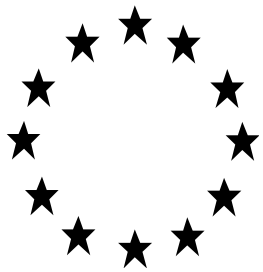
Directive 98/8/EC concerning the placing biocidal products on the market

Inclusion of active substances in Annex I or IA to Directive 98/8/EC

Assessment Report



Methyl nonyl ketone

Product-type 19
(Repellents and attractants)

October 2011

RMS – Spain

Methyl nonyl ketone (PT 19)

Assessment report

Finalised in the Standing Committee on Biocidal Products at its meeting on 9 December 2011 in view of its inclusion in Annex I to Directive 98/8/EC

CONTENTS

1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Introduction

This assessment report has been established as a result of the evaluation of methyl nonyl ketone (CAS no. 112-12-9) as product-type 19 (Repellents and attractants), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market , with a view to the possible inclusion of this substance into Annex I or IA to the Directive.

Methyl nonyl ketone (CAS no. 112-12-9) was notified as an existing active substance, by Guaber UK Limited, hereafter referred to as the applicant, in product-type **19.** The risks to human health and the environment (including any risks from physico-chemical properties and possible unacceptable effects) and the efficacy have been assessed in accordance with the Directive 98/8/EC for the use of methyl nonyl ketone as a product type 19. The report includes an evaluation of data submitted on one product formulation with methyl nonyl ketone necessary to evaluate the risk of use of the active substance.

The report will help Member States to make national decisions on the individual biocidal products containing methyl nonyl ketone, in accordance with the provisions of Article 5(1) of the Directive 98/8/EC. This report shall not be used to support any authorisation/registration outside the context of Directive 98/8/EC.

1.2. Application form

1.1.	**Applicant**	Name:	Graham Mountford
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		Fax number:	+44 (0) 1737 780063
		Contact Point	
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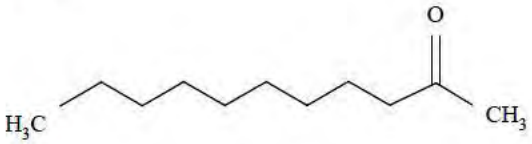
		Fax number:	+44 (0) 01673 885163
		E-mail address:	ms@barkwithassociates.com
1.2.	**Manufacturer of Active Substance**	Name:	[redacted]
		Address:	[redacted]
		Telephone:	[redacted]
		Fax number:	
		E-mail address:	
1.3.	**Manufacturer of Product(s)**	Name:	[redacted]
		Address:	
		Telephone:	
		Fax number:	

2. OVERALL SUMMARY AND CONCLUSIONS

2.1. Presentation of the Active Substance

2.1.1. Identity, Physico-Chemical Properties & Methods of Analysis

CAS-No.	112-12-9
EINECS-No.	*203-937-5*
Other No. (CIPAC, ELINCS)	None
IUPAC Name	Undecan-2-one
Common name, synonym	methyl nonyl ketone (MNK)
Molecular formula	$C_{11}H_{22}O$
Structural formula	
Molecular weight (g/mol)	170.29
Purity:	97.5% (w/w)

Methyl nonyl ketone (MNK) is a clear mobile liquid, with a strong characteristic smell at room temperature that presents a vapour pressure of 11.8 Pascals at 20° C. It has a very low solubility in water and high solubility in organic solvents such as n-heptane, p-xylene, 1,2-dichloroethane, methanol, acetone and ethyl acetate. MNK is not considered highly flammable or explosive or oxidizing. The identity, physico-chemical properties and analytical methods are listed in Appendix I of this assessment report. Moreover, a detailed description and discussion of these is presented in the Competent Authority Report.

2.1.2. Intended Uses and Efficacy

Vapet® Get Off™ Spray is an animal repellent formulated as a liquid (EC) containing approximately 3.58 % MNK. It is provided as a ready to use spray and it is applied only indoors as a spot treatment to areas of the home to discourage dogs from fouling. It is intended to be used only by non-professionals. Non-professional users are usually general public who may or may not read a product label. Although they may not have access to formal PPE, it is expected that the general public will follow some basic recommendation such as do not eat, drink or smoke when working with animal repellent in general, avoid contact with eyes and skin and do not inhale vapour.

Due to the lack of appropriate test-guidelines for repellents and as no guidance, concerning the efficacy testing of products of PT19 was provided; two tests in house were submitted, one in dog and the other in cat and one user trial where samples of a product containing methylnonylketone were placed with amateur users who completed a questionnaire in their

experience. Additionally, after CA meeting in February 2011 new studies were performed to demonstrate the repellent efficacy of methyl nonyl ketone, using a product with 3.58% MNK and without essential oils. The results showed that the product had effect against dogs. .

There are no known reports of resistance to methyl nonyl ketone among dogs. Due to its volatility methyl nonyl ketone does not persist in the environment and hence does not continuously select resistance mechanisms in target organisms.

2.1.3. Classification and Labelling

Classification and labelling of the active substance

Classification	Irritant
Class of danger	Xi
R-phrases	R38 Irritating to skin
S-phrases	S37 Wear suitable gloves S46 If swallowed, seek medical advice immediately and show this container or label S64 If swallowed, rinse mouth with water (only if the person is conscious)
Classification for the Environment	Dangerous for the environment
Class of danger	N
R-phrases	R50/53: Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
S-phrases	S29: Do not empty into drains. S35: This material and its container must be disposed of in a safe way S61: Avoid release to the environment. Refer to special instruction/safety data sheet

Classification according to the Regulation (EC) No 1272/2008 of the European Parliament and of the Council and the Globally Harmonised System of Classification and Labelling of Chemicals (hereinafter referred to as "the GHS"):

GHS Pictograms		
Signal Word	Warning	
Classification for human health	Hazard class and category: Hazard statement	Category 2; Skin Irrit. 2 H315: Causes skin irritation
Prevention precautionary statement	P264: Wash … thoroughly after handling P280: Wear protective gloves/protective clothing/eye protection/ face protection	
Response precautionary statements	P302+P352: IF ON SKIN: Wash with plenty of soap and water P321: Specific treatment (see … on this label). P332+P313: If skin irritation occurs: Get medical advice/attention. P362: Take off contaminated clothing and wash before reuse	

GHS Pictograms		
Signal Word	Warning	
Classification for the Environment	Hazard class and category: Hazard statement	Hazardous to the aquatic compartment, Acute hazard, Category 1,chronic toxicity, Category 1 H400: Very toxic to aquatic life H410: Very toxic to aquatic life with long lasting effects
Prevention precautionary statement	P273: Avoid release to the environment	
Response precautionary statements	P391: Collect spillage	
Disposal precautionary statements	P501: Dispose of contents/container to…	

Classification and labelling of the product

Classification	-
S-phrases	S24 Avoid contact with skin S46 If swallowed, seek medical advice immediately and show this container or label S64 If swallowed, rinse mouth with water (only if the person is conscious)
Classification for the Environment	Dangerous for the environment
Class of danger	N
R-phrases	R51/53: Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
S-phrases	S29: Do not empty into drains. S35: This material and its container must be disposed of in a safe way S61: Avoid release to the environment. Refer to special instruction/safety data sheet

The product contains citronella and eucalyptus oils, which are classified as sensitising. In this sense, the label on the packaging of mixtures containing at least one substance classified as sensitising and present in a concentration equal to or greater than 0.1 %, shall bear the statement: "Contains Citronella and eucalyptus oils. May produce an allergic reaction" (the essential oils are classified as sensitising and present in a concentration equal to or greater than 0.1 %).

Classification according to the Regulation (EC) No 1272/2008 of the European Parliament and of the Council and the Globally Harmonised System of Classification and Labelling of Chemicals (hereinafter referred to as "the GHS"):

GHS Pictograms		

Signal Word		
Classification for human health	Hazard class and category: Hazard statement	EUH208 — 'Contains Citronella and eucalyptus oils. May produce an allergic reaction'
Prevention precautionary statement	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.	
Response precautionary statements	P302+P352: IF ON SKIN: Wash with plenty of soap and water P321: Specific treatment (see … on this label). P333+P313: If skin irritation or rash occurs: Get medical advice/ attention. P363: Wash contaminated clothing before reuse	
Precautionary Statement Disposal	P501: Dispose of contents/container to …	
GHS Pictograms		
Signal Word	No signal word	
Classification for the Environment	Hazard class and category: Hazard statement	Hazardous to the aquatic compartment, chronic toxicity, Category 2 H411: Toxic to aquatic life with long lasting effects
Prevention precautionary statement	P273: Avoid release to the environment	
Response precautionary statements	P391: Collect spillage	
Disposal precautionary statements	P501: Dispose of contents/container to…	

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1. Hazard identification

A read-across for chronic toxicity, carcinogenicity and teratogenicity and reproduction using data coming from other aliphatic (lineal and branched) ketones was also performed in this dossier. This read-across is justified because:

1 The only subchronic effect displayed by all other studied aliphatic ketones was a nephropathy that accounts through a mechanism that is not relevant for humans since this species does not express the protein that aggregates in the kidney for causing the renal injury.

2 The absence of carcinogenicity in all subchronic studies performed with MNK and other aliphatic ketones, the absence of genotoxicity in MNK and the absence of structural chemical alerts for ketones.

3 The absence of teratogenic effects in the study with MNK included in the dossier together with the absence of reproductive effects and injuries in reproductive organs reported for all studies with other ketones.

Acute toxicity

Methyl nonyl ketone (MNK) exhibited low acute toxicity, with both oral and dermal LD_{50} higher than 2 g / kg bw for rat and rabbit respectively. Regarding the inhalative route it is remarkable that the LC_{50} of MNK was higher than 5.43 mg/L for males and for females as well.

MNK caused reversible erythema and oedema and was classified as skin irritant, while the compound only caused reversible moderated conjunctival irritation. The symbol "Xi" and the risk phrase R38 "Irritating to skin" are therefore required for MNK. MNK did not induced sensitisation in guinea pig skin.

Absorption

In absence of appropriate studies 100% of dermal and gastric absorption must be assumed.

Biotransformation

There are no available data about toxicokinetics of MNK. However, three routes of biotransformation are proposed for MNK through comparison with published information regarding other aliphatic ketones of shorter carbon chain. These three routes are: 1) biotransformation to the corresponding secondary alcohols (i.e., 2-nonanol is the corresponding secondary alcohol of 2-nonanone), that are rapidly excreted in the urine mainly as glucuronic acid conjugates; 2) oxidation to α-ketoacids and cleavage to yield shorter chain acids which will be further introduced in the endogenous fatty acids pathway; 3) formation of potentially neurotoxic ω-diketones (e.g. 2,5-hexadione), although it is expectable that neurotoxicity of ketones with more than 7 atoms of carbon accounts only after exposures near to the lethal dose.

A kinetics study of methyl ethyl ketone in man suggests that most of the administered dose is converted to products of intermediary metabolism, probably through the fatty acid pathway and citric acid cycle. Therefore it is expectable that the formation of 2,5-undeconedione (the potentially neurotoxic ω-diketones of MNK) is not a relevant pathway because: 1) this biotransformation route is not favoured in humans and; 2) the neurotoxic effect for ketones with 7 or 9 atoms of carbon only accounts at lethal doses and therefore the same situation should be expected for ketones of 11 atoms of carbon.

Genotoxicity

MNK displayed no indications of genotoxicity or clastogenicity under in vitro test.

Teratogenicity and reproductive toxicity

There was no evidence of maternal toxicity following oral administration of MNK during organogenesis at 1000 mg/kg bw/day to rats. At this maximum level there was no evidence of embriotoxicity. Litter size, foetal weight and the incidence of foetal abnormalities were not affected by treatment. The NOAEL established in this study was 1000 mg/ kg bw/day for both the developing embryo and the pregnant rat.

The effects on reproductive and developmental toxicity of several lineal and branched aliphatic ketones was analyzed and given the lack of any significant reproductive effects in the reproductive/developmental screening studies and the absence of any significant effects to the reproductive organs of animals in subchronic and chronic repeat dose studies, it is conc1uded that aliphatic ketones and alkyl-substituted cyc1ohexanones exhibits a very low order of reproductive toxicity.

Repeated toxicity

In a subchronic toxicity test groups of twenty (10 males and 10 females) Sprague-Dawley Crl:CD rats were daily dosed by gavage with vehicle, 5, 50 or 1000 mg MNK/kg bw/day during ninety days. The only treatment-related adverse effect was a histological renal change detected in male rats exposed to the highest dose. Females exposed to 1000 mg MNK/kg bw/day and males and females exposed to 5 and 50 mg MNK/kg bw/day exhibited no treatment-related adverse effects. This study was considered the critical endpoint for acute, short and medium term and chronic exposure.

A read across study has been performed with available toxicological information coming form other aliphatic ketones and in all cases the common toxicological effect were nephrotoxic effects caused by accumulation of aggregates of alpha-2- microglobulin, which is a protein that is not expressed in humans and therefore this nephrotoxic effect is not relevant for humans.

Carcinogenicity

The absence of carcinogenicity potential observed in studies with aliphatic ketones (other than MNK), together with the lack of genotoxicity potential of MNK, the absence of signs of carcinogenicity in the subchronic studies performed with all other studies aliphatic (lineal and branched) ketones and the lack of structural alerts for carcinogenic effects in relationship with the chemical structure of ketones suggest no carcinogenicic hazard for MNK.

2.2.1.2. Effects assessment

Acceptable Operator Exposure Levels (AEL)

The AEL were set as follows:

Exposure	Critical study	Critical NOAEL	Safety Factor	AEL
Acute	90 day repeated oral dose in rat	50 mg/kg bw	100	0.50 mg/kg bw/day

Short and medium term	90 day repeated oral dose in rat	50 mg/kg bw/day	100	0.50 mg/kg bw/day
Long term	90 day repeated oral dose in rat	50 mg/kg bw/day	300	0.17 mg/kg bw/day

The AEL for long term exposure was calculated using a safety factor of 300 instead of 100 because is obtained through a single subchronic study and because there is a lack of other toxicity studies as a second study of teratogenicity, carcinogenicity, chronic toxicity, toxicity to fertility and studies with technical product Vapet® Get Off™ Spray.

Acceptable daily intake (ADI)

In predicting the ADI, long term/chronic studies in the rodent are considered to be the most appropriate. The ADI is derived from the most sensitive species in appropriate studies, divided by a safety factor. Considering that chronic studies are not presented for MNK a NOEL of 50 mg/kg bw/day from a 90 day oral toxicity study in rat has been used in determining the ADI. The incorporation of a safety factor of 300 (the same factor employed for setting the chronic AEL) leads to an ADI of 0.17 mg/kg bw/day.

Maximum allowable concentration (MAC) in drinking water

In the absence of human and animal studies on the toxicity of MNK in drinking water, it is acceptable to base the MAC on the dietary ADI. In order to derive the MAC for drinking water, it is appropriate to divide the ADI of 0.17 mg/kg bw/day by an additional factor of 10, thus giving an intake value of 0.017 mg/kg bw/day for drinking water. Based on a human bodyweight of 65 kg and a daily intake of 1.4 litres, the proposed parametric value for MNK is 0.79 mg MNK/litre.

2.2.1.3. Exposure assessment

The product is intended for non professional use only, therefore, the primary exposure has been assessed for an amateur applying Vapet® Get Off™ Spray by spraying, using the models from the TNsG and Consexpo 4.1. The task considered is the application of the product; the process of mixing and loading is not applicable since Vapet® Get Off™ Spray is supplied as a ready-to-use product. The application of MNK as repellent (PT 19) in home environment can result in direct exposure via skin contact or via inhalation, but the oral ingestion is not considered as a potential direct route. The exposure has been estimated using the **Consumer product spraying and dusting – model 2**, hand-held trigger spray, provided in the TNsG, and the estimated systemic doses of MNK, are 5.47×10^{-2} mg/kg bw/day without PPE (Tier 1) and 4.89×10^{-2} mg/kg bw/day considering that long sleeve shirt and trousers (Tier 2) are worn. Using the **ConsExpo 4.1**: Targeted spot application, the estimated systemic doses of MNK is 4.35×10^{-3} mg/kg bw/day.

Secondary exposure has also been assessed through acute (children and infant in contact with wet sprayed surface) and chronic (inhalation of volatilised residues indoors by infants and adults) scenarios. The acute scenario for children and infants involve a systemic dose of 5.575×10^{-2} and 7.77×10^{-2} mg/kg bw/day, respectively. Regarding the chronic scenarios, the estimated doses after inhaling volatilised residues are 2.533×10^{-6} mg/kg bw/day for an adult and 3.286×10^{-6} mg/kg bw/day for an infant. Finally, the total systemic doses when touching

surfaces treated are 1.03 x 10^{-3} mg/kg bw/day for children and 4.12 x 10^{-3} mg/kg bw/day for infants. If ConsExpo 4.1 is used, the estimated exposure of children crawling on a treated surface is 7.6 x 10^{-3} mg/kg bw/day.

2.2.1.4. Risk characterisation

Professional users

The biocidal product is not intended for professional users.

Non professional users

The estimated total uptake for non-professional users spraying the product without and with protective clothes were 5.47 x 10^{-2} and 4.89 x 10^{-2} mg MNK/kg bw/day. The comparison of these exposures with the above stated AEL yields ratios always lower than 1. In the same way, MOEs for both scenarios were higher than 100. Therefore, the use of MNK for spraying yields an acceptable risk.

Secondary exposure

Acute scenario:

The secondary exposure assessment for the acute scenario under worst case assumptions yielded acute exposures ranging from 5.575 x 10^{-2} (for children in contact with wet sprayed surface) to 7.77 x 10^{-2} mg/kg (for infants in contact with wet sprayed surface). The comparison to the relevant endpoints gives rise to MOEs ranging from 643 to 1136, which are above 300 while the exposure/AEL ratios were always lower than 1, indicating an acceptable risk. Table 2.2.1.5 displays a summary of the total uptakes and risk assessment parameters.

Regarding the secondary exposure of a child licking a treated surface, a worst case reverse reference scenario has been described to estimate the surface that needs to be licked to achieve the AEL, and $1.75 \cdot 10^{-2}$ m^2 has been obtained. This represents a surface of approximately 14 x 14 cm, which might be considered small. However, the product is applied as a spot treatment and it would be unlikely to have a spot surface of 14 x 14 cm totally treated, and difficult that a child would lick it completely.

Chronic scenario:

Four different situations were described for the chronic secondary exposure, the adult inhalation of indoors volatised residues, the infant inhalation of indoors volatised residues, the children touching surfaces treated with the animal repellent and the infants touching surfaces treated with the animal repellent and oral exposure. The respective exposures in these four situations are 2.533 x 10^{-6}, 3.286 x 10^{-5}, 1.03 x 10^{-3}, 4.12 x 10^{-3} mg/kg/day. Using the above stated AEL of 0.17 mg/kg/day, the relevant NOAEL of 50 mg/kg/day and the assessment factor of 300, it is concluded that the risk for the chronic secondary exposure is acceptable, because the exposure/AEL ratios are always lower than 1 while the MOEs are lower than 300. Table 2.2.1.5 displays a summary of the total uptakes and risk assessment parameters.

Conclusion of the risk assessment

No unacceptable risks are expected from the use of MNK in the biocidal product.

Table 2.2.1.4: Estimated internal exposure and summary of risk assessment of non-professionals. Spraying and dusting model 2: hand held trigger spray.

Exposure Scenario		Estimated Internal Exposure				Relevant NOAEL/ LOAEL [mg/kg b.w/day] & Reference Value e.g: AEL (acute or medium or chronic)	AF MOE_{ref}	MOE	Exposure /AEL
		Estimated oral uptake [mg/kg b.w/day]	Estimated inhalation uptake [mg/kg b.w/day]	Estimated dermal uptake [mg/kg b.w/day]	Estimated total uptake [mg/kg b.w/day]				
Animal repellent formulated as a liquid (EC), applied by spraying	**Tier 1** (no PPE)	-	2.6×10^{-4}	5.45×10^{-2}	5.47×10^{-2}	50	300	914	0.32
	Tier 2 (Long sleeve t-shirt and trousers)	-	2.6×10^{-4}	4.87×10^{-2}	4.89×10^{-2}	50	300	1022	0.28

Table 2.2.1.5: Estimated internal exposure and summary of risk assessment of non-professionals. ConsExpo 4.1: Targeted spot application by trigger spray.

Exposure Scenario	Estimated Internal Exposure				Relevant NOAEL/ LOAEL [mg/kg b.w/day] & Reference Value e.g: AEL (acute or medium or chronic)	AF MOE_{ref}	MOE	Exposure /AEL
	Estimated oral uptake [mg/kg b.w/day]	Estimated inhalation uptake [mg/kg b.w/day]	Estimated dermal uptake [mg/kg b.w/day]	Estimated total uptake [mg/kg b.w/day]				
Animal repellent formulated as a liquid (EC), applied by spraying.	2.88×10^{-4}	1.09×10^{-6}	4.06×10^{-3}	4.35×10^{-3}	50	300	11494	2.6×10^{-2}

Table 2.2.1.6: Estimated internal exposure and summary of risk assessment. Indirect exposure

Exposure Scenario (indicate duration)				Estimated Internal Exposure				Relevant NOAEL/ LOAEL [mg/kg b.w/day] & Reference Value e.g: AEL (acute or medium or chronic)	AF MOE_{ref}	MOE	Exposure /AEL
				Estimated inhalation uptake [mg/kg b.w/day]	Estimated dermal uptake [mg/kg b.w/day]	Estimated oral uptake [mg/kg b.w/day]	Estimated total uptake [mg/kg b.w/day]				
Tier 1 (Worst Case)	Short term Scenario	Animal repellent formulated as a liquid (EC), applied by spraying	Children	-	5.575×10^{-2}	-	5.575×10^{-2}	50	100	897	0.11
			Infant	-	7.064×10^{-2}	7.064×10^{-3}	7.77×10^{-2}	50	100	643	0.16
Tier 2 (Worst Case)	Long term Scenario	Animal repellent formulated as a liquid (EC), applied by spraying	Adult	2.533×10^{-6}	-	-	2.533×10^{-6}	50	300	2.0×10^{7}	1.5×10^{-5}
			Children		1.03×10^{-3}	-	1.03×10^{-3}	50	300	4.9×10^{4}	6.1×10^{-3}
			Infant	3.286×10^{-6}	2.06×10^{-3}	2.06×10^{-3}	4.123×10^{-3}	50	300	1.2×10^{4}	2.4×10^{-2}

2.2.2. Environmental Risk Assessment

2.2.2.1. Environmental fate and behaviour and ecotoxicological profile

Methyl nonyl ketone (MNK) is used as active substance for the manufacture of olfactory repellent products (product type 19.02: attractants and repellents not applied directly on human or animal skin) in indoor uses in no food/feed areas in homes. **In its normal use as a repellent it is used inside homes against dogs.**

The biocidal product *Vapet® Get Off™ Spray* is the generic formulation used for the evaluation. Vapet® Get Off™ Spray is an animal repellent formulated as a liquid (EC) containing approximately 3.58% (w/v) of Methyl Nonyl Ketone (MNK). *Vapet® Get Off™ Spray* is intended for use as a repellent which is effective against dogs. It is applied to areas of the home to discourage animals from fouling. The highly volatile product releases a strong odour, which confuses the sense of smell of the animal and thus discourages them from visiting the treated area. Over a period of time the animals are trained to move away from and not to foul the treated area. It is intended for use by non-professionals indoors on doorways, carpets and furnishings. *Vapet® Get Off™ Spray* is supplied as a ready to use preparation in trigger spray packaging. It has a localised low volume use, and is applied to small areas as a spot treatment. It is not recommended for use outdoors.

There are no emission scenario documents (ESDs) currently available for repellent liquid sprays used indoors. The RIVM ESD for PT 2 “Private area and public health area disinfectants and other biocidal products” under the scenario entitled “tiles and surfaces” accommodates products used for the disinfection of air, surfaces, materials, equipment and furniture not used for direct food or feed contact in private, public and industrial areas. The tonnage approach is considered for this scenario. The release to wastewater is 100% by default, and the receiving STP is considered as a point source.

We do not use the indoor spray application scenario for PT 18 **because the intended uses of the biocidal product are not the same as an insecticide.** The biocidal product Vapet® Get Off™ Spray is not used in air-space treatment or treatment of a specific surface in m^2, and the intended uses of the product are not the same as an insecticide. Thus, scenario for PT18 was not considered. The product is applied to small areas as a spot treatment. **The scenario for calculating the releases of disinfectants used for sanitary purposes (tiles and surfaces) based on the annual tonnage applied was therefore, considered in this risk assessment as it provides the closest estimates of environmental exposure for PT 19 liquid sprays used indoors. This scenario is incorporated into the risk assessment model USES 4.0 and EUSES 2.0.3 (as assessment of biocides on local scale only: private use; (2) disinfectants: (2.2) Sanitary sector), which carries out quantitative assessments of the risks posed by biocides to man and the environment. The environmental exposure assessment described in the following sub-sections will follow the recommendations of the TGD (2003) for Risk Assessment.**

Exposure to the primary receiving environmental compartments such as soil, water and air depends on the physical-chemical properties of the substance as well as its formulation type, mode of application, use and disposal. Therefore, taking into account

that *Vapet® Get Off™ Spray* is recommended for use indoors only at low volume of application and at localized areas, and that most MNK once incorporated in the environment will be displaced from other environmental compartments *via* volatilisation into the air (*see following section*) where it will undergo a rapid degradation by photochemical processes, it is unlikely that soil and water may be exposed to significant amounts of MNK.

However, according to "Data requirements for biocidal product types, Version 4.3.2' (October, 2000)", air and soil should be considered as possible routes of exposure for PT 19. Indoor application may also result in environmental exposure *via* the sewage system (*i.e.* rinsing cloths used to wash areas with *Vapet® Get Off™ Spray* or during cleaning processes following treatment). This poses a risk of the product entering STPs and subsequently being released *via* effluent into surface water. This is a worst-case assumption as the product is intended only for non-professional household use and is applied until the dog or cat is discouraged from marking their territory, thus the use pattern of the product is localized and of low volume. Furthermore, label recommendations advise against the use of the product in areas where water may become contaminated. Hence, exposure to STP's and consequently water and soil is negligible. However, given the heightened awareness of the fate of chemicals in the aquatic environment and the risk they pose in Europe, a risk assessment has been carried out to address the fate of *Vapet® Get Off™ Spray* in sewage treatment plants and surface water.

The fate and behaviour of MNK in the environment as well as the impact on non-target organisms is reflected in this document.

2.2.2.1.1. Fate and behaviour in air

According to Level I Mackay Fugacity Model (*see ref. Report: Doc.III-A7.3.2*). Methyl Nonyl Ketone was predicted to partition predominantly to air (98.7537%) due to its high VP and low water solubility (1.44 mg/L), and with much lower amounts anticipated to be distributed to aerosols in the atmosphere (0.0010%), to soil (0.7461%), to water (0.3450%), to sediment (0.1492%), to suspended sediment (0.0047%) and to fish (0.000379%). Following Level III fugacity model, MNK was predicted to partition differently than modelled by Level I, and the percentage distribution in air resulted in 7.62 %.

However, this substance is unstable in the atmosphere to react with OH radicals of troposphere. Its half-life in this compartment was calculated to be 1.16 days.

Therefore, it is expected that the concentrations of MNK in air will be negligible.

2.2.2.1.2. Fate and behaviour in aquatic compartment (incl. Sediment)

MNK is characterized in the aquatic compartment by:

- To have a low water solubility, 1.44 mg/L at 20ºC
- To be a non-ionisable substance
- To be hydrolytically stable in water at 25ºC in the pH-range from 5 to 9.

- Not to be readily biodegradable under test conditions in a CO_2 evolution test (OECD 301 B).
- Its lowest value of K_{oc} was estimated to be 1,511 L/kg. Consequently, the amount of MNK that will bind to sediment essentially will depend on the organic matter content that characterizes the sediment.

2.2.2.1.3. Fate and behaviour in soil

Methyl Nonyl Ketone once incorporated into soil, it is rapidly degraded under aerobic conditions in microbially active soils. The aerobic degradation of this substance in the dark seems to consist mainly in progressive oxidation of lineal hydrocarbon chain to give 4-hydroxy-2-undecanone and/or 10-hydroxy-2-undecanone; 2,4-undecanone and/or 2,10-undecanone and 4-hydroxypentanoic acid. No metabolite above 3% TAR could be detected at any sample point in the soil samples.

Concurrent with the declination of MNK in soil there is a formation of bound residues. The bound ^{14}C-residues in the soil increased from 0.59% of the Initial Measured Dose (IMD) at Day 0 to 58.2% of IMD at Day 1 and then gradually decreased to 38.3% of the IMD at the study's termination (30 days). The level of ^{14}C-volatile degradation products was 3.21% of the IMD at 4 hours and increased to 60.7% of the IMD after 30 days.

The majority of the ^{14}C-volatile activity (> 80%) was confirmed to be $^{14}CO_2$. The majority of the remaining ^{14}C-volatile activity corresponded with MNK that was volatilised, 3.0% of the IMD (at 4 hours) was increased up to 11.78% of the IMD after 30 days. $^{14}CO_2$ accounted for 48.7% of the IMD after 30 days. Based on the structures of the parent compound and the metabolites identified during the study, it can be theorized that the test compound will further metabolise to CO_2 following the classical β-oxidation sequence.

The half-life determination was calculated by using first-order kinetics using Microsoft Excel. The overall net half-life (Day 0 through 1 month) at 12ºC was estimated to be of 11.5 days.

Adsorption/desorption study characterizes MNK as a compound with a high adsorption capacity in soils, the minimum estimated K_{oc} value in the tests was 1,511 L/kg. From this data it is deduced that its high binding capacity essentially depends on the organic matter percentage that characterizes the soils. Thus, it can be expected that MNK once incorporated into the soil, will bind tightly to the soil particles of the first centimetres being nearly immobile on this layer.

2.2.2.1.4. Effects on aquatic organisms

The toxicity tests of MNK for the estimation of $PNEC_{water}$ are summarized in the following table (effects on sediment-dwelling organisms are discussed in the next section).

Table 1. Summary of toxicity tests of MNK for water phase

Guideline / Test method	Species	Endpoint / Type of test	Exposure		Results (mg/L)		Related to conc[1]
			Design	Durat.	NOEC	L(E)C_{50}	
US EPA 72-1	*L. macrochirus*	Mortality and toxic signs	Flow-through	96 h	0.74	2.1	Measured
OECD 202	*D. magna*	Mobility	Semi-static	48 h	0.002	0.23	Measured
OECD 201	*P. subcapitata*	Growth rate: Biomass:	Static (closed bottle)	24 h	0.38 0.38	1.9 1.4	Measured

[1]Concentrations were measured in all tests. If deviation of measured concentration from nominal value > 20%, effects were related to measured concentrations.

The acute toxicity tests for three trophic levels (fish, invertebrates and algae) are available. No chronic toxicity test was conducted in fish and invertebrates because they were considered unnecessary, taking into account the fate and distribution in the environment of MNK and the intended use of the biocidal product.

Concerning the PNEC, to its estimation the lowest endpoint available was selected. This endpoint was the EC_{50} for immobilization in *Daphnia magna*. This result was supported by Another study related to the evaluation of MNK from the U.S-EPA ("Registration Eligibility Decision (RED): Methyl Nonyl Ketone"), in wich the EC_{50} derived from an acute toxicity test with *Daphnia magna* and MNK was estimated to be 0.54 mg/l.

An extrapolation factor of 1,000 was used as recommended by the TGD. Thus, the PNEC for aqueous phase organism was estimated to be 0.00023 mg a.s./L.

2.2.2.1.5. Effects on sediment organisms

Assessment using the equilibrium partitioning method (EPM)

The concentration of the substance in sediment-dwelling organisms was predicted by using the equilibrium partitioning method. The formula of the EPM only considers uptake *via* the water phase, assuming partitioning equilibrium between water and suspended matter. The equation is as follows:

$$PNEC_{sediment} = \frac{\mathrm{PNEC}_{water} \cdot \mathrm{K}_{susp\text{-}water} \cdot 1{,}000}{\mathrm{RHO}_{susp}} = 0.00023 \cdot 38.67 \cdot 1{,}000/1{,}150 = 0.007734\ mg/kg$$

Where:

- $PNEC_{water}$ = Predicted No Effect Concentration in water given in [$mg \cdot L^{-1}$]. *See the previous section*
- $K_{sed.\text{-}water}$ = Sediment-water partitioning coefficient. Calculated value according to equation 24 of the TGD: 38.67 [$m^3_{sed.} \cdot m^{-3}_{water}$]

- RHO_{susp} = Bulk density of (wet) suspended matter, by default a value of 1,150 [$kg_{susp} \cdot m_{soil}^{-3}$] can be assumed

2.2.2.1.6. Effects on sewage treatment plant micro-organisms

PNEC value for micro-organisms of sewage treatment plant (STP) is estimated to be 6 mg MNK/L. This PNEC value was derived from the NOEC value of the respiration inhibition test using a safety factor of 10 as the the TGD recommends.

Table 2. Effects of MNK on microbial activity (aquatic)

Guideline / Test method	Species / Inoculum	Endpoint / Type of test	Exposure		Results (mg/L)			Reference
			Design	Duration	NOEC	EC_{20}	EC_{50}	
OECD 209	Activated sludge	Respiration inhibition test	-	180 min	60	121.75	379.49	A7.4.1.4

2.2.2.1.7. Effects on terrestrial organisms

Assessment by using the Equilibrium Partitioning Method (EPM)

According to the TGD (section 3.6.2.2) if only one terrestrial test result is available (case of MNK), the risk assessment should be also performed on the basis of the outcome of the aquatic toxicity data to provide an indication of the risk.

The PNEC was calculated as follows:

$$PNEC_{soil} = \frac{PNEC_{water} \cdot K_{soil\text{-}water} \cdot 1000}{RHO_{soil}}$$

$$PNEC_{soil} = 0.00023 \cdot 45.6478 \cdot 1{,}000/1{,}700 = 0.00618 \text{ mg/kg}$$

Where:

- $PNEC_{water}$ = Predicted No Effect Concentration in water given in [$mg \cdot L^{-1}$]. *See section 2.2.3.4*
- $K_{soil\text{-}water}$ = Soil-water partitioning coefficient. Calculated value according to equation 24 of the TGD: 45.6478 [$m^3_{soil} \cdot m^{-3}_{water}$]
- RHO_{soil} = Bulk density of (wet) soil, by default a value of 1,700 [$kg_{soil} \cdot m_{soil}^{-3}$] can be assumed

2.2.2.1.8. Non compartment specific effects relevant to food chain (secondary poisoning)

No specific data has been submitted. However, an initial assessment of the secondary poisoning through the aquatic food chain was done in order to rule out whether or not MNK can move up into the higher levels of the trophic chain.

The $PNEC_{oral}$ was calculated from mammalian tests according to section 3.8.3.5 of the TGD.

$PNEC_{oral}$ for predators can be calculated from the oral toxicity data of mammals as follows:

$$NOEC_{mammal,\ food\ \_\ chr} = NOAEL_{mammal,\ food\ \_\ chr} \cdot CONV_{mammal} = 50 \cdot 20 = 1000\ \frac{mg\ MNK}{kg_{food}}$$

$$PNEC_{oral} = \frac{TOX_{oral}}{AF_{oral}} = \frac{NOAEL_{mammals,\ oral,\ chr}}{90\ (**)} = \frac{1000}{90} = 11.1 \frac{mg\ MNK}{kg_{food} \cdot d}$$

Where:

- The $NOAEL_{mammals,\ food,\ chr}$ = 50 mg a.s./(kg_{bw}·d). *See reference report: Doc. III-A 6.4.1*. In a Repeated Dose 90-Day Oral Toxicity Study in Rats, the severest effects were observed in male rats at the highest dose tested (1,000 mg a.s./kg_{bw}/d): a minimal body gain, reduced grip strength and kidney changes consistent with the male rat specific condition, hydrocarbon nephropathy. Thus, the NOAEL for male rats (*i.e.* the lowest endpoint for rats) was established to be 50 mg a.s./(kg_{bw}·day). The usual approach is based on the consideration that effects on populations will not occur if the survival rate, reproduction rate and development of individuals are not affected. Mammalian tests are designed for human risk assessment.
- Conversion factor from NOAEL to NOEC. Conversion factor (bw/dfi) for *Rattus norvegicus* (> 6 weeks) of 20 (*see Table 22 section 3.8.3.5 of TGD*).
- 90 (**) is the assessment factor applied for sub-chronic tests (duration of the oral tests: 90 days).

For predators (birds) was not possible to carry out the corresponding approach to derive $PNEC_{oral}$ since no information about oral toxicity data in birds was provided with the Dossier.

2.2.2.1.9. PBT, POP and ED assessment

Assessment of PBT criteria

A substance must be regarded as a PBT substance if it fulfils the combined set of criteria of identification summarized in the Table 30 of the TGD (section 4.4, Page 164). The combined set of criteria is based on inherent properties:

- Persistence (P)
- Bioaccumulation (B)
- Toxicity (T)

When it is clear that the P criterion is fulfilled a stepwise approach should be followed to elucidate the B criterion, eventually followed by clarifying the T criterion.

Persistence: the P criterion

MNK does not to fulfil the P criterion for soil since its half-life in this medium is below 120 d. Under laboratory conditions its DT_{50} value at 12ºC was estimated to be 11.5 days. However, MNK fulfils the P criterion for freshwater because this substance is not dissociated nor biodegraded, and is not hydrolysed at pH 5, 7 and 9 either.

Nevertheless, taking into account its high VP (11.8 Pa at 20ºC) and its low water solubility (1.44 mg/l at 20ºC), it is expected that most of this substance on reaching the environment (soil and water) will be quickly displaced from these compartments to air (*via* volatilization) where it will undergo a rapid photochemical degradation (its DT_{50} was estimated to be 1.16 days).

Therefore, it is unlikely that MNK persists in the soil and the water compartments.

Bioaccumulation: the B criterion

The assessment of the (potential for) bioaccumulation in the context of PBT or vPvB evaluation makes use of measured bioconcentration factor. When not available, BCF value may be estimated from the octanol/water partition coefficient (K_{ow}) by using (Q)SAR models. This is the case of MNK. For this substance the estimated BCF for fish is about 978.81 L/kg. Therefore, MNK does not fulfil the B criterion, its BCF is under the cut-off values proposed in the TGD (BCF > 2,000 for PBT assessment and > 5,000 for vPvB assessment).

Toxicity: the T criterion

According to section 4.4.5.3 of the TGD: "*Where data on chronic effects are not available short-term toxicity data for freshwater organisms can be used to determine whether a substance is a potential PBT provided the screening criteria for P and B are fulfilled. In the context of the PBT assessment a substance is considered to be potentially toxic when the L(E)C$_{50}$ to aquatic organisms is less than 0.1 mg/L"*.

Therefore, MNK cannot be regarded as a potentially toxic substance because the EC_{50} for the most sensitive organism (*D. magna*) is 0.23 mg/L.

Assessment of POPs criteria

The following P (persistent) O (organic) P (pollutants) criteria are laid down in Executive Body decision 1998/2.

Long-range transport potential:

- Vapour pressure <1000 Pa and
- half-life in air > 2 days or
- Monitoring data in remote area showing that the substance is found in remote regions.

Toxicity:

- Potential to adversely affect human health and/or environment

Persistence:

- Half-life in water > 2 months, or
- in sediment >6 months, or
- in soils > 6 months

Bioaccumulation :

- BCF or BAF >5000 or log Pow > 5
- Alternatively, if the bio-accumulative potential is significantly lower than (i) above, other factors, such as the high toxicity of the substance, that make it of concern within the scope of the protocol.

The vapour pressure of MNK is 11.8 Pa at 20°C, the half-life in air is of 1.16 daysof 3.8 hours, indicating that the criterion for long-range transport potential is not fulfilled. In soil, the overall net half-life at 12 °C was estimated to be of 11.5 days, hence MNK fails the persinstence criterion.

The calculated BCF values using (Q)SAR models for fish and earthworm was 978.81 and 264.58 L/kg, respectively, hence <5000. Thus, the bioaccumulation criterion is not fulfilled for MNK.

In conclusion, considering the the above rationale, it can be concluded that MNK does not fulfil the POPs criteria.

Assessment of Endocrine Disruption (ED)

In relation to the potential of MNK to interfere with the hormone system, MNK is not present in any of the lists of the Commission staff working document on implementation of the Community Strategy for Endocrine Disrupters - a range of substances suspected of interfering with the hormone systems of humans and wildlife (COM (1999) 706). In addition a literature search was performed in scientific databases (ISI Web of Knowledge, PubMed, Sciencedirect and Toxnet) on this issue and no results were found. Thus, It can be stated that, to date, no evidence of endocrine disruption activity can be attributed to MNK.

Conclusion:

MNK must not be regarded as a PBT or vPvB, POP or ED substance because it does not fulfil the criteria.

2.2.2.2. Risk characterisation

2.2.2.4.1. Sewage treatment plant micro-organisms (STP)

In order to estimate the risk posed the predicted MNK concentration in the aeration tank of STP ($3.38 \cdot 10^{-5}$ mg/L) is compared with the PNEC for micro-organisms (6 mg/L).

$$\frac{PEC_{STP}}{PNEC_{micro-organisms}} = \frac{3.38 \cdot 10^{-5}}{6} = 5.63 \cdot 10^{-6}$$

Conclusion:

No risk is expected to micro-organisms of STPs since the risk characterization ratio is negligible.

2.2.2.4.2. Aquatic organisms

The risk characterization in this compartment is made by comparing the calculated concentration of MNK in a river ($3.38 \cdot 10^{-6}$ mg/L) with the PNEC for aquatic phase organisms (0.00023 mg/L).

$$\frac{PEClocal_{water}}{PNEC_{aquatic\ phase\ organisms}} = 3.31 \cdot 10^{-6}/0.00023 = 1.44 \cdot 10^{-2}$$

Conclusion:

No potential risk is expected for aquatic phase organisms (fish, aquatic invertebrates and algae) exposed to MNK (as an animal repellent) since PEC/PNEC value is below 1.

2.2.2.4.3. Sediment organisms

The risk characterization for sediment-dwelling organisms can be calculated as follows, based on the equilibrium partitioning method (EPM).

$$\frac{PEClocal_{sed}}{PNEC_{sed\,orgaims}} = \frac{PEClocal_{sed} \cdot RHO_{sed}}{PNEC_{aquaticphaseorganisms} \cdot K_{sed-water} \cdot 1000}$$

$$\frac{PEClocal_{sed}}{PNEC_{sed\ orgaisms}} = 2.06 \cdot 10^{-4} \cdot 1{,}300/0.00023 \cdot 38.67 \cdot 1{,}000 = 0.03129$$

Where:

- $PEClocal_{sed}$ = Concentration in sediment, calculated value (*see section 8.4.2.3 of Doc. II-B*): $2.06 \cdot 10^{-4}$ [$mg \cdot kg_{sed.}^{-1}$]
- $RHO_{sed.}$ = Bulk density of (wet) sediment, default value: 1,300 [$kg \cdot m^{-3}$]
- $PNEC_{aquatic\ phase\ organisms}$ = Predicted no effect environmental concentration for aquatic phase organisms, calculated value (*see section 4.3.1.1 of Doc. II-A*): 0.00023 [$mg \cdot L^{-1}$]
- $K_{sed.-water}$ = Sediment-water partitioning coefficient, calculated value in the *section 8.3.1.2 of Doc. II-A*: 38.67 [$m^3_{sed.} \cdot m^{-3}_{water}$]

Conclusion:

No potential risk is expected to sediment phase organisms to be exposed to MNK (as an animal repellent) since PEC/PNEC value is below 1.

2.2.2.4.4. Terrestrial organisms

Assessment by using the equilibrium partitioning method (EPM)

The risk assessment was also performed (according to the TGD recommendations, section 3.6.2.2) on the basis of the outcome of the aquatic toxicity data to provide an indication of the risk. The risk characterization for soil organisms was calculated as follows, by using the equilibrium partitioning method (EPM).

$$\frac{PEClocal_{soil}}{PNEC_{terrestrial\ organisms}} = \frac{PEClocal_{soil} \cdot RHO_{soil}}{PNEC_{aquatic\ phase\ organisms} \cdot K_{soil\text{-}water} \cdot 1000} = 3.09 \cdot 10^{-4} \cdot 1{,}700 / 0.00023 \cdot 45.648 \cdot 1{,}000 = 5.01 \cdot 10^{-2}$$

Where:

- $PEClocal_{soil}$ = Concentration in agricultural soil averaged over 30 days after application of sludge, calculated value (*see section 10.1.4 of Doc. II-B*): $3.09 \cdot 10^{-4}$ [$mg \cdot kg_{soil}^{-1}$]
- RHO_{soil} = Bulk density of (wet) soil, default value: 1,700 [$kg \cdot m^{-3}$]
- $PNEC_{aquatic\ phase\ organisms}$ = Predicted no effect environmental concentration for aquatic phase organisms, calculated value (*see section 4.3.1.1 of Doc. II-A*): 0.00023 [$mg \cdot L^{-1}$]
- $K_{soil\text{-}water}$ = Soil-water partitioning coefficient, calculated value (*see section 4.3.2 of Doc. II-A*): 45.648 [$m^3_{soil} \cdot m^{-3}_{water}$]

Conclusion:

No potential risk is expected for terrestrial organisms exposed to MNK (as an animal repellent) since PEC/PNEC values obtained is much lower than 1.

2.2.2.4.5. Groundwater

The concentration in groundwater was calculated for indirect exposure of humans through drinking.

The estimations of the PEC in groundwater were performed as the TGD recommends (section 2.3.8.6.), from the concentration in porewater of agricultural soil by using the partitioning equation. The concentration in porewater of agricultural soil is taken as an indication of the potential groundwater level. This is a worst-case assumption, neglecting transformation and dilution in deeper soil layers.

$$PEC_{groundwater} = PEClocal_{soil,\ porewater} = \frac{PEClocal_{soil} \cdot RHO_{soil}}{K_{soil\text{-}water} \cdot 1{,}000}$$

Where:

- $PEClocal_{soil,\ porewater}$ = Predicted environmental concentration in soil porewater given in [mg/L]
- $PEClocal_{soil}$ = Predicted concentration in local soil given in [mg/kg_{wwt}]
- RHO_{soil} = Bulk density of wet soil by default a value of 1,700 kg/m^3 can be assumed
- $K_{soil\text{-}water}$ = Soil-water partitioning coefficient, calculated value according to equation 24 of the TGD: 38.67 [$m_{soil}^3 \cdot m_{water}^{-3}$]

Table 3. $PEC_{groundwater}$ due to the indirect emissions of MNK to soil

Scenario		Average time (d)	$PEC_{groundwater}$ [mg/L]
STP sludge	**Agriculture**	30	**$1.36 \cdot 10^{-5}$**
	Agriculture	180	**$2.27 \cdot 10^{-6}$**
	Grassland	180	**$4.54 \cdot 10^{-7}$**

Conclusion:

The estimated concentrations of MNK in groundwater (according to the approach of the TGD) do not exceed for any scenarios the pesticides drinking water standard of 0.1 µg/L (EU Drinking Water Directive, 98/83/EC).

2.2.2.4.6. Non compartment specific effects relevant to food chain (secondary poisoning)

For predators (birds) was not possible to carry out the corresponding risk characterization since no information about oral toxicity data in birds was provided with the Dossier.

2.2.2.4.6.1. Assessment of secondary poisoning via the aquatic food chain

The risk to fish-eating predators (mammals) is calculated as the ratio between the concentration in the food ($PECoral_{fish\text{-}predator}$) and the no-effect-concentration for oral intake (PNECoral).

$$\frac{PECoral_{fish\text{-}predator}}{PNEC_{predator}} = 2.98 \cdot 10^{-3} / 11.1 = 2.68 \cdot 10^{-4}$$

Conclusion:

No risk is expected to fish-eating predators (mammals) since the risk characterization ratio is below 1.

2.2.2.4.6.2. Assessment of secondary poisoning via the terrestrial food chain

A similar approach as for the aquatic route was used here. The risk to worm-eating predators (mammals) was calculated as the ratio between the concentration in the food ($PECoral_{worm\text{-}predator}$) and the no-effect-concentration for oral intake (PNECoral).

Table 4. PEC/PNEC ratios for Mammal predators in an exposure situation

Exposure Scenario		Avg. time (d)	$PECoral_{worm\text{-}predator}$ [mg/kg_{diet}]	$PNEC_{oral}$ [mg/kg_{diet}]	PEC/PNEC
STP sludge	Agriculture	30	$3.27 \cdot 10^{-3}$	11.1	$2.95 \cdot 10^{-4}$
	Agriculture	180	$5.44 \cdot 10^{-4}$		$4.90 \cdot 10^{-5}$
	Grassland	180	$1.09 \cdot 10^{-4}$		$9.82 \cdot 10^{-5}$

Conclusion:

No risk is expected to worm-eating predators (mammals) since the risk characterization ratios are negligible.

2.2.3. Listing of endpoints

In order to facilitate the work of Member States in granting or reviewing authorisations, and to apply adequately the provisions of Article 5(1) of Directive 98/8/EC and the common principles laid down in Annex VI of that Directive, the most important endpoints, as identified during the evaluation process, are listed in Appendix I.

3. PROPOSAL FOR THE DECISION

3.1. Background to the Proposed Decision

The risk assessment for methyl nonyl ketone and its formulated product Vapet® Get Off™ Spray used as repellents and attractants has been performed following the directions from Directive 98/8/EC and extended in the TGD and ESD documents and agreed decisions in Technical Meetings on Biocide Evaluation.

Vapet® Get Off™ Spray is an animal repellent formulated as a liquid (EC) containing approximately 3.58 % methyl nonyl ketone. It is a ready-to-use product, only applied indoors by non-professionals by spraying to areas of the home to discourage dogs from fouling.

Regarding **efficacy**, the product demonstrated an efficacy against dogs.

The overall conclusion from the **human health** evaluation of methyl nonyl ketone used in product type 19 is that no potential risk to non-professional users would be related to dermal and inhalation routes of exposure. It has been demonstrated in the Tier 1 assessment that repellent containing 3.58% w/w methyl nonyl ketone do not pose risks (MOE > 300) to non-professional users. In the Tier 2 approach, the comparison of the estimated exposure to the proposed AEL gives rise to a ratio <1, indicating an acceptable risk. Finally, it has also been demonstrated using the calculations obtained with ConsExpo 4.1 that repellent containing 3.58% w/w methyl nonyl ketone poses acceptable risk to consumers.

The results of the secondary exposure risk assessment demonstrate that adult, children and infants will not be exposed to unacceptable levels of methyl nonyl ketone during the realistic worst case scenarios presented. Neither acute secondary exposure of children crawling on treated surface, nor chronic exposure of adults inhaling volatilised residue, children touching surfaces and infants inhaling volatilised residue or touching surfaces, show an unacceptable risk.

From the **environmental** point of view, taking into consideration the results of the risk assessment carry out with the realistic worst-case scenarios presented, it can be concluded that Methyl nonyl ketone used for the formulation of biocidal products type 19 does not represent a potential risk for the environment.

3.2. Proposed Decision regarding Inclusion in Annex I

It is recommended that methyl nonyl ketone is included in Annex I to Directive 98/8/EC as an active substance for use in product-type **19** (Repellents and attractants), subject to the following specific provisions:

a) The active substance methyl nonyl ketone shall have a minimum purity of 975 g/kg.

b) Products containing methyl nonyl ketone are restricted to indoor application by non-professional users, unless data is submitted allowing the assessment of those uses or exposure scenarios and those risks to human populations and to environmental

compartments that are relevant to the particular product and have not been representatively addressed in the Union level risk assessment, and demonstrating that the product will meet the requirements of Article 5 and Annex VI.

3.3. Factors to be taken into account by Member States when authorising products

No particular restrictions are proposed associated with the inclusion of methyl nonyl ketone in Annex I of Council Directive 98/8/EC.

Nevertheless, further efficacy data will be required to support authorisation of products with methyl nonyl ketone at the Member State level (studies will include both untreated controls and comparison formulations to assess the effects of perfumes within the supported product).

Regarding the storage stability test, it should also be required at national level authorisation.

Finally, in order to avoid food having contact with the product, a warning statement that product should not be used on areas where food is prepared, stored or consumed should be added to the labelling.

3.4. Requirement for further information

It is considered that the evaluation has shown that sufficient data have been provided to verify the outcome and conclusions, and permit the proposal for the inclusion of Methyl nonyl ketone in Annex I to Directive 98/8/EC.

Nevertheless, it has to be clearly pointed out, that further data requirements are requested for the assessment of the environmental part at national level product authorisation, if other pathways of exposure become more relevant.

3.5. Updating this Assessment report

This report may need to be updated periodically in order to take account of scientific developments and results from the examination of any of the information referred to in articles 7, 10.4 and 14 of Directive 98/8/EC. Such adaptations will be examined and finalised in connection with any amendment of the conditions for the inclusion of methyl nonyl ketone in Annex I to the Directive.

Appendix I: Listing of end points

Chapter 1: Identity, Physical and Chemical Properties, Classification and Labelling

Active substance (ISO Common Name)	methyl nonyl ketone
Product-type	Repellent (PT19)

Identity

Chemical name (IUPAC)	Undecan-2-one
Chemical name (CA)	2-Undecanone
CAS No	112-12-9
EC No	203-937-5
Other substance No.	None
Minimum purity of the active substance as manufactured (g/kg or g/l)	> 975 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	no additives no (eco)toxicologically relevant impurities
Molecular formula	$C_{11}H_{22}O$
Molecular mass	170.29
Structural formula	

Physical and chemical properties

Melting point (state purity)	12.2° C (99.5%)
Boiling point (state purity)	235.5°C (99.5%)
Temperature of decomposition	Not applicable
Appearance (state purity)	Clear mobile liquid, with a strong characteristic smell (99.5%)
Relative density (state purity)	0.826 at 20°C (99.5%)
Surface tension	62.3 mN/m at 20°C for a 90 % saturated solution. 66.0 mN/m at 40ºC for a 90% saturated solution.
Vapour pressure (in Pa, state temperature)	11.8 Pa at 20°C
Henry's law constant (Pa m^3 mol^{-1})	1395.4 Pa m^3/mol at 20 ºC
Solubility in water (g/l or mg/l, state temperature)	1.44 mg/L at 20° C at pH 7
Solubility in organic solvents (in g/l or mg/l, state temperature)	250 g/L soluble in n-heptane, p-xylene, 1,2-dichloroethane, methanol, acetone and ethyl acetate
Stability in organic solvents used in biocidal products including relevant breakdown products	Not applicable
Partition coefficient (log P_{OW}) (state temperature)	Log Pow = 4.342 at 21.5°C
Dissociation constant	Not applicable as MNK does not dissociate in water
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	λ_{max}: 275 nm Molar absorption coefficient: 22.4 dm^3/mol/cm (pH 1.8) Molar absorption coefficient: 20.4 dm^3/mol/cm (pH 6.6) Molar absorption coefficient: 20.7 dm^3/mol/cm (pH 12.2)
Photostability (DT_{50}) (aqueous, sunlight, state pH)	λ_{max} for MNK: 275 nm. It is assumed that those chemicals that have absorption maxima below 290nm cannot undergo direct photolysis in sunlight. Based on a theoretical study, if MNK photo-transforms in an aqueous system, two main photo-degradation products could result: acetone and 1-octene.
Quantum yield of direct phototransformation in water at Σ > 290 nm	Not evaluated
Oxidizing properties	Non-oxidising
Flammability	Not flammable Auto ignition temperature: 207ºC Flash-point: 97 ºC
Explosive properties	Non-explosive

Classification and proposed labelling

with regard to physical/chemical data	No classification
with regard to toxicological data	Xi: Irritant (Category 2; Skin Irrit. 2) R38: Irritating to skin (H315)
with regard to environmental fate and behaviour data	N: Dangerous for the environment R53: May cause long-term adverse effects in the aquatic environment
with regard to ecotoxicological data	N: Dangerous for the environment R50: Very toxic to aquatic organisms
for the environment according to the Regulation (EC) No 1272/2008 and the GHS	Hazardous to the aquatic environment, Chronic toxicity, Category 1 H400: Very toxic to aquatic life H410: Very toxic to aquatic life with long lasting effects

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	GC-FID
Impurities in technical active substance (principle of method)	GC-FID

Analytical methods for residues

Soil (principle of method and LOQ)	Not relevant
Air (principle of method and LOQ)	GC-MS LOQ: 5.56 µg/m^3
Water (principle of method and LOQ)	GC-MS (only validated for drinking water) LOQ: 0.103 µg/l
Body fluids and tissues (principle of method and LOQ)	Not relevant
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Not relevant
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not relevant

CRITICAL ENDPOINTS

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	100% default value
Rate and extent of dermal absorption:	100% default value

Distribution:	Not evaluated
Potential for accumulation:	Rapidly eliminated from the blood.
Rate and extent of excretion:	Although ketones and secondary alcohols are readily interconverted in animals, reduction of the ketones by cytosolic carbonyl reductases is favoured yielding the corresponding secondary alcohols that are rapidly excreted in the urine mainly as glucuronic acid conjugates.
Toxicologically significant metabolite(s)	Parent compound MNK

Acute toxicity

Rat LD_{50} oral	> 2000 mg/kg bw
Rat LD_{50} dermal	> 2000 mg/kg bw
Rat LC_{50} inhalation	> 5.43 mg/L
Skin irritation	Irritating
Eye irritation	Non irritating
Skin sensitization (test method used and result)	Non sensitising

Short-term repeated dose toxicity

Species/ target / critical effect	Rat/Kidney/Histological changes consistent with nephropathy
Oral NOAEL / LOAEL	NOAEL = 50 mg/kg/day for males and 1000 mg/kg/day for females (90 day rat oral study) / LOAEL = 1000 mg/kg/day for males (90 day rat oral study) and not determined for females
Dermal NOAEL / LOAEL	Not evaluated
Inhalation NOAEL / LOAEL	Not evaluated

Genotoxicity	Non mutagenic in an in vitro bacterial mutation assay and an in vitro gene mutation mammalian cells assay. Non clastogenic in an in vitro chromosome aberration mammalian cells assay.

Chronic Toxicity/Carcinogenicity

Species/ target / critical effect	Not evaluated
Relevant dermal NOAEL / NOEL	Not evaluated
Carcinogenicity	Not evaluated

Reproductive toxicity

Reproduction toxicity

Species/ Reproduction target / critical effect	Not evaluated

Parental NOAEL / LOAEL	Not evaluated
Reproductive NOAEL / LOAEL	Not evaluated
Offspring NOAEL / LOAEL	Not evaluated
Developmental toxicity	
Developmental target/critical effect	No treatment related teratogenic effect detected at the highest assayed dose
Relevant maternal NOAEL	1000 mg / kg bw / day
Relevant developmental NOAEL	1000 mg / kg bw / day

Neurotoxicity

Acute neurotoxicity	Not evaluated
Repeated neurotoxicity	Not evaluated
Delayed neurotoxicity	Not evaluated

Other studies

.....	Not relevant

Medical data

.....	No incidents of poisoning have been reported. In the historical data of 1Pet and Garden Manufacturing Ltd.`s employees, no incidents related to exposure to MNK have been recorded. No epidemiological studies were found pertaining to exposure to MNK. No poisoning incidents or symptoms have been reported despite its widespread use. MNK has been used over the last 40 years as a repellent for cats and dogs. No observations of sensitisation or allergenicity have been made following use of MNK.

Summary	Value	Study	Safety factor
Non-professional user			
ADI (acceptable daily intake, external long-term reference dose)	0.17 mg / kg bw / day	90 day rat oral	300
AEL-S (Operator Exposure)	0.50 mg / kg bw / day	90 day rat oral	100
ARfD (acute reference dose)	Not applicable		
Professional user			
Reference value for inhalation (proposed OEL)	Not determined	-	-
Reference value for dermal absorption	Not determined	-	-
AEL values			

Acute	0.50 mg/kg bw/day	90 day repeated oral dose in rat	100
Short and medium term	0.50 mg/kg bw/day	90 day repeated oral dose in rat	100
Long term	0.17 mg/kg bw/day	90 day repeated oral dose in rat	300

Acceptable exposure scenarios (including method of calculation)

Professional users	Not intended for professional users
Non-professional users	• Method of calculation based on **Consumer product spraying and dusting – model 2**, hand-held trigger spray, of TNsG: - Without protective clothing: 5.47 x 10^{-2} mg/kg bw/day (MOE = 914; exposure/AOAEL = 0.32) - With protective clothing: 4.89 x 10^{-2} mg/kg bw/day (MOE = 1022; exposure/AEL = 0.28) • Method of calculation based on **ConsExpo 4.1**: 4.35 x 10^{-3}mg/kg bw/day (MOE = 11494; exposure/AOAEL = 2.6 x 10^{-2})
Indirect exposure as a result of use	• <u>Acute scenario:</u> - Child in contact with wet sprayed surface: 5.575 x 10^{-2} mg/kg bw/day (MOE = 897) - Infant in contact with wet sprayed surface 7.77 x 10^{-2} mg/kg bw/day (MOE = 643) - Children crawling on a treated surface (Method of calculation based on ConsExpo 4.1): 4.4 x 10^{-2} mg/kg bw/day (MOE=1136) • <u>Chronic scenario:</u> - Adult inhalating volatilised residues indoors: 2.533 x 10^{-6} mg/kg bw/day (MOE = 2.0 x 10^{7}; exposure/AEL = 1.5 x 10^{-5}) - Infant inhalating volatilised residues indoors: 3.286 x 10^{-5} mg/kg bw/day (MOE = 1.5 x 10^{6}; exposure/AEL = 1.9 x 10^{-4}) - Child touching surfaces treated with the animal repellent: 1.03 x 10^{-3} mg/kg bw/day (MOE= 4.9 x 10^{4}; exposure/AEL = 6.1 x 10^{-3}) - Infant touching surfaces treated with the animal repellent and oral exposure: 4.12 x 10^{-3} mg/kg bw/day (MOE= 1.2 x 10^{4}; exposure/AEL = 2.4 x 10^{-2}) - Children crawling on a treated surface (Method of calculation based on ConsExpo 4.1): 7.6 x 10^{-3}mg/kg bw/day (MOE=6.6 x 10^{3}; exposure/AEL=4.5 x 10^{-2})

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water (Annex IIA, point 7.6, IIIA, point XII.2.1, 2.2)

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	pH___5___: at 25°C the following % of Initial Measured Dose (IMD) as MNK was recovered at the end of the study: 84.7 – 98.9. Indicating that MNK was hydrolytically stable at pH 5.
	pH___7___: at 25°C the following % of IMD as MNK was recovered at the end of the study: 94.0 – 103.1. Indicating that MNK was hydrolytically stable at pH 7.
	pH__9____: 25°C the following % of IMD as MNK was recovered at the end of the study: 90.7 – 101.5. Indicating that MNK was hydrolytically stable at pH 9.
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	λ_{max} for MNK: 275 nm. It is assumed that those chemicals that have absorption maxima below 290nm cannot undergo direct photolysis in sunlight. Based on a theoretical study, if MNK photo-transforms in an aqueous system, two main photo-degradation products could result: acetone and 1-octene.
Readily biodegradable (yes/no)	No (according to guideline OECD 301B)
Biodegradation in seawater	Not relevant. Utilization in seawater is not intended
Non-extractable residues	Not relevant
Distribution in water / sediment systems (active substance)	Not relevant
Distribution in water / sediment systems (metabolites)	Not relevant

Route and rate of degradation in soil (Annex IIIA, point VII.4, XII.1.1, XII.1.4; Annex VI, para. 85)

Mineralization (aerobic)	MNK is mineralised in soil (laboratory test at 25ºC). The level of CO_2 was 0.2% of the IMD at 4 hours and increased to 48.7% of the IMD at the study's termination (30 days).
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} (25°C, aerobic): 4.07 days (correlation = 0.807). DT_{50lab} (12°C, aerobic): 11.5 days
Field studies (state location, range or median with number of measurements)	Not relevant
Anaerobic degradation	Not relevant
Soil photolysis	Not relevant
Non-extractable residues	The bound residues in the soil increased from 0.59% of

	the Initial Measured Dose (IMD) at day 0 to 58.2% of IMD at the day 1 and then gradually decreased to 38.3% of the IMD at the study's termination (30 days).
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	No metabolite was present at > 3% of the applied radioactivity.
Soil accumulation and plateau concentration	Not relevant. Accumulation studies were not required because the half life of MNK in soil was significantly shorter than 1 year.

Adsorption/desorption (Annex IIA, point XII.7.7; Annex IIIA, point XII.1.2)

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	**Silt loam:** pH = 7.4 K_{oc} (ml/g)= 1,511 (worst-case for water phase) Desorption in $Ca(NO_3)_2$ solution = 82.1 **Sandy loam:** pH = 8.5 K_{oc} (ml/g)= 2,512 Desorption in $Ca(NO_3)_2$ solution = 10.2 **Clay loam:** pH = 6.4 K_{oc} (ml/g)= 2,825 (worst-case for sediment) Desorption in $Ca(NO_3)_2$ solution = 51.4 **Sand:** pH = 7.4 K_{oc} (ml/g) = 1,700 Desorption in $Ca(NO_3)_2$ solution = 34.6 K_{oc} (arithmetic mean) = 2,147 ml/g

Fate and behaviour in air (Annex IIIA, point VII.3, VII.5)

Direct photolysis in air	Not documented
Quantum yield of direct photolysis	Not documented
Photo-oxidative degradation in air	DT_{50} in air = 1.16 days (assuming on a 24-hours basis), as a result of gas phase reactions with photochemically produced OH radicals.
Volatilization	High potential for Volatilisation

Monitoring data, if available (Annex VI, para. 44)

Soil (indicate location and type of study)	No data provided
Surface water (indicate location and type of study)	No data provided
Ground water (indicate location and type of study)	No data provided

Air (indicate location and type of study)	No data provided

Chapter 5: Effects on Non-target Species

Toxicity data for aquatic species (most sensitive species of each group)
(Annex IIA, point 8.2, Annex IIIA, point 10.2)

Species	Time-scale	Endpoint	Toxicity
Fish			
Bluegill sunfish, *(Lepomis macrochirus)*	96 h	Mortality	LC_{50} = 2.1 mg/L
Invertebrates			
Daphnia magna	48 h	Mobility	EC_{50} = 0.23 mg/L **(the lowest endpoint for water phase)**
Algae			
Pseudokirchnerriella subcapitata	24 h*	Growth rate Biomass	E_rC_{50} = 1.9 mg/L E_bC_{50} = 1.4 mg/L NOEC = 0.38 mg/L
Microorganisms			
Activated sludge from the waste-water treatment plant	3 h	Respiration inhibition	EC_{20} = 121.75 mg/L EC_{50} = 379.49 mg/L NOEC = 60.00 mg/L **(key endpoint for sewage microorganisms)**

***** In a 72 h toxicity test, MNK disappeared from the test solution after 24 h, the highest inhibitory effect on the growth of the algae was determined within this exposure period.

Effects on earthworms or other soil non-target organisms

Acute toxicity to non-target organisms (Annex IIIA, point XIII.3.2)	Spider mites *(Tetranychus urticae)* Endpoint: Contact toxicity, residual activity, egg viability Duration of test: 7 days 24-hrs EC_{50} = 1.64 mg/ml equivalent to 24-hrs EC_{50} = 51.01151 mg/kg **(key endpoint for terrestrial compartment)**
Reproductive toxicity to…….. (Annex IIIA, point XIII.3.2)	Not evaluated

Effects on soil micro-organisms (Annex IIA, point 7.4)

Nitrogen mineralization	Not relevant
Carbon mineralization	Not relevant

Effects on terrestrial vertebrates

Acute toxicity to mammals (Annex IIIA, point XIII.3.3)	---

Acute toxicity to birds (Annex IIIA, point XIII.1.1)	Not evaluated
Dietary toxicity to birds (Annex IIIA, point XIII.1.2)	Not evaluated
Reproductive toxicity to birds (Annex IIIA, point XIII.1.3)	Not evaluated

Effects on honeybees (Annex IIIA, point XIII.3.1)

Acute oral toxicity	Not evaluated
Acute contact toxicity	Not evaluated

Effects on other beneficial arthropods (Annex IIIA, point XIII.3.1)

Acute oral toxicity	Not evaluated
Acute contact toxicity	Not evaluated
Acute toxicity to ……	Not evaluated

Bioconcentration (Annex IIA, point 7.5)

Bioconcentration factor (BCF)	No data provided BCF_{fish} = 978.81 L/kg, calculated value by using a (Q)SAR model $BCF_{earthworm}$ = 264.58 L/kg, calculated value by using a (Q)SAR model
Depuration time(DT_{50}) (DT_{90})	Not evaluated
Level of metabolites (%) in organisms accounting for > 10 % of residues	Not evaluated

Chapter 6: Other End Points

No other end points are available for MNK.

Appendix II: List of intended uses

Summary of intended uses

Object and/or situation	Member State or Country	Product name	Organisms controlled	Formulation		Application			Applied amount per treatment			Remarks:
				Type	Conc.	method	number	interval between applications (min)	g as/L	water L/m^2	g as/m^2	
(a)			(c)	(d-f)	of as (i)	kind (f-h)	min max (k)		min max	min max	min max	(m)
Indoor use	Northern and Southern EU	Vapet® Get Off™ Spray	Dogs	EC	35.8 g/L	Spraying	Repeat as necessary	12 hours	35.8 g/L	NA	0.143 – 0.286	Product is applied undiluted as a ready to use spray.

NA – Not applicable

(a) *e.g.* biting and suckling insects, fungi, molds; (b) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(c) GCPF Codes - GIFAP Technical Monograph No 2, 1989 ISBN 3-8263-3152-4); (d) All abbreviations used must be explained
(e) g/kg or g/l;(f) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench;
(g) Kind, *e.g.* overall, broadcast, aerial spraying, row, bait, crack and crevice equipment used must be indicated;
(h) Indicate the minimum and maximum number of application possible under practical conditions of use;
(i) Remarks may include: Extent of use/economic importance/restrictions

Appendix III: List of studies

Data protection is claimed by the applicant in accordance with Article 12.1(c) (i) and (ii) of Council Directive 98/8/EC for all study reports marked "Y" in the "Data Protection Claimed" column of the table below. For studies marked Yes(i) data protection is claimed under Article 12.1(c) (i), for studies marked Yes(ii) data protection is claimed under Article 12.1(c) (ii). These claims are based on information from the applicant. It is assumed that the relevant studies are not already protected in any other Member State of the European Union under existing national rules relating to biocidal products. It was however not possible to confirm the accuracy of this information.

Doc IIIA: Active substance

Section No./Reference No.	Author(s)	Year	Title, Source (where different from company) Company, Report No. GLP (where relevant) / (Un) Published	Data Protection Claimed (Yes/No)	Owner
IIIA, 3.1	Drake, R.M.	2004	Determination of Relative Density Boiling Point and Freezing Point of MNK TECH. Chemex Environmental International Limited, Report No. ENV5983/120136, GLP (unpublished).	Yes	[1]Pet and Garden Manufacturing Ltd.
IIIA 3.2	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.
IIIA, 3.2.1	ChemIDplus Advanced	2005	Methyl Nonyl Ketone. Source: Not applicable, Report No. RN 112-12-9, Non-GLP (published).	No	Public Literature
IIIA 3.3	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.
IIIA, 3.4	White, D.F. and Mullee, D.M.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	Pet and Garden Manufacturing Ltd.
IIIA 3.4/1	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.
IIIA 3.4/2	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.

Section No./Reference No.	Author(s)	Year	Title, Source (where different from company) Company, Report No. GLP (where relevant) / (Un) Published	Data Protection Claimed (Yes/No)	Owner
IIIA 3.4/3	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.
IIIA 3.4/4	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.
IIIA 3.5	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.
IIIA 3.7	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.
IIIA 3.9	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.
IIIA 3.10	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.
IIIA 3.11	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.
IIIA 3.12	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.
IIIA 3.13	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.
IIIA 3.14	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.

Section No./Reference No.	Author(s)	Year	Title, Source (where different from company) Company, Report No. GLP (where relevant) / (Un) Published	Data Protection Claimed (Yes/No)	Owner
IIIA, 4.1	DGF	2000	Gaschromatographie: Analyse der Fettsäuren und Fetsäureverteilung. DGF, Report No.: DGF C-VI 10, non GLP (published).	No	DGF
IIIA, 4.2.b/1	Smith, J.S.C	2007a	Validation of GC Laboratories Ltd. Analytical Method M630 "Determination of Residues of Methyl Nonyl Ketone (MNK, 2-Undecanone) in Air Monitoring Tubes". GC Laboratories Ltd, Report no: J16446, GLP (unpublished).	Yes	[1]Spotless UK Ltd.
IIIA, 4.2.c/1	Smith, J.S.C	2007 b	Validation of GC Laboratories Ltd. Analytical Method M631 "Determination of Residues of Methyl Nonyl Ketone (MNK, 2-Undecanone) in Water". GC Laboratories Ltd, Report no: J16447, GLP (unpublished).	Yes	Spotless UK Ltd.
IIIA, 6.1.1	Brunt, P.	2003a	Methyl Nonyl Ketone: Acute Oral Toxicity in the Rat – Acute Toxic Class Safepharm Laboratories Limited, Report no. 672/005, GLP (unpublished)	Yes	[1]Pet and Garden Manufacturing Plc.
IIIA, 6.1.2	Brunt, P.	2003 b	Methyl Nonyl Ketone: Acute Dermal Toxicity (Limit Test) in the Rat Safepharm Laboratories Limited, Report no. 672/006, GLP (unpublished)	Yes	[1]Pet and Garden Manufacturing Plc.
IIIA, 6.1.3	Hershman, R.J.	1991	MGK® Dog and Cat Repellent (Methyl Nonyl Ketone) – Code #150-91, Acute Inhalation Toxicity, LC_{50}, 4-hour Exposure – Rats, Part I Biosearch Incorporated, Report no. 91-7236A, GLP (unpublished)	Yes	[3]McLaughlin Gormley King Company
IIIA, 6.1.4/1	Brunt, P.	2003c	Methyl Nonyl Ketone: Acute Dermal Irritation in the Rabbit Safepharm Laboratories Limited, Report no. 672/007, GLP (unpublished)	Yes	[1]Pet and Garden Manufacturing Plc.

Section No./Reference No.	Author(s)	Year	Title, Source (where different from company) Company, Report No. GLP (where relevant) / (Un) Published	Data Protection Claimed (Yes/No)	Owner
IIIA, 6.1.4/2	Brunt, P.	2003 d	Methyl Nonyl Ketone: Acute Eye Irritation in the Rabbit Safepharm Laboratories Limited, Report no. 672/008, GLP (unpublished)	Yes	[1]Pet and Garden Manufacturing Plc.
IIIA, 6.1.5	Brunt, P.	2003e	Methyl Nonyl Ketone: Skin Sensitisation in the Guinea Pig – Magnusson and Kligman Maximisation Method Safepharm Laboratories Limited, Report no. 672/009, GLP (unpublished)	Yes	[1]Pet and Garden Manufacturing Plc.
IIIA, 6.2/1	DiVincenzo, G.D., Kaplan, C.J., Dedinas, J.	1976	Characterisation of the Metabolites of Methyl *n*-Butyl Ketone, Methyl iso-Butyl Ketone and Methyl Ethyl Ketone in Guinea Pig Serum and their Clearance *Toxicology and Applied Pharmacology* 36: 511-522, non-GLP (published)	No	Public literature
IIIA, 6.2/2	Dugay, A.B., Plaa, G.L.	1994	Tissue Concentrations of Methyl Isobutyl Ketone, Methyl n-Butil Ketone and Their Metabolites After Oral or Inhalation Exposure *Toxicology Letters*, 75: 51-58, non-GLP (published)	No	Public literature
IIIA, 6.2/3	Liira, J., Riihimäki, V., Pfäffli, P.	1988	Kinetics of Methyl Ethyl Ketone in Man: Absorption, Distribution and Elimination in Inhalation Exposure *Int Arch Occup Environ Health, 60: 195-200, non-GLP (published)*	No	Public literature
IIIA, 6.2/4	Thrall, K.D., Soelberg, J.J., Weitz, K.K., Woodstock, A.D.	2002	Development of a Physiologically Based Pharmacokinetic Model for Methyl Ethyl Ketone in F344 Rats *Journal of Toxicology and Environmental Health, Part A, 65: 881-896, non-GLP (published)*	No	Public literature
IIIA, 6.2/5	Eastman Chemical Company	2004	Test Plan for Ketone Bottoms (KB4/KB3) Facility: Not applicable, Report no. 201-15014A, non GLP (published)	No	Public literature

Section No./Reference No.	Author(s)	Year	Title, Source (where different from company) Company, Report No. GLP (where relevant) / (Un) Published	Data Protection Claimed (Yes/No)	Owner
IIIA, 6.4.1	McRae, L.A., Mullee, D., Brooks, P.N.	2005	Ninety day Repeated Dose Oral (Gavage) Toxicity Study in the Rat Safepharm Laboratories Limited, Report no. 672/004, GLP (unpublished)	Yes	[1]Pet and Garden Manufacturing Plc.
IIIA, 6.6.1	San, R.H.C and Shelton, J.B.	1991	Salmonella/Mammalian-Microsome Plate Incorporation Mutagenicity Assay (Ames Test) Microbiological Associates, Report no. T9487.501, GLP (unpublished)	Yes	[3]McLaughlin Gormley King Company
IIIA, 6.6.2	Béres, E.	2003a	*In vitro* Mammalian Chromosomal Aberration Study of Test Item Methyl Nonyl Ketone Toxicological Research Centre Limited, Report no. 02/688-020C, GLP (unpublished)	Yes	[1]Pet and Garden Manufacturing Plc.
IIIA, 6.6.3	Béres, E.	2003 b	Mutagenic Evaluation of Test Item Methyl Nonyl Ketone in CHO/HPRT Assay Toxicological Research Centre Limited, Report no. 02/688-015C, GLP (unpublished)	Yes	[1]Pet and Garden Manufacturing Plc.
IIIA, 6.8.1	Irvine, L.F.H.	1992	Methyl Nonyl Ketone (MNK) Rat Developmental Toxicity (Teratology) Study Toxicol Laboratories Limited, Report no. MCA/5/91, GLP (unpublished)	Yes	[3]McLaughlin Gormley King Company
IIIA, 6.12.1	US EPA	1995	Reregistration Eligibility Decision (RED) – Methyl Nonyl Ketone Facility: Not applicable, Report no. EPA 738-R-95-038, non GLP (published)	No	Public literature
IIA, 4.1.1.1.1 (IIIA, 7.1.1.2.1)	Drake, R.M.	2003 b	Determination of the ready biodegradability of MNK TECH. Chemex Environmental International Limited, Report No. ENV5820/120136, GLP (unpublished).	Yes	[1]Pet and Garden Manufacturing Ltd.
IIA, 4.1.1.1.2 (IIIA, 7.2.1)	Williams, M.	1992	Aerobic Soil Metabolism of Methyl Nonyl Ketone: Lab Project Number: 39430. Unpublished study prepared by ABC Laboratories.	Yes	[2]McLaughlin Gormley King Company (MGK)

Section No./Reference No.	Author(s)	Year	Title, Source (where different from company) Company, Report No. GLP (where relevant) / (Un) Published	Data Protection Claimed (Yes/No)	Owner
IIA, 4.1.1.2.1 (IIIA, 7.1.1.1)	Gorman, M.	1991	Hydrolysis of Methyl Nonyl Ketone as a Function of pH at 25º C: Lab Project Number: 39313. Unpublished study prepared by ABC Laboratories.	Yes	[2]McLaughlin Gormley King Company (MGK)
IIA, 4.1.1.3.1 (IIIA, 7.2.3.1)	Williams, M.	1992	Soil/Sediment Adsorption-Desorption of Methyl Nonyl Ketone: Lab Project Number: 39436. Unpublished study prepared by ABC Laboratories.	Yes	[2]McLaughlin Gormley King Company (MGK)
(IIIA, 7.3.1)	Drake, R.M.	2003a	The Estimation of the Adsorption Coefficient (K_{oc}) of MNK TECH. Chemex Environmental International Limited, Report No. ENV5982/120136, GLP (unpublished).	Yes	[1]Pet and Garden Manufacturing Ltd.
IIIA 4.2.1.1 (IIIA, 7.4.1.1/01)	Sword, M.; Herzig, R.	1991	Acute Flow-Through Toxicity of Methyl Nonyl Ketone to Bluegill (Lepomis macrochirus): Lab Project Number: 391198. Unpublished study prepared by ABC Laboratories.	Yes	[2]McLaughlin Gormley King Company (MGK)
IIA, 4.2.1.2 (IIIA, 7.4.1.2/01)	Craig, W.J.	2003a	The toxicity to *Daphnia magna* of MNK technical. Chemex Environmental International Limited, Report No. ENV 5981/120136, GLP (unpublished).	Yes	[1]Pet and Garden Manufacturing Ltd.
IIA, 4.2.1.3 (IIIA, 7.4.1.3/01)	Craig, W.J.	2003 b	The growth inhibition of the alga *Selenastrum capricornutum* by MNK technical. *Chemex Environmental International Limited, Report No. ENV5817/120136, GLP (unpublished).*	Yes	[1]Pet and Garden Manufacturing Ltd.
IIA, 4.2.1.4 (IIIA, 7.4.1.4)	McMurray, A.	2002	An evaluation of the effect of Methyl Nonyl Ketone on the inhibition of activated sludge respiration according to OECD 209. Chemex Environmental International Limited, Report No. ENV5816/120136, GLP (unpublished).	Yes	[1]Pet and Garden Manufacturing Ltd.

Section No./Reference No.	Author(s)	Year	Title, Source (where different from company) Company, Report No. GLP (where relevant) / (Un) Published	Data Protection Claimed (Yes/No)	Owner
IIA, 4.2.3 (IIIA, 7.5.6)	Chatzivasileidis E.A. and Sabelis M.W.	1997	Toxicity of methyl ketones from tomato trichomes to *Tetranychus urticae Koch*. *The Institute of Systematics and Populations Biology, University of Amsterdam, In Experimental & Applied Acarology, Vol. 21, pp. 473 – 484, Non-GLP (published).*	No	Public Literature

1Pet and Garden Manufacturing Limited and Guaber UK Limited are fully owned by Spotless UK Ltd.

Doc IIIB: Biocidal Product

Section No./Reference No.	Author(s)	Year	Title, Source (where different from company) Company, Report No. GLP (where relevant) / (Un) Published	Data Protection Claimed (Yes/No)	Owner
IIIB, 3.1	Pet and Garden Manufacturing Plc.	2005	MSDS Vapet® Get Off™ Spray. Pet and Garden Manufacturing Plc., Report No. Not applicable, Non-GLP (unpublished).	No	[1]Pet and Garden Manufacturing Plc.
IIIB, 3.4	Pet and Garden Manufacturing Plc.	2005	MSDS Vapet® Get Off™ Spray Pet and Garden Manufacturing Plc., Report No. Not applicable, Non-GLP (unpublished).	No	[1]Pet and Garden Manufacturing Plc.
IIIB, 3.4	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.
IIIB, 3.5	White, G.A.	2010	Determination of the pH of Get Off Spray G C Laboratories Ltd., (unpublished)	Yes	[1]Spotless UK Ltd.
IIIB, 3.6	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.
IIIB, 3.10	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.
IIIB, 3.11	Parsons, A.H.	2007	Physical Chemistry Testing of Methyl Nonyl Ketone Technical material and 'Get off Spray'. G C Laboratories Ltd., Report no. J16413 (unpublished)	Yes	[1]Spotless UK Ltd.

Section No./Reference No.	Author(s)	Year	Title, Source (where different from company) Company, Report No. GLP (where relevant) / (Un) Published	Data Protection Claimed (Yes/No)	Owner
IIIB, 4.1/1	White, G.A	2006	Validation of analytical method M591 "High performance liquid chromatography determination of Methyl Nonyl Ketone (MNK) in technical material and Formulations" for the "Get Off Spray" and "Get Off My Garden" formulations, G.C. Laboratories, 6 Fen End, Astwick Road, Stotfold, Hitchin SG5 4BA, United Kingdom, unpublished report no: J15715.	Yes	[1]Guaber UK Limited
IIIB, 5.10/1	Mugford, R.	Date not available	Report of preliminary trials of get Off My Garden. WBC Technology Limited, Norfolk House, Great Chesterford Court, Great Chesterford, Saffron Walden, Essex, CB10 1PF, unpublished report no: MNK/E3	Yes	[1]Guaber UK Limited
IIIB, 5.10/2	WBC Technology Limited	Date not available	Testing of dog repellent (urination). WBC Technology Limited, Ontario Nutri Lab, 855 St. David St. N., Fergus, Ontario, N1M2L1, Canada, unpublished report no: MNK/E4	Yes	[1]Guaber UK Limited
IIIB, 5.10/3	-	1993	User trial with the product GET OFF MY GARDEN in south-west England during the summer of 1993	Yes	[1]Guaber UK Limited
IIIB, 5.10/4	Kawani, H.J.	2011	Repellency trials of test formulation in the beagle dog. Jai Research Foundation, Department of Toxicology, Valvada-396 108, Dist. Valsad, Gujarat (India). JRF Research Number: R-571/2011	Yes	Spotless Punch Limited
IIIB, 5.10/5	Ramírez, D.	2011	Avoidance study of get off spray in cats. Harlan Laboratoris, S.A., C/. Argenters, 6; 08130 – Santa Perpètua de Mogoda (Barcelona). Study number: S33111	Yes	Spotless Punch Limited

1Pet and Garden Manufacturing Limited and Guaber UK Limited are fully owned by Sp

Appendix IV: List of standard terms and abbreviations

(Adapted from: (i) Guidelines and criteria for the preparation of PPP dossiers[1]; (ii) TNsG on Data Requirements[2])

Stand. term / Abbreviation	**Explanation**
A	ampere
ACh	acetylcholine
AChE	acetylcholinesterase
ADI	acceptable daily intake
ADME	administration distribution metabolism and excretion
ADP	adenosine diphosphate
AE	acid equivalent
AF	assessment factor
AFID	alkali flame-ionisation detector or detection
A/G	albumin/globulin ratio
ai	active ingredient
ALD_{50}	approximate median lethal dose, 50%
ALT	alanine aminotransferase (SGPT)
Ann.	Annex
AOEL	acceptable operator exposure level
AMD	automatic multiple development
ANOVA	analysis of variance
AP	alkaline phosphatase
approx	approximate
ARC	anticipated residue contribution
ARfD	acute reference dose
as	active substance
AST	aspartate aminotransferase (SGOT)
ASV	air saturation value
ATP	adenosine triphosphate
BAF	bioaccumulation factor
BCF	bioconcentration factor
bfa	body fluid assay
BOD	biological oxygen demand

Stand. term / Abbreviation	**Explanation**
bp	boiling point
BPD	Biocidal Products Directive
BSAF	biota-sediment accumulation factor
BSE	bovine spongiform encephalopathy
BSP	bromosulfophthalein
Bt	*Bacillus thuringiensis*
Bti	*Bacillus thuringiensis israelensis*
Btk	*Bacillus thuringiensis kurstaki*
Btt	*Bacillus thuringiensis tenebrionis*
BUN	blood urea nitrogen
bw	body weight
c	centi- (x 10^{-2})
°C	degrees Celsius (centigrade)
CA	controlled atmosphere
CAD	computer aided design
CADDY	computer aided dossier and data supply (an electronic dossier interchange and archiving format)
cd	candela
CDA	controlled drop(let) application
cDNA	complementary DANN
CEC	cation exchange capacity
cf	confer, compare to
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CL	confidence limits
cm	centimetre
CNS	central nervous system
COD	chemical oxygen demand
CPK	creatinine phosphatase
cv	coefficient of variation

Stand. term / Abbreviation	**Explanation**
Cv	ceiling value
d	day(s)
DES	diethylstilboestrol
DIS	draft international standard *(ISO)*
DMSO	dimethylsulfoxide
DNA	deoxyribonucleic acid
dna	designated national authority
DO	dissolved oxygen
DOC	dissolved organic carbon
dpi	days post inoculation
DRP	detailed review paper *(OECD)*
$DT_{50(lab)}$	period required for 50 percent dissipation (under laboratory conditions) (define method of estimation)
$DT_{90(field)}$	period required for 90 percent dissipation (under field conditions) (define method of estimation)
dw	dry weight
DWQG	drinking water quality guidelines
ε	decadic molar extinction coefficient
EC_{50}	median effective concentration
ECD	electron capture detector
ED_{50}	median effective dose
EDI	estimated daily intake
EINECS	European inventory of existing commercial substances
ELINCS	European list of notified chemical substances
ELISA	enzyme linked immunosorbent assay
e-mail	electronic mail
EMDI	estimated maximum daily intake
EN	European norm
EPMA	electron probe micro-analysis
ERL	extraneous residue limit

Stand. term / Abbreviation	**Explanation**
ESPE46/51	evaluation system for pesticides
EUSES	European Union system for the evaluation of substances
F	field
F_0	parental generation
F_1	filial generation, first
F_2	filial generation, second
FBS	full base set
FELS	fish early-life stage
FIA	fluorescence immuno-assay
FID	flame ionisation detector
F_{mol}	fractional equivalent of the metabolite´s molecular weight compared to the active substance
FOB	functional observation battery
f_{oc}	organic carbon factor (compartment dependent)
fp	freezing point
FPD	flame photometric detector
FPLC	fast protein liquid chromatography
g	gram(s)
GAP	good agricultural practice
GC	gas chromatography
GC-EC	gas chromatography with electron capture detector
GC-FID	gas chromatography with flame ionisation detector
GC-MS	gas chromatography-mass spectrometry
GC-MSD	gas chromatography with mass-selective detection
GEP	good experimental practice
GFP	good field practice
GGT	gamma glutamyl transferase
GI	gastro-intestinal
GIT	gastro-intestinal tract
GL	guideline level

Stand. term / Abbreviation	**Explanation**
GLC	gas liquid chromatography
GLP	good laboratory practice
GM	geometric mean
GMO	genetically modified organism
GMM	genetically modified micro-organism
GPC	gel-permeation chromatography
GPS	global positioning system
GSH	glutathione
GV	granulosevirus
h	hour(s)
H	Henry's Law constant (calculated as a unitless value)
ha	hectare(s)
Hb	haemoglobin
HC5	concentration which will be harmless to at least 95 % of the species present with a given level of confidence (usually 95 %)
HCG	human chorionic gonadotropin
Hct	haematocrit
HDT	highest dose tested
hL	hectolitre
HEED	high energy electron diffraction
HID	helium ionisation detector
HPAEC	high performance anion exchange chromatography
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography - mass spectrometry
HPPLC	high pressure planar liquid chromatography
HPTLC	high performance thin layer chromatography
HRGC	high resolution gas chromatography
H_S	Shannon-Weaver index

Stand. term / Abbreviation	**Explanation**
Ht	haematocrit
HUSS	human and use safety standard
I	indoor
I_{50}	inhibitory dose, 50%
IC_{50}	median immobilisation concentration or median inhibitory concentration 1
ICM	integrated crop management
ID	ionisation detector
IEDI	international estimated daily intake
IGR	insect growth regulator
im	intramuscular
IMD	initial measured dose
inh	inhalation
INT	2-p-iodophenyl-3-p-nitrophenyl-5-phenyltetrazoliumchloride testing method
ip	intraperitoneal
IPM	integrated pest management
IR	infrared
ISBN	international standard book number
ISSN	international standard serial number
IUCLID	International Uniform Chemical Information Database
iv	intravenous
IVF	*in vitro* fertilisation
k *(in combination)*	kilo
k	rate constant for biodegradation
K	Kelvin
Ka	acid dissociation constant
Kb	base dissociation constant
K_{ads}	adsorption constant
K_{des}	apparent desorption coefficient
kg	kilogram
K_H	Henry´s Law constant (in atmosphere per cubic metre per

Stand. term / Abbreviation	**Explanation**
	mole)
K_{oc}	organic carbon adsorption coefficient
K_{om}	organic matter adsorption coefficient
K_{ow}	octanol-water partition coefficient
Kp	solid-water partition coefficient
kPa	kilopascal(s)
l, L	litre
LAN	local area network
LASER	light amplification by stimulated emission of radiation
LBC	loosely bound capacity
LC	liquid chromatography
LC-MS	liquid chromatography- mass spectrometry
LC_{50}	lethal concentration, median
LCA	life cycle analysis
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
ln	natural logarithm
LOAEC	lowest observable adverse effect concentration
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOEC	lowest observable effect concentration
LOEL	lowest observable effect level
log	logarithm to the base 10
LOQ	limit of quantification (determination)
LPLC	low pressure liquid chromatography
LSC	liquid scintillation counting or counter
LSD	least squared denominator multiple

Stand. term / Abbreviation	**Explanation**
	range test
LSS	liquid scintillation spectrometry
LT	lethal threshold
m	metre
M	molar
µm	micrometre (micron)
MAC	maximum allowable concentration
MAK	maximum allowable concentration
MC	moisture content
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
MDL	method detection limit
MFO	mixed function oxidase
µg	microgram
mg	milligram
MHC	moisture holding capacity
MIC	minimum inhibitory concentration
min	minute(s)
MKC	minimum killing concentration
mL	millilitre
MLT	median lethal time
MLD	minimum lethal dose
mm	millimetre
MMAD	mass median aerodynamic diameter
mo	month(s)
MOE	margin of exposure
mol	mole(s)
MOS	margin of safety
mp	melting point
MRE	maximum residue expected
MRL	maximum residue level or limit
mRNA	messenger ribonucleic acid
MS	mass spectrometry

Stand. term / Abbreviation	**Explanation**
MSDS	material safety data sheet
MTD	maximum tolerated dose
MT	material test
MW	molecular weight
n.a.	not applicable
n-	normal (defining isomeric configuration)
n	number of observations
NAEL	no adverse effect level
nd	not detected
NEDI	national estimated daily intake
NEL	no effect level
NERL	no effect residue level
ng	nanogram
nm	nanometre
NMR	nuclear magnetic resonance
no, n°	number
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOED	no observed effect dose
NOEL	no observed effect level
NOIS	notice of intent to suspend
NPD	nitrogen-phosphorus detector or detection
NPV	nuclear polyhedrosis virus
NR	not reported
NTE	neurotoxic target esterase
OC	organic carbon content
OCR	optical character recognition
ODP	ozone-depleting potential
ODS	ozone-depleting substances
OEL	occupational exposure limit
OH	hydroxide
OJ	Official Journal

Stand. term / Abbreviation	**Explanation**
OM	organic matter content
Pa	pascal
PAD	pulsed amperometric detection
2-PAM	2-pralidoxime
pc	paper chromatography
PC	personal computer
PCV	haematocrit (packed corpuscular volume)
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
PED	plasma-emissions-detector
pH	pH-value
PHED	pesticide handler’s exposure data
PIC	prior informed consent
pic	phage inhibitory capacity
PIXE	proton induced X-ray emission
pKa	negative logarithm (to the base 10) of the acid dissociation constant
pKb	negative logarithm (to the base 10) of the base dissociation constant
PNEC	predicted no effect concentration (compartment to be added as subscript)
po	by mouth
POP	persistent organic pollutants
ppb	parts per billion (10^{-9})
PPE	personal protective equipment
ppm	parts per million (10^{-6})
PPP	plant protection product
ppq	parts per quadrillion (10^{-24})

Stand. term / Abbreviation	**Explanation**
ppt	parts per trillion (10^{-12})
PSP	phenolsulfophthalein
PrT	prothrombin time
PRL	practical residue limit
PT	product type
PT(CEN)	project team CEN
PTDI	provisional tolerable daily intake
PTT	partial thromboplastin time
QA	quality assurance
QAU	quality assurance unit
(Q)SAR	quantitative structure-activity relationship
r	correlation coefficient
r^2	coefficient of determination
RA	risk assessment
RBC	red blood cell
REI	restricted entry interval
RENI	Registry Nomenclature Information System
Rf	retardation factor
RfD	reference dose
RH	relative humidity
RL_{50}	median residual lifetime
RNA	ribonucleic acid
RP	reversed phase
rpm	revolutions per minute
rRNA	ribosomal ribonucleic acid
RRT	relative retention time
RSD	relative standard deviation
s	second
S	solubility
SAC	strong adsorption capacity
SAP	serum alkaline phosphatase
SAR	structure/activity relationship
SBLC	shallow bed liquid chromatography

Stand. term / Abbreviation	**Explanation**
sc	subcutaneous
sce	sister chromatid exchange
SCAS	semi-continous activated sludge
SCTER	smallest chronic toxicity exposure ratio (TER)
SD	standard deviation
se	standard error
SEM	standard error of the mean
SEP	standard evaluation procedure
SF	safety factor
SFC	supercritical fluid chromatography
SFE	supercritical fluid extraction
SIMS	secondary ion mass spectroscopy
S/L	short term to long term ratio
SMEs	small and medium sized enterprises
SOP	standard operating procedures
sp	species (only after a generic name)
SPE	solid phase extraction
SPF	specific pathogen free
spp	subspecies
SSD	sulphur specific detector
SSMS	spark source mass spectrometry
STEL	short term exposure limit
STER	smallest toxicity exposure ratio (TER)
STMR	supervised trials median residue
STP	sewage treatment plant
t	tonne(s) (metric ton)
$t_{½}$	half-life (define method of estimation)
T_3	tri-iodothyroxine
T_4	thyroxine
T_{25}	tumorigenic dose that causes tumours in 25 % of the test animals
TADI	temporary acceptable daily intake
TBC	tightly bound capacity

Stand. term / Abbreviation	**Explanation**
TCD	thermal conductivity detector
TG	technical guideline, technical group
TGD	Technical guidance document
TID	thermionic detector, alkali flame detector
TDR	time domain reflectrometry
TER	toxicity exposure ratio
TER_I	toxicity exposure ratio for initial exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
tert	tertiary (in a chemical name)
TEP	typical end-use product
TGGE	temperature gradient gel electrophoresis
TIFF	tag image file format
TLC	thin layer chromatography
Tlm	median tolerance limit
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TMRC	theoretical maximum residue contribution
TMRL	temporary maximum residue limit
TNsG	technical notes for guidance
TOC	total organic carbon
Tremcard	transport emergency card
tRNA	transfer ribonucleic acid
TSH	thyroid stimulating hormone (thyrotropin)
TTC	2,3,5-triphenylterazoliumchloride testing method
TWA	time weighted average
UDS	unscheduled DNA synthesis
UF	uncertainty factor (safety factor)
ULV	ultra low volume

Stand. term / Abbreviation	**Explanation**
UR	unit risk
UV	ultraviolet
UVC	unknown or variable composition, complex reaction products
UVCB	undefined or variable composition, complex reaction products in biological material
v/v	volume ratio (volume per volume)
vis	visible
WBC	white blood cell
wk	week
wt	weight
w/v	weight per volume
ww	wet weight
w/w	weight per weight
XRFA	X-ray fluorescence analysis
yr	year
<	less than
≤	less than or equal to
>	greater than
≥	greater than or equal to

Abbreviations of Organisations and Publications

(adapted from: (i) Guidelines and criteria for the preparation of PPP dossiers[1]; (ii) TNsG on Data Requirements[2])

Abbreviation	**Explanation**
ASTM	American Society for Testing and Materials
BA	Biological Abstracts (Philadelphia)
BART	Beneficial Arthropod Registration Testing Group
BBA	German Federal Agency of Agriculture and Forestry
CA(S)	Chemical Abstracts (System)
CAB	Centre for Agriculture and Biosciences International
CAC	Codex Alimentarius Commission
CAS	Chemical Abstracts Service
CCFAC	Codex Committee on Food Additives and Contaminants
CCGP	Codex Committee on General Principles
CCPR	Codex Committee on Pesticide Residues
CCRVDF	Codex Committee on Residues of Veterinary Drugs in Food
CE	Council of Europe
CEC	Commission of the European Communities
CEFIC	European Chemical Industry Council
CEN	European Committee for Normalisation
CEPE	European Committee for Paints and Inks
CIPAC	Collaborative International Pesticides Analytical Council Ltd
CMA	Chemicals Manufacturers Association
COREPER	Comite des Representants Permanents
COST	European Co-operation in the field

Abbreviation	**Explanation**
	of Scientific and Technical Research
DG	Directorate General
DIN	German Institute for Standardisation
EC	European Commission
ECB	European Chemicals Bureau
ECCO	European Commission Co-ordination
ECDIN	Environmental Chemicals Data and Information Network of the European Communities
ECDIS	European Environmental Chemicals Data and Information System
ECE	Economic Commission for Europe
ECETOC	European Chemical Industry Ecology and Toxicology Centre
EDEXIM	European Database on Export and Import of Dangerous Chemicals
EEC	European Economic Community
EHC	Environmental Health Criteria
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMIC	Environmental Mutagens Information Centre
EPA	Environmental Protection Agency
EPAS	European Producers of Antimicrobial Substances
EPFP	European Producers of Formulated Preservatives
EPO	European Patent Office
EPPO	European and Mediterranean Plant Protection Organization
ESCORT	European Standard Characteristics

Abbreviation	**Explanation**
	of Beneficials Regulatory Testing
EU	European Union
EUPHIDS	European Pesticide Hazard Information and Decision Support System
EUROPOEM	European Predictive Operator Exposure Model
EWMP	European Wood Preservation Manufacturers
FAO	Food and Agriculture Organization of the UN
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
FRAC	Fungicide Resistance Action Committee
GATT	General Agreement on Tariffs and Trade
GAW	Global Atmosphere Watch
GIFAP	Groupement International des Associations Nationales de Fabricants de Produits Agrochimiques (now known as GCPF)
GCOS	Global Climate Observing System
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GEDD	Global Environmental Data Directory
GEMS	Global Environmental Monitoring System
GRIN	Germplasm Resources Information Network
IARC	International Agency for Research on Cancer
IATS	International Academy of Toxicological Science
ICBP	International Council for Bird Preservation
ICCA	International Council of Chemical Associations
ICES	International Council for the Exploration of the Seas
ILO	International Labour Organization

Abbreviation	**Explanation**
IMO	International Maritime Organisation
IOBC	International Organization for Biological Control of Noxious Animals and Plants
IPCS	International Programme on Chemical Safety
IRAC	Insecticide Resistance Action Committee
ISCO	International Soil Conservation Organization
ISO	International Organization for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JECFA FAO/WHO	Joint Expert Committee on Food Additives
JFCMP	Joint FAO/WHO Food and Animal Feed Contamination Monitoring Programme
JMP	Joint Meeting on Pesticides (WHO/FAO)
JMPR	Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
MITI	Ministry of International Trade and Industry, Japan
NATO	North Atlantic Treaty Organization
NAFTA	North American Free Trade Agreement
NCI	National Cancer Institute (USA)
NCTR	National Center for Toxicological Research (USA)
NGO	non-governmental organisation
NTP	National Toxicology Program (USA)
OECD	Organization for Economic Co-operation and Development
OLIS	On-line Information Service of OECD
OPPTS	Office of Prevention, Pesticides and

Abbreviation	**Explanation**
	Toxic Substances (US EPA)
OSPAR	Oslo Paris Convention (Convention for the Protection of the Marine Environment of the North-East Atlantic)
PAN	Pesticide Action Network
RIVM	Netherlands National Institute of Public Health and Environmental Protection
RNN	Re-registration Notification Network
RTECS	Registry of Toxic Effects of Chemical Substances (USA)
SETAC	Society of Environmental Toxicology and Chemistry
SI	Système International d'Unitès

Abbreviation	**Explanation**
SITC	Standard International Trade Classification
TOXLINE	Toxicology Information On-line
UBA	German Environmental Protection Agency
UN	United Nations
UNEP	United Nations Environment Programme
WFP	World Food Programme
WHO	World Health Organization
WPRS	West Palearctic Regional Section
WTO	World Trade Organization
WWF	World Wildlife Fund

[1] EU (1998a): European Commission: Guidelines and criteria for the preparation of complete dossiers and of summary dossiers for the inclusion of active substances in Annex I of Directive 91/414/EC (Article 5.3 and 8,2). Document 1663/VI/94 Rev 8, 22 April 1998

[1] European Chemicals Bureau, ECB (1996) Technical Guidance Documents in support of the Commission Directive 93/67/EEC on risk assessment for new notified substances and the Commission Regulation (EC) 1488/94 for existing substances

[1] EU (1998a): European Commission: Guidelines and criteria for the preparation of complete dossiers and of summary dossiers for the inclusion of active substances in Annex I of Directive 91/414/EC (Article 5.3 and 8,2). Document 1663/VI/94 Rev 8, 22 April 1998

[2] European Chemicals Bureau, ECB (1996) Technical Guidance Documents in support of the Commission Directive 93/67/EEC on risk assessment for new notified substances and the Commission Regulation (EC) 1488/94 for existing substances