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

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

Assessment Report

METOFLUTHRIN

Product-type 18
(Insecticides, acaricides and products to control other arthropods)

Annex I

METOFLUTHRIN (PT 18)

Assessment Report

Finalised in the Standing Committee on Biocidal Products at its meeting in May 2010 in view of its inclusion in Annex I to Directive 98/8/EC

CONTENTS

1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Procedure followed

This assessment report has been established as a result of the evaluation of Metofluthrin as product-type 18 (Insecticides, acaricides and products to control other arthropods), carried out in the context of the evaluation of new active substances provided for in Article 8(2) of Directive 98/8/EC concerning the placing of biocidal products on the market[1], with a view to the possible inclusion of this substance into Annex I to the Directive.

Metofluthrin (CAS no. 240494-70-6) was notified as a new active substance, by Sumitomo Chemical (UK) Plc, hereafter referred to as the applicant, in product-type 18. The United Kingdom was chosen as Rapporteur Member State to carry out the assessment on the basis of the dossier submitted by the applicant.

On 23rd December 2005 the UK competent authority received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 2nd May 2006.

On 19th June 2008 the Rapporteur Member State submitted to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report. The Commission made the report available to all Member States by electronic means on 1st July 2008. The competent authority report included a recommendation for the inclusion of Metofluthrin in Annex I to the Directive for PT 18.

In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the Commission. Revisions agreed upon were presented at the TMIII09 Technical Meeting held in October 2009 and the competent authority report was amended accordingly.

The present assessment report contains the conclusions of the Standing Committee on Biocidal Products, as discussed during its meeting held on 27th May 2010.

1.2. Purpose of the assessment report

This assessment report has been developed and finalised in support of the decision to include Metofluthrin in Annex I to Directive 98/8/EC for product-type 18. The aim of the assessment report is to facilitate the authorisation in Member States of individual biocidal products in product-type 18 that contain Metofluthrin. In their evaluation, Member States shall apply the provisions of Directive 98/8/EC, in particular the provisions of Article 5 as well as the common principles laid down in Annex VI.

[1] Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing biocidal products on the market. OJ L 123, 24.4.98, p.1

For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report, which is available at the Commission website[2], shall be taken into account.

However, where conclusions of this assessment report are based on data protected under the provisions of Directive 98/8/EC, such conclusions may not be used to the benefit of another applicant, unless access to these data has been granted.

1.3. Overall conclusion in the context of Directive 98/8/EC

The overall conclusion from the evaluation is that it may be expected that there are products containing Metofluthrin for the product-type 18 which will fulfil the requirements laid down in Article 10(1) and (2) of Directive 98/8/EC. This conclusion is however subject to:

i. compliance with the particular requirements set out in this assessment report,

ii. the implementation of the provisions of Article 5(1) of Directive 98/8/EC, and

iii. the common principles laid down in Annex VI to Directive 98/8/EC.

Furthermore, these conclusions were reached within the framework of the uses that were proposed and supported by the applicant (see Appendix II). Extension of the use pattern beyond those described will require an evaluation at product authorisation level in order to establish whether the proposed extensions of use will satisfy the requirements of Article 5(1) and of the common principles laid down in Annex VI to Directive 98/8/EC.

[2] http://ec.europa.eu/comm/environment/biocides/index.htm

2. OVERALL SUMMARY AND CONCLUSIONS

2.1. Presentation of the Active Substance

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

The common name (ISO) metofluthrin refers to an unspecified mixture of all 8 possible isomers of the substance, 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl(EZ)-(1RS,3RS;1SR,3SR)-2,2-dimethyl-3-prop-1-enylcyclopropanecarboxylate, CAS no: 240494-70-6. However, metofluthrin is marketed (currently outside the EU) with a specific isomer profile; the major isomer, 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl-(1R,3R)-2,2-dimethyl-3-[(Z)-prop-1-enyl]cyclopropanecarboxylate (CAS no: 240494-71-7) is present at >80%. Strictly speaking this ISO name should not be used for this substance as not all isomers are present in equal amounts, however as metofluthrin is already marketed and the substance used in the EU would be identical, it has been agreed that the name metofluthrin can be used.

As the major isomer is present at >80% the substance has been identified, as has been agreed at the biocides CA meeting (i.e. according to the REACH guidance), as a mono-constituent substance rather than a mixture of all the isomers. This is indicated in Doc IIA (Section 1.1) & Doc IIIA (Section A2). Wherever the name metofluthrin is mentioned this relates to the purity profile as given in the confidential annex with the major component as identified. Unless otherwise stated any purities given relate to metofluthrin (i.e. the sum of all the isomers) and not just the major isomer.

The main identification characteristics and the physico-chemical properties of metofluthrin are given in Appendix I to this document. The active substance must be technically equivalent to the specification given.

The methods of analysis for the active substance as manufactured and for the determination of impurities have been validated. The methods of analysis in environmental matrices, as appropriate for the areas of use assessed, have been validated and shown to be sufficiently sensitive with respect to the levels of concern.

2.1.2. Intended Uses and Efficacy

The assessment of the biocidal activity of the active substance demonstrates that it has a sufficient level of efficacy against the target organism(s) and the evaluation of the summary data provided in support of the efficacy of the accompanying product, establishes that the product may be expected to be efficacious.

In addition, 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 intended uses of the substance, as identified during the evaluation process, are listed in Appendix II.

2.1.3. Classification and Labelling

Active Substance (Metofluthrin)

Current Classification

As metofluthrin is a new active substance to the EU, there is no current classification assigned according to Annex I of Council Directive 67/548/EEC.

Proposed Classification

On the basis of a review of the data submitted, the UK CA proposes the classification, given in Table 1.1. For information a classification proposal according to the CLP Regulation 1272/2008/EC is also provided in Table 1.1a. These classification & labelling proposals are not supported by the Applicant (specifically, T with the associated risk phrase R25) and they will be discussed further at the European Chemical Agency (ECHA) Risk Assessment Committee (RAC); therefore there is no guarantee that they will remain unchanged.

Table 1.1 Proposed classification for metofluthrin

Classification	Proposed classification for metofluthrin following evaluation
Class of danger	T: Toxic Xn: Harmful N: Dangerous for the environment.
R-phrases	R25: Toxic if swallowed[3]. R20: Harmful by inhalation. R48/20: Harmful: Danger of serious damage to health by prolonged exposure if inhaled. R50/53: Very toxic to aquatic organisms. May cause long-term adverse effects in the aquatic environment.

Table 1.1a Proposed CLP classification for metofluthrin

Classification	Proposed Classification for Metofluthrin according to the CLP criteria
Signal Word	Danger Warning
Hazard Statement (H-Phrase)	Acute Tox 3 - H301 - Toxic if Swallowed[3] Acute tox 4 - H332 - Harmful if Inhaled STOT - RE2 - H373 STOT RE2 - H373 (inhalation) Causes Damage to Organs Through Prolonged or Repeated Exposure Aquatic Acute 1 - H400 - Very Toxic to Aquatic Life Aquatic Chronic 1 - H410 -Very Toxic to Aquatic Life with Long Lasting Effects

[3] The Applicant does not agree with the proposal to classify metofluthrin with T; R25/Acute Tox 3 – H301. A justification for their position is provided at Annex I of Document IIA

Biocidal Product (SumiOne® Liquid Vapouriser)

Current Classification

As metofluthrin is a new active substance to the EU, there is no current classification assigned according to Annex I of Council Directive 67/548/EEC.

Proposed Classification

Based on the proposed classification for metofluthrin, and information available on the co-formulants, the classification of the representative solvent-based product (SumiOne® Liquid Vapouriser) can be determined. The proposed classification for the product, given in Table 1.2 and 1.2a, will also be subject to the decision reached at the ECHA RAC, regarding metofluthrin; therefore there is no guarantee that they will remain unchanged.

Table 1.2 Proposed classification for representative solvent-based product (SumiOne® Liquid Vapouriser)

Classification	Proposed classification for SumiOne® Liquid Vapouriser following evaluation
Class of danger	Xn: Harmful N: Dangerous for the environment.
R-phrases	R65: Harmful: may cause lung damage if swallowed R52/53: Toxic to aquatic organisms. May cause long-term adverse effects in the aquatic environment.

Table 1.2a Proposed CLP classification for representative solvent-based product (SumiOne® Liquid Vapouriser)

Classification	Proposed Classification for SumiOne® Liquid Vapouriser according to the CLP criteria
Signal Word	Danger
Hazard Statement (H-Phrase)	Asp Tox 1 - H304 - May be Fatal if Swallowed and Enters Airways Aquatic Chronic 3 - H412 - Harmful to Aquatic Life with Long Lasting Effects

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1 Hazard identification

2.2.1.1.1 Toxicology Hazard Summary

The toxicology studies, with the exception of those investigating toxicokinetics, were performed on metofluthrin containing a minimum 80.2 % of the RTZ isomer (see Document IIA Section 3 and Document IIIA2 – Confidential for more details).

For the oral toxicokinetic studies, the RTZ and RTE isomers of metofluthrin have been purified and investigated separately; while in the *in vivo* dermal study a mixture of the purified RTZ and RTE isomers (ratio RTZ:RTE of 84:11) was used (see Document IIA Section 3 and Document IIIA2 – Confidential for more details).

The potential of metofluthrin and the representative product SumiOne® Liquid Vapouriser (S-1264 Liquid) to cause adverse health effects has been investigated in animal studies. For repeated oral and dermal toxicity, genotoxicity, carcinogenicity and reproductive toxicity, information on metofluthrin and the co-formulant has been used to predict the likely human health hazards of S-1264 Liquid.

RTZ and RTE isomers of metofluthrin are well absorbed (100 %) following oral and inhalation exposure, with a conservative estimate of 53 % becoming systemically available following dermal exposure. RTZ and RTE isomers of metofluthrin are extensively metabolised following oral dosing with evidence that first pass metabolism is occurring. A wide range of Phase I reactions were identified, including C-oxidation, epoxidation and ester hydrolysis. The principal Phase II reactions are epoxide ring opening, glutathione conjugation and glucuronidation. Subsequent distribution of the metabolites of RTZ and RTE isomers of metofluthrin is widespread. Elimination was rapid via both the urine and faeces. There were no marked gender-related differences in absorption, distribution, metabolism or excretion.

Following oral administration of neat metofluthrin to rats, in a standard study, only a single mortality was observed at 2000 mg/kg, the highest dose tested. In contrast, when metofluthrin is administered in a corn oil vehicle, mortality was reported in 7/20 rats at the highest dose of 100 mg/kg (though no deaths were reported in 5 animals/sex at this dose level in a sighting study) and in 2/10 mice at the highest dose of 60 mg/kg. The UK CA considers that the studies using corn oil are relevant for hazard identification and for classification purposes. The use of corn oil as a vehicle to facilitate testing is a standard approach. Given that corn oil is inert (i.e. non-toxic) the observed toxicity must be due to metofluthrin, providing unequivocal evidence of some inherent toxicity. The specific reason why metofluthrin is more toxic in corn oil than when it is used neat is not clear. Therefore the UK CA considers the more conservative studies in rats and mice the most appropriate on which to base classification. Consequently, T; R25 is

proposed[4]. Following inhalation exposure of rats to an aerosol of metofluthrin, an LC_{50} value of between 1 – 2 mg/l is reported, indicating classification with Xn; R20 is appropriate. It is noted that signs of neurotoxicity were noted in all animals exposed to 0.5 mg/l and above. Metofluthrin was found to be of low toxicity to rats in single dermal exposure studies, with no classification considered appropriate. S-1264 Liquid was of low toxicity in rats following single oral, dermal and inhalation exposures and no classification for acute toxicity is proposed. Therefore, this endpoint will not be considered further in the risk characterisation.

Data from standard studies show that metofluthrin and S-1264 Liquid do not meet the EU criteria for classification as a skin or eye irritant. Also data from single and repeated dose inhalation studies show that metofluthrin and S-1264 Liquid are not respiratory tract irritants. The end points will not be taken forward for risk characterisation.

Neither metofluthrin nor S-1264 Liquid showed skin sensitisation potential in guinea pig maximisation tests and so, no classification is proposed. Therefore, this end point will not be taken forward for risk characterisation.

There is insufficient information to determine whether or not metofluthrin can cause occupational asthma. However, in the absence of structural alerts for metofluthrin for this endpoint, the UK CA concludes that metofluthrin is unlikely to have the potential to cause occupational asthma. There is no information on the potential of S-1264 Liquid to induce respiratory sensitisation/occupational asthma. However, the co-formulant of metofluthrin in S-1264 Liquid, is not classified as a respiratory sensitiser. Therefore, it is concluded that S-1264 Liquid has low potential to cause respiratory sensitisation/ occupational asthma. Consequently, it does not meet the EU criteria for classification.

The repeated dose toxicity of metofluthrin has been investigated by the oral route in rats (dietary studies of between 28 days to 2 years duration), mice (dietary studies of 13 weeks and 2 years duration) and dogs (capsule dosing studies of 13 weeks and 1 year duration); in addition, a specific 90 day dietary study in rats has been conducted to investigate its neurotoxic potential. The repeated dermal toxicity of metofluthrin has been investigated in a 13-week study in rats and the repeated inhalation toxicity of metofluthrin has been investigated in a 28-day study in rats.

The most prominent findings, from the oral repeated dose studies were neurotoxicity in rats and dogs, hepatotoxicity in rats and mice and indications of nephrotoxicity in rats (high dose level only in a lifetime study).

Metofluthrin has neurotoxic potential, causing tremors in both rats and dogs but not in mice or rabbits. The dog is identified as the more sensitive species with regard to metofluthrin-induced neurotoxicity with tremors usually occurring 2 – 6 h post-administration of the dose via capsule (indicating this is an acute effect); NOAEL values of 10 mg/kg/d being established following exposure for 90 days and 1 year. In a rat study specifically designed to investigate neurotoxic

[4] The Applicant does not agree with the proposal to classify metofluthrin with T; R25. A justification for their position is provided at Annex I of Document IIA.

potential, an increased incidence of tremor and a single treatment-related mortality (female) was reported at the top dose (60 mg/kg/d). No supporting neurotoxicological histopathological changes were observed in this study. There is no clear explanation as to why rabbits and mice appear to be less sensitive to the neurotoxic potential of metofluthrin. Overall, neurotoxicity is considered to be relevant for human health.

With regard to hepatotoxicity, increased liver weight, increased levels of plasma cholesterol and phospholipids, and histopathological changes such as hepatocellular hypertrophy, have been observed in dietary studies in rats and mice, but not in capsule studies in the dog. In the rat and mice studies, the most sensitive marker of hepatotoxicity is considered to be increased incidences of hepatocellular hypertrophy; the rat being the more sensitive to metofluthrin-induced hepatotoxicity. The NOAEL values in the rat studies were 29, 6.9, 26 and 8 mg/kg/d following exposure for 28 days, 90 days, 26 weeks and 2 years, respectively. Mechanistic investigations in rats show that dietary administration of metofluthrin can induce hepatic xenobiotic metabolising enzymes, which is a well-established cause of hepatocyte hypertrophy. The profile of enzyme induction following metofluthrin exposure (in particular CYP 2B1/2) is similar to that produced by phenobarbitone. Although, hepatocyte hypertrophy secondary to phenobarbitone-type enzyme induction can be regarded as an adaptive response, for metofluthrin, this is also associated with statistically significant increases in plasma levels of cholesterol and phospholipids, which are likely to be an expression of liver toxicity. Therefore, for the purposes of the risk characterisation, the hepatotoxicity observed in these studies will be considered to be of relevance to human health, and hepatocyte hypertrophy will be considered to be the most sensitive marker of hepatotoxicity.

Indications of nephrotoxicity were noted in animals in the top dose group only (78 mg/kg/d males, 96 mg/kg/d females) in the lifetime study in rats, however, it should be noted that in general the findings showed only weak dose-response relationships. The nephrotoxicity was characterised by statistically significant increases in the incidence of lipofuscin deposition in males and females; statistically significant increases in the incidence of tubular casts and interstitial fibrosis in top dose females; and statistically significant increases in the incidence of tubular vacuolation in males. These changes did not lead to any physiological disturbance or progression to tumours in these animals. A NOAEL for nephrotoxicity of 38 mg/kg/d can be derived. Despite similar changes not being observed in studies in either mice or dogs, these kidney changes in rats are considered to be relevant for human health, but only for long-term exposures, as they occurred only in a lifetime exposure study.

Following oral exposure, the appearance of hepatocyte hypertrophy occurs at dose levels at which classification with Xn; R48/22 could be considered appropriate. The appearance of hepatocyte hypertrophy is not in itself considered as serious damage to health. Therefore, no classification for repeat dose toxicity following oral exposure is considered appropriate. No classification for repeat dose toxicity following oral exposure is proposed for S-1264 Liquid, given that the co-formulant is also not classified for repeat dose toxicity.

Following repeated inhalation exposure of rats for 28 days to an aerosol of metofluthrin, mortality and tremors (suggestive of neurotoxicity) were observed at 0.2 mg/l, the highest concentration tested (it is noted that this is equivalent to a systemic dose of around 32

mg/kg/d). There were no histopathological changes observed either at the site of contact or to other organs and tissues. It is possible to identify a rat NOAEC of 0.1 mg/l from this study for systemic toxicity (equivalent to a NOAEL of 15 mg/kg/bw/d for systemic exposure) Classification with Xn; R48/20 is considered appropriate as mortalities occurred throughout this study and are therefore not considered to be a manifestation of the acute inhalation toxicity of metofluthrin. A 28 day repeat inhalation study is also available in rats exposed to S-1264 Liquid. In this study, no mortalities, clinical signs of toxicity or histopathological changes were observed at vapour concentrations of up to 0.022 mg/l, the highest concentration tested. Given that no toxicity was reported at this concentration of S-1264 Liquid, there is some uncertainty regarding the appropriate classification for S-1264 Liquid, as metofluthrin meets the EU criteria for classification with Xn; R48/20. However, S-1264 Liquid contains metofluthrin at a concentration of 0.5 %, and the other constituent is not classified as being harmful following repeated inhalation exposure. Therefore, according to the Dangerous Preparations Directive, no classification for toxicity following repeated inhalation exposure is appropriate for S-1264 Liquid.

Following repeated dermal application of up to 1000 mg/kg/d metofluthrin to rats for 13 weeks, no toxicologically significant, treatment-related changes were observed at doses of up to 300 mg/kg/d. At the highest dose of 1000 mg/kg/d, 2/12 female animals died within 3 days of the start of the study; tremor was noted in one of these females prior to death. The only histopathological changes observed occurred locally and comprised an increased incidence of slight squamous cell hyperplasia in top dose females. Based on the mortality, single incidence of tremor and local histopathological changes reported in top dose females, it is possible to identify a NOAEL of 300 mg/kg/d from this study for both local and systemic effects. These data on repeated dermal exposure do not support classification of metofluthrin for repeated dose toxicity. No classification for repeat dose toxicity following dermal exposure is proposed for S-1264 Liquid, given that the co-formulant is also not classified for repeat dose toxicity.

Metofluthrin gave negative results *in vitro* (Ames chromosomal aberration and MCGM) and *in vivo* (mouse micronucleus) genotoxicity studies. Overall, it can be concluded that metofluthrin does not have genotoxic potential, and no classification is proposed. The co-formulant is also not classified for mutagenicity, therefore, no mutagenicity classification is proposed for S-1264 Liquid.

The carcinogenic potential of metofluthrin has been investigated in standard dietary lifetime studies in rats and mice. Metofluthrin induced clear increases in the incidence of liver carcinomas in male and female rats, and liver adenomas in male rats. However, no changes in tumour incidence were observed in mice at doses of up to 277 mg/kg/day, the highest dose tested. The liver tumours in rats occurred against a background of hepatic enzyme induction and hepatocyte proliferation. There is no evidence of genotoxicity from well-conducted studies. The Applicant has proposed a mode of action for the onset of liver tumours observed in the rat to justify the non-classification of metofluthrin for carcinogenicity. The UK CA has accepted this argument. The detailed proposal (Unpublished, Yamada 2008) can be found at Annex II to Document IIA. In brief, metofluthrin is a constitutive androstane receptor (CAR) agonist. Activation of this receptor leads to enzyme induction, hepatocyte proliferation and the generation of altered hepatic foci (preneoplastic foci) which can progress to adenomas and

carcinomas in rats and mice. All of these stages leading to tumour induction have been identified in rats dosed with metofluthrin. This is identical to the mode of action for the induction of liver tumours in rats by phenobarbitone. The mode of action document also indicates that mice are much less sensitive to metofluthrin-induced preneoplastic changes, providing a mechanistic basis for the observed difference in tumour profile between rats and mice dosed with metofluthrin. There is no clear evidence for tumour induction in humans administered therapeutic levels of phenobarbitone for very long periods, at dose levels that would induce liver tumours in rats. This supports the view that humans are much less sensitive to liver tumour induction than rats. However, phenobarbitone can induce hepatic enzymes and cause some liver cell hypertrophy in humans, although it is uncertain whether this occurs via the CAR or another receptor.
Overall, metofluthrin induced liver tumours in rats via a phenobarbitone-like mode of action. Humans are much less sensitive than rats to liver tumour induction by this mode of action; therefore, classification for carcinogenicity is not considered to be appropriate.

The co-formulant in S-1264 Liquid is also not classified for carcinogenicity, therefore, no carcinogenicity classification for S-1264 Liquid is proposed.

The potential for metofluthrin to cause developmental toxicity has been investigated in standard studies in rats and rabbits. No evidence of developmental toxicity was observed in rats, at doses of up to 30 mg/kg/day, and in rabbits at doses of up to 250 mg/kg/day, and so no classification for developmental toxicity is considered appropriate. Similarly, no classification for S-1264 Liquid is appropriate given that the co-formulant is also not classified as a developmental toxicant.

The potential for metofluthrin to cause adverse effects on fertility has been investigated in a standard 2-generation study in rats. No treatment-related adverse effects on fertility were observed at doses of up to 176 mg/kg/day, the highest dose tested. Therefore, no classification for fertility is considered appropriate. Similarly, no classification for S-1264 Liquid is appropriate given that the co-formulant is also not classified as having an adverse effect on fertility.

2.2.1.1.2 Critical Endpoints

The key health effects to consider for primary exposure scenarios are those arising from acute dermal exposure. The key health effects to consider for secondary exposure scenarios are those arising from acute and medium-term oral, acute and medium-dermal and medium-term inhalation exposure.

Oral
Neurotoxicity is considered to be the key health effect following acute and medium-term oral exposures. Neurotoxicity is observed in both rats and dogs with the dog being the more sensitive species. However, there is no information with regards to human exposure and the susceptibility or otherwise to metofluthrin-induced neurotoxicity. Therefore, neurotoxicity observed in rats and dogs repeatedly exposed to metofluthrin orally are considered to be potentially relevant to human health. A NOAEL of 10 mg/kg/d is identified from a 1 year study

in dogs, based on an increased incidence of tremors, and is proposed for use in the risk characterisation of acute and medium-term oral exposures.

Dermal
In a 90 day rat dermal study, mortality, signs of neurotoxicity and local irritation were observed at the top dose only (1000 mg/kg/d); a NOAEL of 300 mg/kg/d (equivalent to a systemic dose of 159 mg/kg/d) being identified. There are no data available on species differences in susceptibility to these effects or whether or not humans will be more susceptible. Therefore, these effects following dermal exposure are considered relevant to human health. The NOAEL will be used in the risk characterisation of acute and medium-term dermal scenarios.

Inhalation
In a 28-day repeat dose inhalation study in rats, the key health effects noted were mortality and tremor at the highest exposure concentration of 0.2 mg/l; a NOAEL of 0.1 mg/l being identified. There are no data available on species differences in susceptibility to these effects or whether or not humans will be more susceptible. Therefore, these effects following inhalation exposure are considered relevant to human health. Consequently, the NOAEL of 0.1 mg/l (equivalent to a systemic dose of 15 mg/kg/d) will be used as the basis for the risk characterisation of medium-term inhalation exposure scenarios.

2.2.1.1.3 Uncertainties

Dermal Absorption Values Used in the Risk Assessment

No dermal penetration studies have been conducted with the product S-1264 Liquid, however data are available on metofluthrin. In an *in vivo* dermal penetration study, 0.002 mg/cm^2 radiolabelled metofluthrin a 10% aqueous tween 80 vehicle was applied to the shorn skin of rats under a non-occlusive dressing for 6 or 24 hours. The UK CA considers the dermal absorption value obtained following the 24-hour time period to be the most appropriate for risk characterisation. Consequently, a worst-case dermal absorption value of 53 % is considered appropriate for metofluthrin.

The applicant has submitted a waiver for not conducting this test on S-1264 Liquid. The waiver is based on the marked vapour pressure differences between the co-formulant and the active substance. The active substance, metofluthrin, and the co-solvent have very different vapour pressures, 1.87 x 10^{-3} Pa, at 25°C and < 66.64 Pa, at 38˚C, respectively; the co-solvent being the more volatile. Thus, during vaporisation, the co-solvent and active substance will evaporate at different rates, and any material deposited on skin (or other surfaces) after evaporation will no longer be representative of the proportions in the product. Any co-solvent that is deposited on the skin is also likely to re-evaporate at body temperature. Therefore any residues on the skin may be anticipated to have a higher proportion of metofluthrin than is present in the formulation. Consequently, the UK CA considers that dermal exposure will be primarily to the metofluthrin and the waiver is acceptable. Therefore, the dermal penetration value of 53 % is also appropriate following exposure to metofluthrin from S-1264 Liquid.

Inter- and Intra-species Variability

Oral

Following oral exposure to metofluthrin, neurotoxicity is observed in rats and dogs, hepatotoxicity is observed in rats and mice and indications of nephrotoxicity are observed in rats. With regard to neurotoxicity and the indications of nephrotoxicity, there is no definitive information available to identify the relative sensitivities of humans compared to experimental animals in relation to the ability of metofluthrin to cause these effects. Similarly, there are no data to reliably inform on the potential for inter-individual variability in susceptibility to these effects. Given these uncertainties, standard default assessment factors of 10 to account for potential inter-species (human compared to rats) and of 10 to account for intra-species (human to human) variability will be included in the risk characterisation for these effects, giving an overall assessment factor of 100.

With regard to the hepatotoxicity observed, this is considered to be a result of enzyme induction through a mechanism similar to that of phenobarbitol. It is unlikely that humans are more sensitive than rats to these effects. Therefore, it could be argued that the interspecies factor of 10 could be lowered where hepatotoxicity is the key health effect driving the risk characterisation. However, in this risk assessment the UK CA will adopt a conservative approach and use standard default assessment factors of 10 to account for potential inter-species and of 10 to account for intra-species variability.

Inhalation

Following inhalation exposure, mortality and signs of neurotoxicity are observed in rats. There is no definitive information available to identify the relative sensitivities of humans compared to experimental animals in relation to the ability of metofluthrin to cause these effects. Similarly, there are no data to reliably inform on the potential for inter-individual variability in susceptibility to these effects. Given these uncertainties, for short-term exposures standard default factors of 10 to account for potential inter-species (human compared to rats) and of 10 to account for intra-species (human to human) variability will be included in the risk characterisation. No long-term inhalation exposure scenarios are considered in the risk characterisation.

Dermal

Following dermal exposure, mortality, indications of neurotoxicity and local irritation were observed in rats. There is no definitive information available to identify the relative sensitivities of humans compared to experimental animals in relation to the ability of metofluthrin to cause these effects. Similarly, there are no data to reliably inform on the potential for inter-individual variability in susceptibility to these effects. Given these uncertainties, standard default factors of 10 to account for potential inter-species (human compared to rats) and of 10 to account for intra-species (human to human) variability will be included in the risk characterisation, giving an overall assessment factor of 100.

Route to Route Extrapolation

Given that extensive first pass metabolism occurs following oral exposure, extrapolation from oral to dermal and inhalation exposure scenarios for systemic effects is not considered to be valid. However, there are repeated exposure studies available for both the dermal (rat, 13 week) and inhalation (rat, 28 day) routes. From both these studies the external dose will be transformed, using an appropriate absorption value, to establish route-specific systemic NOAELs. These values will then form the basis of route-specific AELs that will be used as appropriate in the risk characterisation.

Dose-response/severity of key health effect

There are 4 key studies that can be used for risk characterisation. A 1-year dog study for acute and medium -term oral exposure scenarios, a 2-year rat study for long-term oral exposure scenarios, a 28-day rat inhalation study for inhalation exposure scenarios and a 13-week rat dermal study for dermal exposure scenarios. It is noted that no long-term exposure scenarios are predicted to occur by any exposure route. The dose-response characteristics of each study are briefly described below.

In the 1-year dog capsule study, the NOAEL of 10 mg/kg/d is based on an increased incidence of tremor in 5 animals at 30 mg/kg/d (4/4 males, 1/4 females). At 100 mg/kg/d, the top dose level, tremor was observed in 7 animals (4/4 males, 3/4 females). The tremors occurred 2 – 6 h post-administration. Based on these data, no additional assessment factors are considered appropriate for acute and medium term oral exposure scenarios. Thus, an overall assessment factor of 100 is proposed, equivalent to an Acceptable Exposure Level (AEL) value of 0.1 mg/kg/d.

In the 2-year rat dietary study, increased incidences of non-neoplastic hepatotoxicity and indications of nephrotoxicity are identified as the key health effects. An overall NOAEL of 8 mg/kg/d is identified from this study. This is based on hepatotoxicity, manifested as increased incidences of hepatocellular hypertrophy (12/50 females) and increased plasma concentrations of cholesterol, triglycerides and phospholipids in males (24 %, 62 % and 26 %, respectively, compared with control levels) at the next dose level (38 mg/kg/d males, 47 mg/kg/d females).. At the top dose level (78 mg/kg/d males, 96 mg/kg/d females), hepatotoxicity, manifested as increased incidences of hepatocellular hypertrophy and eosinophilic foci in males (13/50 and 10/50, respectively) and clear cell foci and mixed cell foci in females (32/50 and 12/50, respectively), and increased plasma concentrations of cholesterol, triglycerides and phospholipids in males (37 %, 49 % and 41 %, respectively, compared with control levels) was observed; and indications of nephrotoxicity, manifested as an increased incidence of lipofuscin deposition in males (12/50 compared to 3/50 in controls) and females (40/50 compared to 21/50 in controls), tubular casts (48/50 compared to 40/50 in controls) and interstitial fibrosis (10/50 compared to 3/50 in controls) in females, tubular vacuolation (8/50 compared to 0/50 in controls) was also observed. Based on these data, no additional assessment factor is considered appropriate for long term oral exposure scenarios. Thus, an overall assessment factor of 100 is proposed, equivalent to an AEL value of 0.08 mg/kg/d.

In the 28-day inhalation study in rats exposed to an aerosol of metofluthrin, the NOAEL of 0.1 mg/l (equivalent to a systemic dose of 15 mg/kg/d) is based on mortalities (7/10 males; 3/10 females) and tremor (5/10 males; 5/10 females), at the highest exposure concentration of 0.2 mg/l. Based on these data no additional assessment factor is considered appropriate for acute inhalation exposure scenarios. Thus, an overall assessment factor of 100 is proposed. An absorption value of 100 % is predicted following inhalation exposure of rats, therefore the external NOAEL from this study is equivalent to a systemic NOAEL of 15 mg/kg/d. This is equivalent to an inhalation systemic AEL_{acute} value of 0.15 mg/kg/d. For medium and long term inhalation exposure scenarios additional assessment factors of 3 and 6, respectively, are considered appropriate (to account for extrapolation from a subacute study to subchronic and chronic studies, respectively; as described in the TGD on risk characterisation and the biocides specific TNsG on Risk Characterisation of Systemic Effects[5]). Thus, for medium term inhalation exposure scenarios, an overall assessment factor of 300 is proposed, equivalent to an inhalation systemic $AEL_{medium\text{-}term}$ value of 0.05 mg/kg/d; while for long term inhalation exposure scenarios, an overall assessment factor of 600 is proposed, equivalent to an inhalation systemic $AEL_{long\text{-}term}$ value of 0.025 mg/kg/d.

In the 13-week dermal study in rats, the NOAEL of 300 mg/kg/d is based on treatment-related mortality in 2/12 females (tremor was also note in one of these females) and an increased incidence of slight irritation at the site of administration (5/10 females) at 1000 mg/kg/d, the highest dose tested. Based on these data, no additional assessment factors are considered appropriate for acute and medium term dermal exposure scenarios. Thus, an overall assessment factor of 100 is proposed. An absorption value of 53 % is predicted following dermal exposure of rats, therefore the external NOAEL from this study is equivalent to a systemic NOAEL of 159 mg/kg/d. This is equivalent to a dermal systemic $AEL_{acute/medium\text{-}term}$ value of 1.59 mg/kg/d. For long term dermal exposure scenarios, an additional assessment factor of 2 is considered appropriate (to account for extrapolation from a subchronic study to a chronic study). Thus, for long term dermal exposure scenarios, an overall assessment factor of 200 is proposed, equivalent to a dermal systemic $AEL_{long\text{-}term}$ value of 0.8 mg/kg/d.

2.2.1.2 Exposure assessment

The active substance, metofluthrin, and the representative product, SumiOne® Liquid Vapouriser, are not manufactured, formulated or packaged within the EU. Therefore, exposures during manufacture, formulation and packaging have not been evaluated.

2.2.1.2.1 Application of product

SumiOne® Liquid Vapouriser is specifically designed for small-scale use in residential properties for the control of mosquitoes. It is to be marketed solely for the amateur-use market.

[5] http://ec.europa.eu/environment/biocides/pdf/tnsg_4_1.pdf

The design of the product (i.e. SumiOne® Liquid Vapouriser is marketed in bottles containing only 45 ml of the vapouriser fluid and is only for use in small-scale electrically-heated vapouriser units), would exclude use by professional operators on economic and practical grounds. Therefore, exposures from professional operators have not been assessed. The primary and secondary exposure scenarios considered in the risk assessment from the use of SumiOne® Liquid Vapouriser are described below.

Primary exposure

SumiOne® Liquid Vapouriser is specifically designed for small-scale use in residential properties and is to be marketed solely for the amateur-use market. Potential dermal exposure could occur during insertion of the SumiOne® Liquid Vapouriser bottle into, and the removal of the spent bottle from, the vapouriser unit. This task is to be undertaken by an adult (60 kg bw) and would be an acute exposure. As the product is only to be used by amateurs, the use of Personal Protective Equipment (PPE) is not applicable and has not been considered in the assessments.

Quantification of the potential primary dermal exposures during amateur application of the SumiOne® Liquid Vapouriser has been presented within Section 3 of Document IIB. The exposure assessment has been conducted using guidance provided in the Technical Notes for Guidance, TNsG document (European Commission, 2002). Dermal exposures have been estimated using the dermal absorption value of 53 % (Document IIA, Section 3.1).

In line with the TNsG on Human Exposure to Biocidal Products, the UK CA has carried out for this product (SumiOne® Liquid Vapouriser) and its specified uses exposure assessments for human health based on a tiered approach. The UK has started each exposure assessment using worst-case assumptions (e.g. for duration of exposure, residues on surfaces etc.). If the risks to human health following exposure to metofluthrin were considered to be acceptable following comparison of the predicted systemic dose with the appropriate NOAEL/NOAEC from animal studies, then no further refinement of the exposure scenario was carried out. The UK CA accepts that in many cases (e.g. Tier 1 assessments) the exposure scenarios presented are highly conservative but consider further refinement of the exposure scenarios is unnecessary, if no unacceptable risk is identified. If an unacceptable risk is identified for a particular exposure scenario, then a further refinement of the exposure/risk assessment was carried out using additional parameters (e.g. submitted residue data etc.).

Secondary exposure

When the vapouriser unit is in operation, occupants of treated premises will be exposed, via inhalation, to airborne residues and via dermal, oral and inhalation routes, to residues that have deposited from the air onto surfaces. For SumiOne® Liquid Vapouriser the following potential exposure scenarios are considered possible:

- acute oral exposure – infant breaks open the SumiOne® Liquid Vapouriser bottle and drinks the contained Liquid;

- medium-term oral exposure – infant, child or adult is exposed to metofluthrin residues condensing out of air and depositing on food and onto surfaces on which food is placed;
- acute-term dermal exposure – infant breaks open the SumiOne® Liquid Vapouriser bottle and is dermally exposed to the contained Liquid;
- medium-term dermal exposure – infant contacts surfaces (e.g. a floor/carpet) upon which volatilised metofluthrin condensing from the air has deposited;
- medium-term dermal exposure – volatilised metofluthrin condensing on body surface of infants, children and adults;
- medium-term inhalation exposure – infant, child or adult inhales for 12 or 24 hours/d to metofluthrin volatilised into the air by the vapouriser unit; and
- medium-term inhalation exposure – people are exposed to metofluthrin re-volatilised from surfaces upon which it has deposited.

The following exposure scenarios are adjusted for body weight; which is 10 kg for an infant, 34.4 kg for a child and 60 kg for an adult:

Oral exposure

Scenario 1: Infant breaks open SumiOne® Liquid Vapouriser bottle and drinks the Liquid, and assuming 100 % oral absorption. This is an acute oral exposure.

Scenario 2: Infant, child or adult is exposed to metofluthrin that has condensed out of the air and deposits on food, or on surfaces on which food may be placed. This is a medium-term oral exposure.

(a) *Tier 1 Assessment*
An infant, child or adult is exposed to either sandwiches or apples onto which metofluthrin has deposited for either 12 or 24 hours and assumes 100 % oral absorption.

(b) *Tier 2 Assessment*
As in the Tier 1 assessment, above, with the application of a 100-fold assessment factor.

(c) *Tier 3 Assessment*
As in the Tier 1 assessment above, but using a study conducted to measure the surface residues of prallethrin following volatilisation of ETOC (Matoba Y. and Takimoto Y., 1996). Assuming the worst case for prallethrin deposition (75 µg prallethrin/m^2 for the wall with the air outlet).

(d) *Tier 4 Assessment*
As in the Tier 3 assessment, above, with the application of a 100-fold assessment factor.

The Tier 4 assessment (presented in Table 2.2), is based on deposition figures from a study using ETOC, a pyrethroid-based insecticide which is considered suitable and relevant for this risk assessment (See Document III-B, Section 6.6 – 05. Matoba, Y., Takimoto, Y., (1996); Indoor distribution of Etoc®. Evaporated by an Electric Vapouriser). In the ETOC study a vapouriser, similar to the product (SumiOne® Liquid Vapouriser), is used in a room of the same dimensions as the product is to be used in (30 m^3). The active ingredient used in the ETOC study is prallethrin. Both of these active ingredients are not considered volatile at room

temperature based on the vapour pressures of 9.47 x 10^{-4} Pa (i.e. 0.947 mPa) at 20 ºC and 1.33 x 10^{-2} mPa at 23.1 ºC for metofluthrin and prallethrin, respectively. This is an accordance with Curry (1995), which states as a general rule, it is considered a substance should be considered volatile only if it has a vapour pressure > 10 mPa at 20^{o}C [Reference - Curry, P.B., Iyengar, S., Maloney, P.A. and Maroni, M., (1995). 'Methods of Pesticide Exposure Assessment'. Plenum Press, New York. ISBN 0-306-45130-1]. The UKCA has also taken into consideration that the emission rates of both devices is different (0.79 mg/hr for prallethrin, and 0.28 mg/hr for metofluthrin), therefore a factor of 0.35 has been applied to the ETOC study results, to represent this change. With this conversion factor applied, and considering the similar use patterns and the fact that both active ingredients are pyrethroids, the UK CA believes that the Tier 4 assessments can be considered as realistic worst-case exposure scenarios.

Dermal exposure

Scenario 1: An infant breaks open a full SumiOne® Liquid Vapouriser bottle and is dermally exposed to the contents. It is assumed the infant is exposed to 5 % of the contents. This is an acute dermal exposure scenario.

Scenario 2: An infant comes into contact with surface (i.e. floor/carpet), onto which metofluthrin has condensed and deposited. This is a medium-term dermal exposure scenario.

(a) *Tier 1 Assessment*

Following 8 hours use per day over a 90-d period, the a cumulative residue value of 0.002 mg metofluthrin/m^2, 100 % skin contact with the floor/carpet is assumed and a 30 % transfer coefficient (from floor/carpet to skin) is applied.

(b) *Tier 2 Assessment*

An assessment using the ConsExpo Model Version 4.1 has also been undertaken to estimate dermal exposure for infants contacting a surface (e.g. floor/carpet) upon which volatilised metofluthrin from the ait has condensed. The ConsExpo default value of 30 % for the transfer of dislodgeable surface residue to skin has been used in the assessment.

(c) *Tier 3 Assessment*

(1) As in the Tier 1 assessment above, but using a study conducted to measure the surface residues of prallethrin following volatilisation of ETOC for 12 hours (Matoba Y. and Takimoto Y., 1996). Using the worst case for prallethrin deposition (75 µg prallethrin/m^2 for the wall with the air outlet), the residue of metofluthrin on a surface following 12 hours release, can be calculated to be 15.6 x 10^{-5} mg metofluthrin/cm^2.

(2) As above, but using a deposition value of 5.9 x 10^{-5} mg metofluthrin/m^2 (calculated from ETOC study value of 28 µg prallethrin/m^2 for the floor residues).

Scenario 3: An infant, child or adult comes into contact with metofluthrin condensing onto the body. This is a medium-term dermal exposure scenario.

(a) *Tier 1 Assessment*

Based on a metofluthrin deposition value of 6.6 x 10^{-5} mg/cm^2 on horizontal surfaces over 24 h and assuming 100 % of the body surface is exposed.

(b) *Tier 2 Assessment*
As in the tier 1 assessment above, but using a deposition value of 5.2 x 10^{-6} mg metofluthrin/cm^2 (as calculated in ETOC study by Matoba Y. and Takimoto Y., 1996).

Inhalation exposure
Scenario 1: Infants, children or adults exposed via inhalation in an enclosed, unventilated and/or ventilated space for 12 or 24 h/d to metofluthrin volatilised into the air by the vapouriser unit. These are medium-term inhalation exposure scenarios.

(a) *Tier 1 Assessment*
Assuming 100 % adsorption and applying a saturated vapour concentration (SVC) (see Doc IIB, Appendix II for calculation) of 0.2851 mg/m^3, at 25 °C in air.

(b) *Tier 2 Assessment*
Potential inhalation exposure to infants, children and adults was calculated using the ConsExpo model 4.1. Assuming a room size of 30 m^3, 100 % absorption via inhalation and a formulation emission rate of 0.28 mg metofluthrin/hour. Figures were calculated for both 12 and 24 h exposure and in ventilated and unventilated rooms.

(c) *Tier 3 Assessment*
A study (Matsunaga T. *et al*, 2002) investigated air concentrations of metofluthrin 120 cm above the floor of a room containing a 45 ml bottle of 0.533 % w/v metofluthrin in a solvent heated by an electric heating unit. The room was ventilated at a rate of 1.5 times/hour. The maximum concentration of metofluthrin in air over 11 hours was 44 x 10^{-4} mg/m^3. Exposure to infants, children and adults were calculated.

2.2.1.3 Risk Characterisation

Primary exposure

The exposure, MOE and Exposure/AEL values are given in Table 2.1 below.

Table 2.1 Non-professional users – primary exposure

Exposure Scenario (indicated duration)		**Estimated Internal Exposure**				**Relevant NOAEL/LOAEL [mg/kg b.w] & Reference Value e.g: AEL (acute or medium or chronic)**	**AF MOE_{ref}**	**MOE**	**Exposure/AEL**
		estimated oral uptake [mg/kg b.w]	**estimated inhalation uptake [mg/kg b.w]**	**estimated dermal uptake [mg/kg b.w]**	**estimated total uptake [mg/kg b.w]**				
Tier 1 (no PPE)	Removal and insertion of bottle into vapouriser unit by adult (acute)	N/A	N/A	0.2120	0.2120	Equivalent systemic NOAEL = 159 AEL = 1.59 (acute)	100	750	0.1333

Following potential worst-case short-term dermal exposure of an adult replacing a SumiOne® Liquid Vapouriser bottle in the electrically heated vapouriser unit, an MOE of 750 (adult) is derived. This shows no cause for concern.

Also, this MOE is based on exposure which is considered an over-estimate of the amount of product that could come into contact with the skin, as the HDPE/PET bottles are robust and are effectively sealed; the enclosed Liquid only exiting the bottle via the ceramic wick when heated. Very little Liquid will remain in the spent bottle and thus it is unlikely a person would be exposed to 2.25 ml of the product Liquid in the spent bottle (i.e. 5 % of the full contents of the 45 ml bottle). In a study, which the UK CA considers acceptable, it reports that between 2.0 and 2.9 % (average 2.3 %), i.e. 1.035 ml, of SumiOne® Liquid Vapouriser remains in the spent bottle (Matsumoto, 2005). Also, the Applicant's proposed product label is to carry the precautionary phrases, 'DO NOT TOUCH WICK' and 'WASH HANDS AFTER HANDLING'. Therefore under normal use there should be very little, if any, dermal contact with the Liquid in the SumiOne® Liquid Vapouriser bottle.

Secondary exposures

Oral

The secondary oral exposures based on reverse reference scenarios are given in Table 2.2 below.

Table 2.2 Indirect exposure as a result of use – secondary oral exposure

Exposure Scenarios	Infant				Child				Adult			
	Tier 1	Tier 2	Tier 3	Tier 4	Tier 1	Tier 2	Tier 3	Tier 4	Tier 1	Tier 2	Tier 3	Tier 4
Acute – amount of SumiOne® Liquid Vapouriser infant would need to drink to achieve the NOAEL of 10 mg/kg bw	18.75 ml (= 41.7 % of contents of one bottle of product)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Medium-term – no. of sandwiches (following 12 hours exposure) to be eaten to achieve the NOAEL of 10 mg/kg bw	10000	100	127000	1270	34400	344	436880	4368	60000	600	762000	7620
Medium-term – no. of sandwiches (following 24 hours exposure) to be eaten to achieve the NOAEL of 10 mg/kg bw	5000	50	63500	635	17200	172	218440	2184	30000	300	381000	3810
Medium-term – no. of apples (following 12 hours exposure) to be eaten to achieve the NOAEL of 10 mg/kg bw	1930	19	24511	245	6640	66	84328	843	11528	115	147104	1471
Medium-term – no. of apples (following 24 hours exposure) to be eaten to achieve the NOAEL of 10 mg/kg bw	965	10	12255	122	3320	33	42164	421	5791	57	73545	735

Note: Shaded cells are considered the most relevant for risk assessment.

As a Tier 1 assessment, a 10 kg infant must consume 18.75 ml of SumiOne® Liquid Vapouriser (equivalent to about 42 % of the contents of one bottle) to reach a systemic exposure equivalent to the NOAEL for acute exposure (from the 1-year oral study in the dog).

An infant, child and adult would need to consume 635, 2184 and 3810 sandwiches exposed to metofluthrin vapour condensing from the air over 24 hours, respectively, to reach the systemic exposure equivalent to the NOAEL for medium-term exposure (from the 1-year oral a study in the dog). These figures are taken from a Tier 4 approach.

An infant, child and adult would need to consume 122, 421 and 735 apples exposed to metofluthrin vapour condensing from the air over 24 hours, respectively, to reach the systemic exposure equivalent to the NOAEL for medium-term exposure. These figures are taken from a Tier 4 approach.

Overall, the UK CA considers the risks to infants, children and adults from the exposure of SumiOne® Liquid Vapouriser via the oral route to be low.

Dermal

The exposures, MOE and Exposure/AEL values for secondary dermal exposure are given in Table 2.3 below.

Table 2.3 Indirect exposure as a result of use - secondary dermal exposure

Exposure Scenario		estimated inhalation uptake [mg/kg bw]	estimated dermal uptake [mg/kg bw]	estimated oral uptake [mg/kg bw]	estimated total uptake [mg/kg bw]	Relevant NOAEL/LOAEL [mg/kg bw/d] & Reference Value e.g. AEL (acute/ medium/ long-term)	AF MOE_{ref}	MOE	Exposure/AEL
Tier 1 Acute scenario	infant skin contact with Liquid	N/A	0.6360	N/A	0.6360	Equivalent systemic NOAEL = 159 AEL = 1.59	100	250	0.4
Tier 1 Medium-term	infant skin contact with floor/ carpet surfaces upon which a.s. from air has condensed	N/A	0.2035	N/A	0.2035	Equivalent systemic NOAEL = 159 AEL = 1.59	100	781	0.1280
Tier 2 Medium-term		N/A	0.0053	N/A	0.0053	Equivalent systemic NOAEL = 159 AEL = 1.59	100	30000	0.0033
Tier 3 (a) Medium-term		N/A	0.0159	N/A	0.0159	Equivalent systemic NOAEL = 159 AEL = 1.59	100	10000	0.0100
Tier 3 (b) Medium-term		N/A	0.0060	N/A	0.0060	Equivalent systemic NOAEL = 159 AEL = 1.59	100	26500	0.0038
Tier 1 Medium-term	exposure to volatilised a.s. which deposits on the body	N/A	infant = 0.0224 child = 0.0121 adult = 0.0120	N/A	infant = 0.0224 child = 0.0121 adult = 0.0120	Equivalent systemic NOAEL = 159 AEL = 1.59	100	infant = 7098 child = 13140 adult = 13250	infant = 0.0141 child = 0.0076 adult = 0.0075
Tier 2 Medium-term		N/A	infant = 0.0017 child = 0.0009 adult = 0.0009	N/A	infant = 0.0017 child = 0.0009 adult = 0.0009	Equivalent systemic NOAEL = 159 AEL = 1.59	100	infant = 93529 child = 176667 adult = 176667	infant = 0.0011 child = 0.0006 adult = 0.0006

Note: Shaded cells are considered the most relevant for risk assessment.

Based on the NOAEL of 300 mg/kg/d from the 13-week dermal study in the rat, the MOE for an infant coming into direct skin contact with 5 % of the contents of a SumiOne® Liquid Vapouriser bottle is 250.

An assessment has been made for dermal contact with surfaces upon which volatilised metofluthrin has condensed from the air. In this scenario it is assumed the infant has 100 % skin contact with the contaminated floor/carpet. For the worst-case scenario (Tier 1 assessment), it is assumed all the metofluthrin in a bottle of the product is deposited onto a carpet in a single day and an infant comes into dermal contact with the carpet. This results in an MOE of 781.

Worst-case estimates of exposure from airborne residue depositing directly on the skin are taken from the Tier 2 assessments figures presented in Table 2.3, which gives MOEs of 93529, 176667 and 176667 for infants, children and adults respectively.

Overall, the UK CA considers the risks to infants, children and adults from the exposure of SumiOne® Liquid Vapouriser via the dermal route to be low.

Inhalation
The exposures, MOE and Exposure/AEL values for secondary inhalation exposure are given in Table 2.4 and 2.5 below.

Table 2.4 Indirect exposure as a result of use - secondary inhalation exposure (12 hours exposure in a day)

Exposure Scenario		Estimated Internal Exposure				Relevant NOAEL/ LOAEL [mg/kg bw/d] & Reference Value e.g. AEL (acute/ medium/long-term)	AF MOE_{ref}	MOE	Exposure/AEL
		estimated inhalation uptake [mg/kg bw]	estimated dermal uptake [mg/kg bw]	estimated oral uptake [mg/kg bw]	estimated total uptake [mg/kg bw]				
12 hours exposure to metofluthrin volatilised by vapouriser									
Tier 1 Medium -term	SVC Model – no ventilation	infant = 0.0642 child = 0.0580 adult = 0.0361	N/A	N/A	infant = 0.0642 child = 0.0580 adult = 0.0361	Equivalent systemic NOAEL = 15 AEL = 0.05	300	infant = 234 child = 259 adult = 416	infant = 1.28 child = 1.16 adult = 0.72
Tier 2 Medium -term	ConsExpo – no ventilation	infant = 7.25 x 10^{-4} child = 6.56 x 10^{-4} adult = 4.08 x 10^{-4}	N/A	N/A	infant = 7.25 x 10^{-4} child = 6.56 x 10^{-4} adult = 4.08 x 10^{-4}	Equivalent systemic NOAEL = 15 AEL = 0.05	300	infant = 20690 child = 22866 adult = 36765	infant = 0.015 child = 0.013 adult = 0.008
	ConsExpo – with ventilation	infant = 5.95 x 10^{-4} child = 5.36 x 10^{-4} adult = 3.34 x 10^{-4}	N/A	N/A	infant = 5.95 x 10^{-4} child = 5.36 x 10^{-4} adult = 3.34 x 10^{-4}	Equivalent systemic NOAEL = 15 AEL = 0.05	300	infant = 25210 child = 27985 adult = 44910	infant = 0.012 child = 0.011 adult = 0.0007
	simulation study	infant = 0.0010 child = 0.0009 adult = 0.0006	N/A	N/A	infant = 0.0010 child = 0.0009 adult = 0.0006	Equivalent systemic NOAEL = 15 AEL = 0.05	300	infant = 15000 child = 16667 adult = 25000	infant = 0.02 child = 0.018 adult = 0.012

Table 2.5 Indirect exposure as a result of use – secondary inhalation exposure (24 hours exposure in a day)

Exposure Scenario		Estimated Internal Exposure				Relevant NOAEL/ LOAEL [mg/kg bw/d] & Reference Value e.g. AEL (acute/ medium/long-term)	AF MOE_{ref}	MOE	Exposure/AEL
		estimated inhalation uptake [mg/kg bw]	estimated dermal uptake [mg/kg bw]	estimated oral uptake [mg/kg bw]	estimated total uptake [mg/kg bw]				
24 hours exposure to metofluthrin volatilised by vapouriser									
Tier 1 Medium -term	**SVC Model** – no ventilation	infant = 0.1283 child = 0.1160 adult = 0.0722	N/A	N/A	infant = 0.1283 child = 0.1160 adult = 0.0722	Equivalent systemic NOAEL = 15 AEL = 0.05	300	infant = 117 child = 129 adult = 208	infant = 2.57 child = 2.32 adult = 1.44
Tier 2 Medium -term	**ConsExpo** – no ventilation	infant = 14.8 x 10^{-4} child = 13.4 x 10^{-4} adult = 8.35 x 10^{-4}	N/A	N/A	infant = 14.8 x 10^{-4} child = 13.4 x 10^{-4} adult = 8.35 x 10^{-4}	Equivalent systemic NOAEL = 15 AEL = 0.05	300	infant = 10135 child = 11194 adult = 17964	infant = 0.030 child = 0.027 adult = 0.017
	ConsExpo – with ventilation	infant = 12.0 x 10^{-4} child = 10.9 x 10^{-4} adult = 6.78 x 10^{-4}	N/A	N/A	infant = 12.0 x 10^{-4} child = 10.9 x 10^{-4} adult = 6.78 x 10^{-4}	Equivalent systemic NOAEL = 15 AEL = 0.05	300	infant = 12500 child = 13762 adult = 22124	infant = 0.024 child = 0.022 adult = 0.014
	simulation study	infant = 0.0020 child = 0.0018 adult = 0.0011	N/A	N/A	infant = 0.0020 child = 0.0018 adult = 0.0011	Equivalent systemic NOAEL = 15 AEL = 0.05	300	infant = 7500 child = 8333 adult = 13636	infant = 0.04 child = 0.036 adult = 0.022
Exposure of occupants (infants, children or adults) to metofluthrin re-volatilised from contaminated surfaces should not exceed those values given above.									

Note: Shaded cells are considered the most relevant for risk assessment.

In a worst-case scenario in which occupants (e.g. an infant, child or adult) of treated premises inhale the saturated vapour of metofluthrin over 24 hours in a day, with no ventilation, MOEs are all less than 300, i.e. 117, 129 and 208 for the infant, child and adult respectively. However, refining the risk characterisation further using data from simulated studies in which metofluthrin concentrations in the air were monitored during application of the product by heated vapouriser, gives MOE values of 7500, 8333 and 13636 for the infant, child and adult respectively.

Overall, the UK CA considers the risks to infants, children and adults from the exposure of SumiOne® Liquid Vapouriser via the inhalation route to be low.

Conclusion
Overall, the UK CA considers that the application of metofluthrin via the SumiOne® Liquid Vapouriser is unlikely to present an unacceptable risk to infants, children and adults, and supports the Applicant's proposal that the following precautionary phrases appear on the product label:

- 'DO NOT TOUCH WICK'
- 'WASH HANDS AFTER HANDLING'
- 'KEEP OUT OF REACH OF CHILDREN'
- 'To prevent contamination of food, DO NOT use the unit in kitchens, or other food storage or preparation areas'

Combined exposure

It is considered that exposure from eating food (sandwiches/apples) which might have become contaminated with the active substance during use of the vapourising unit would be incidental and infrequent and would not contribute significantly to the total daily exposure. (From Tier 4 assessments, to achieve the NOAEL of 10 mg a.s./kg bw, an infant would need to eat 635 sandwiches/122 apples per day; a child, 2184 sandwiches/412 apples per day; and an adult 3810 sandwiches/735 apples per day). The product is marketed in HDPE/PET bottles which are robust and are effectively sealed. Therefore, it is considered dermal contamination for an adult removing/inserting the product bottle into the vapouriser unit and for an infant, oral or dermal exposure, from gaining access to the SumiOne® Liquid Vapouriser bottle would only be due to accident and not a normal part of daily exposure.

Adult
Under normal conditions of use, an adult could be exposed to volatilised residues condensing onto the body surface; Tier 2 = 0.0009 mg/kg bw/d (medium-term exposure) for volatilised residues condensing on the body surface over 24 hours. When compared to the systemic dermal NOAEL of 159 mg/kg bw/d, this exposure gives an MOE of 176667. An adult could also be exposed via inhalation to metofluthrin vapours given off by the unit. As a worst case this could be for 24 hours in a day (Tier 2). Data from simulated studies indicates an adult could be exposed to 0.0011 mg/kg bw/d. Using the NOAEL of 15 mg/kg bw/day, the MOE value by this route for an adult is 13636.

The worse-case combined total systemic exposure for an adult to metofluthrin depositing on the body and from inhaling its vapours produced by the vapourising unit is 0.0020 mg/kg bw/day. Using the NOAEL of 15 mg/kg bw/day, the MOE for this combined total systemic exposure for an adult is 7500.

Child

For a child, a worst-case combined dermal exposures could occur through the deposition of metofluthrin from the air onto the skin; the heating unit having been in operation over 24 hours. Exposure for this scenario (Tier 2) is 0.0009 mg/kg bw/d. Compared to the systemic dermal NOAEL of 159 mg/kg bw/d, this exposure gives an MOE of 176667. The child would also be inhalationaly exposed to airborne metofluthrin during operation of the vapouriser unit. For a worst-case scenario (exposure for 24 hours in a day), using data from simulated studies (Tier 2) indicates a child would be exposed to 0.0018 mg/kg bw/d. Using the NOAEL of 15 mg/kg bw/day, the MOE value exposure via inhalation for a child is 8333.

The worse-case combined total systemic exposure for a child being exposed to a.s. depositing on the body and from inhaling vapours produced by the vapourising unit is 0.0027 mg/kg bw/day. Using the NOAEL of 15 mg/kg bw/day, the MOE for this combined total systemic exposure for a child is 5556.

Infant

For an infant, a worst-case combined dermal exposure could occur through the infant coming into contact with a surface (e.g. a floor/carpet) upon which metofluthrin has condensed and the deposition of metofluthrin from the air onto the skin for 24 hours. Exposures for these scenarios are 0.0159 mg/kg bw/d (Tier 3) and 0.0017 mg/kg bw/d (Tier 2) respectively, giving a combined dermal exposure of 0.0176 mg/kg bw/d. Compared to the systemic dermal NOAEL of 159 mg/kg/d, these exposures give an MOE of 9034. The infant would also be inhalationaly exposed to airborne metofluthrin during operation of the vapouriser unit. For a worst-case scenario, exposure is for 24 hours in a day. Using data from simulated studies indicates an infant would be exposed to 0.0020 mg/kg bw/d (Tier 2). Using the NOAEL of 15 mg/kg bw/day, the MOE value exposure via inhalation for an infant is 7500.

The combined total systemic exposure for an infant dermally exposed to residues on a carpet/floor, and as a worse case being exposed to metofluthrin depositing on the body and from inhaling vapours produced by the vapourising unit is 0.0196 mg/kg bw/day. Using the NOAEL of 15 mg/kg bw/day, the MOE for this combined total systemic exposure for an infant is 765.

2.2.2. Environmental Risk Assessment

Environmental effects of metofluthrin were established using both radiolabelled and non-radiolabelled forms of either, the mixture of all isomers (metofluthrin/S-1264) containing >80% RTZ isomer or various forms of purified RTZ or RTE isomers (see Doc IIA Section 4 and Doc IIIA Section 2- Confidential for more details). Throughout this section RTZ and RTE isomers may simply be referred to as Z and E isomers.

2.2.2.1 Fate and distribution in the environment

Fate in the aquatic compartment (including sediment)

The Z isomer of metofluthrin was shown not to undergo hydrolysis at environmentally relevant pH values, the DT_{50} value being predicted as > 1 year at pH 7 irrespective of the temperature. However, Z and E isomers of metofluthrin were shown to undergo aquatic photolysis with DT_{50} values of 2.2 – 2.6 days. The values were obtained using light intensities equivalent to 40 – 50 ºN latitude respectively, which in a European context, equates to intensities found between Brussels and Prague (at 50 ºN) and Madrid and Naples (at 40 ºN).

Metofluthrin is considered as not readily biodegradable, with only a 2 % degradation reported within the timescale of the 28 day test. No data was supplied for aquatic and/or sediment biodegradation, which was supported by a justification for non-submission of data. Data available on the fate of Z and E isomers of metofluthrin in soil did show that under aerobic conditions, the Z isomer was shown to have a mean DT_{50} value of 7.4 days (at 12 ºC, see Section 4.1.1.2.3 Document II-A), when tested under laboratory conditions. The available adsorption/desorption coefficients (arithmetic mean Koc 6184 l/kg), suggests that this active substance would be expected to bind to sediment. However, due to the absence of data from a sediment water study, it has been assumed that metofluthrin would persist at the levels predicted. Where necessary default data values are available within the TGD.

Fate in air

The data presented predicts that metofluthrin would degrade rapidly in air under daylight conditions. Therefore, the UK CA has concluded that any residues/deposits formed during evening use of the product would be rapidly degraded the following day.

Taking these data into account, along with the fact that the associated product is not a fumigant and is likely to result in very limited atmospheric exposure, the UK CA has accepted the Applicant's justification for non-submission of any further fate in air studies (see Document III-A, Section 7.3.2).

Fate in the terrestrial compartment

Z and E isomers of metofluthrin were shown to degrade in soil with half-lives of 2.3 - 3.5 d (at 25 ºC) and were ultimately mineralized to CO_2 under the conditions tested. However, since metofluthrin is not present in equal quantities of Z and E isomers but in a ratio of 9:1, the UK CA considered that using a combined mean from both data sets would not present a realistic DT_{50}. Therefore, following agreement at the TMIII09 the geometric mean of the Z isomer

data, which is 2.6 d at 25 ˚C or 7.4 d converted to 12 ˚C (using equation 25 of TGD) is proposed for the risk assessment. The available data suggests that metofluthrin would not persist or accumulate in the soil compartment and that non-extractable residues would be < 25 %.

Intermediate major (> 10 %) metabolites MFOA-D and TFPA and M7 were identified with mean estimated half-lives of 52.1 d, 97 d and 1.7 d at 12 ºC respectively. The UK CA has considered the impact of these metabolites when carrying out the risk assessment, and has addressed them in documents II-B and II-C.

The mean adsorption values of 6184 l kg^{-1} (Ka_{oc}) and 10497 l kg^{-1} (Kd_{oc}) derived from the soil study [indicating that once adsorbed to the soil Alc-*Z* is unlikely to be desorbed in the presence of water] suggest that Alc-*Z* exhibits a very low mobility potential in the 4 soils tested. This is further supported by Koc values of 16000 and 17000 (*Z* and E isomers respectively) established by the HPLC method.

2.2.2.2 Effects assessment

The assessment factors (AF) used to define the PNECs for the environmental compartments of concern have been taken from the Technical Guidance Document on Risk Assessment (TGD) in support of Commission Directive 93/67/EEC (new notified substances), Commission Regulation (EC) No. 1499/94 (existing substances) and Directive 98/8/EC (biocidal products) (EC, 2003).

A 3 h respiration inhibition test, carried out according to OECD guideline 209, was submitted to assess the effects of S-1264 on STP microorganisms. Both the EC_{50} and EC_0 were reported as > 1000 mg l^{-1} (nominal). Therefore, from the TGD (Table 17), an AF of 10 was applied to the EC_{10} (as a surrogate NOEC) to derive a $PNEC_{STP}$ of 100 mg l^{-1}. It is also considered acceptable to use the limit of solubility of a substance as the $PNEC_{STP}$ where no effects have been seen at concentrations above solubility. Therefore, an additional $PNEC_{STP}$ 0.5 mg l^{-1} (based on *Z* isomer as highest in ratio of 9:1 *Z*:E) has been considered in this risk assessment.

Metofluthrin has been shown to be acutely toxic to aquatic organisms with the most sensitive endpoint reported for the fish (rainbow trout; *Oncorhynchus mykiss*) with a 96 h LC_{50} of 1.2 µg l^{-1}. In the absence of a suitable long-term fish study the maximum assessment factor of 1000 has been applied, which has resulted in a highly conservative, predicted no effect concentration (PNEC) of 1.2 x 10^{-3} µg l^{-1}. Since the log K_{ow} for metofluthrin is 5, a sediment toxicity study was required since the equilibrium partition method (EPM) cannot be used. A chronic spiked sediment study was supplied which suggested that sediment dwellers were not as sensitive to metofluthrin as the pelagic invertebrates with a 28 d NOEC of 340 µg a.s. kg^{-1} wwt sediment chironomids. The TGD states that, when long-term toxicity test data are available for benthic organisms the $PNEC_{sed}$ is calculated using assessment factors for long-term tests and this result should prevail in the risk assessment (see Section 3.5.4 of the TGD). Therefore, according to the TGD, the $PNEC_{sed}$ for metofluthrin can be derived using the 340 µg a.s. kg^{-1} wwt sediment based on no effects seen on emergence and/or development rate at the highest concentration tested (also close to limit of solubility). The TGD recommends an assessment factor (AF) of 100 is applied where only a single sediment NOEC/EC_{10} is available, hence the $PNEC_{sediment}$ is 0.0034 mg a.s. kg^{-1} wwt sediment.

No data were submitted to address the toxicity of metofluthrin to soil organisms because of the low levels of exposure predicted from the proposed use pattern. However, as metofluthrin was shown to have the potential for adsorption to soil with a Koc > 4000, a first tier risk assessment in this compartment was carried out. To do this the PNEC was predicted using the TGD guidance on the EPM, which gave 1.31 x 10^{-4} mg kg^{-1} [soil].

Acute endpoints were provided to assess the acute toxicity of technical grade metofluthrin to birds. The TGD states that secondary poisoning effects on bird and mammal populations rarely become manifest in short-term studies. For this reason, results from long-term studies are strongly preferred. However, in the absence of long-term data, short-term data can be extrapolated to give a $PNEC_{oral}$ that should be protective to other mammalian and avian species. The TGD also states that acute lethal doses are not acceptable for extrapolation to chronic toxicity, as these are not dietary tests. Depending on the available endpoints, an assessment factor for such extrapolation (AF_{oral}) is applied to take into account interspecies variation, acute/subchronic to chronic extrapolation and laboratory data to field impact extrapolation. From the TGD, an AF_{oral} of 3000 is appropriate for short-term (5 d) LC_{50} data (birds). This endpoint has therefore been used to calculate the $PNEC_{avian}$ of 1.87 mg kg^{-1}. Using the available mammalian toxicity data, a NOAEL of 10 mg kg^{-1} d^{-1} was identified from a 1 year study in dogs. This is equivalent to 400 mg kg^{-1} food, and according to the TGD, this endpoint (chronic exposure) attracts an AF of 30, therefore, the $PNEC_{mammal,\ food,\ ch}$ was derived was 13.33 mg kg^{-1} d^{-1}.

2.2.2.3 Persistent, Bioaccumulative and Toxic (PBT) assessment

According to the TGD, 'The Persistent, Bioaccumulative and Toxic (PBT) assessment is considered to be different from the local and regional assessment approaches, as it seeks to protect ecosystems where risks are more difficult to estimate'. Under the Biocidal Products Directive (BPD), a PBT assessment is needed to demonstrate that a substance does not fulfil selection criteria under the United Nations Environment Programme – Persistent Organic Pollutants convention (UNEP-POPs) to limit emissions to the environment of those chemicals with high potential for persistence, bioaccumulation, long-range transport and adverse effects on human health and the environment. Any substance which is found to be either a PBT or very Persistent very Bioaccumulative (vPvB) substance shall not be allowed on Annex I unless releases to the environment can be effectively prevented.

Persistence

The criterion for persistence according to the TGD is that the DT50 in freshwater is >40 days and/or in sediment is >120 days. No data have been submitted on the persistence in sediment water systems. Data are available on the stability of metofluthrin in water at pH 7 as well as its' stability in light. The former indicates that it is stable to aqueous hydrolysis, whilst the latter indicates that it is rapidly degraded in the presence of light (DT_{50} ~ 6 d). The Applicant has stated that according to the 35th CA meeting (Dec 09) REACH criteria can be used to assist in the classification of a compound. In particular the Applicant highlights that the P criteria under REACH includes a reference to DT_{50} in soil of 120 days. Metofluthrin has a half life in soil of 7.4 days.

The TGD states that in order to determine whether the P criteria has been met that 'other degradation mechanisms such as hydrolysis and photolysis should be taken into account where they can be shown to be relevant'; on the basis of the above metofluthrin is not persistent in the soil, however this does not automatically infer that it will not be persistent in sediment or water. Data on the K_{oc} indicates that it is unlikely to remain in the water phase for long. This may subsequently reduce the potential impact of aqueous photolysis which would only be expected to be significant in the upper surface water layers. No data are available on the potential persistence in sediment. Therefore, in the absence of data on potential persistence in sediment water systems, the UK CA has assumed that metofluthrin could persist in the sediment compartment (P criterion is fulfilled) but that the low levels of environmental exposure resulting from its use in a vapouriser product would not be of concern.

Bioaccumulation

A substance is considered to have the potential to fulfil the criterion of bioaccumulation when the log Kow exceeds 4.5 (according to the TGD) and the log Kow for metofluthrin is 5. However, a 60 d exposure study with carp reported a maximum BCF of 120, which removes the concern of bioaccumulation or biomagnification for this compound. Therefore, as the BCF is < 2000 (trigger according to TGD), metofluthrin does not fulfil the criterion.

Toxic

According to the most sensitive endpoint available for metofluthrin, 96 h LC_{50} of 1.2 µg l^{-1}, the acute endpoint is below the trigger of < 0.1 mg l^{-1}. Therefore, the toxic criterion is fulfilled according to the TGD.

[According to the TGD, where data on chronic effects are not available, short-term toxicity data for aquatic organisms are sufficient, provided the potential for PBT is assessed based on the trigger levels for Persistence and Bioaccumulation assessments.]

Conclusion: Metofluthrin is considered to be toxic, however it is not considered to bioaccumulate. As regards persistence there is a lack of data to clearly indicate whether it is or isn't persistent in sediment. In the absence of such data it is proposed to identify the active substance as persistent. In order to reconsider this proposal, data (e.g. sediment water study) would be required.

2.2.2.4 Exposure assessment

Emissions to the environment

The environmental exposure assessment presented by the UK CA, has been produced using all available information. This has been taken from submitted studies and the Organisation for Economic Co-operation and Development (OECD) 4th Draft Emission Scenario Document (ESD) on Insecticides, acaricides and products to control arthropods (PT 18) for household and professional use (PT18 ESD; OECD, 2007). Information and guidance was also taken from part II of the Technical Guidance Document on risk assessment (TGD; EC, 2003).

At the time of submission there was no available exposure guidance to aid the Applicant with the risk assessment for the vapouriser product. Therefore, the UK CA using all available relevant information presented by the OECD PT18 ESD and TGD has produced the environmental exposure assessment presented.

This document relates to the exposure assessment for the SumiOne® Liquid Vapouriser (0.69 % w/w metofluthrin). The product is supplied as a plug-in electrical vapouriser, with ceramic wick and sealed glass bottle containing the product. The intended usage pattern envisaged for the product is for indoor, amateur use. Thus the UK CA considers the main potential exposure routes for the environment to be:

1) Application phase -volatile residues, resulting in;
    a) direct exposure of the immediate and local air compartment through venting.
2) Cleaning phase - disposal of deposited surface residues via cleaning, resulting in;
    a) direct exposure of a sewage treatment plant (STP) [wet cleaning],
    b) indirect exposure of surface waters via STP effluent,
    c) indirect exposure of soil via disposal of STP sludge,
    d) indirect exposure of birds/mammals via fish and
    e) direct exposure to landfill [dry cleaning].

From the above, the main route of environmental exposure is considered to be via the sewage treatment plant (STP) from wet cleaning of indoor hard surfaces. The emission to landfill is not considered further in the risk assessment, as it is assumed that these residues will be significantly diluted with domestic waste and placed in landfill sites subject to the European Landfill Directive (ELD 99/31/EC). Also due to the use pattern (indoor only) and the predicted fate in air (see Section 3.3.2.3) only the immediate indoor atmosphere is likely to be significantly exposed. If venting to the wider atmospheric compartment was to occur, significant dilution and photo degradation would be expected, hence removing any real concern.

All information used in the exposure assessment refers to metofluthrin as used within the SumiOne® Liquid Vapouriser and the predicted environmental concentrations (PEC) are shown to be extremely low. With regards to metabolites, 3 major (> 10 %) metabolites ‘MFOA-D, TFPA and M7’ have been identified. Although as shown in Document II-A, Section 4.1.1.2.3 ‘Degradation in soil’ the first 2; MFOA-D and TFPA, are secondary and tertiary metabolites respectively. The structures shown in Section 4.1.1.2.3 (Document II-A) strongly suggest that these 2 metabolites are structurally very similar and are sufficiently complex to assume that the chemistry will be very similar to the parent compound, which is also supported by the ecotoxicity studies where degradation was reported. Therefore, the exposure and subsequent risk assessment presented for metofluthrin can be assumed to include any exposure to any subsequent metabolites. However, this does not appear to be the same for M7, nonetheless its DT_{50} of 1.7 d at 12 ºC suggests that this substance is unlikely to exist in the soil environment to any great extent. This is particularly demonstrated by the PEC values predicted for soil being exceptionally low. Therefore, the UK CA considers that by using only the initial (worst-case, with no degradation considered) PEC values for the active substance (a.s.), which are very small despite the gross assumptions made, the exposure assessment is sufficiently precautionary to account for any metabolites formed in the longer term. However for completeness, an additional assessment of potential risks posed by the soil metabolites has been provided in Doc IIC. In this additional assessment, the original parent exposure assessment has

been amended based on the longest metabolite soil DT_{50} of 97 d (for metabolite TFPA) to reflect potential exposure of metabolites as a simple and conservative approach.

The OECD PT18 ESD recognises 2 types of diffuser; electrical (limited [in time] use) and passive (unlimited use); as the SumiOne® Liquid Vapouriser is an electrical plug-in device all relevant defaults, unless stated otherwise, have been taken from the 4th draft PT18 ESD (see Table 3.3.2). In order to calculate the environmental exposure during the use (application phase) and post-use (cleaning) phases the following assumptions have been applied by the UK CA:

1) Only one vapouriser per house is used for 12 hours a day.
2) No degradation occurs either before or during cleaning of the treated property [assuming that the product has been restricted to use during the hours of dusk to dawn, when mosquitoes are most prevalent and to ensure maximum efficacy i.e. as no degradation by photo degradation in air] .
3) Depositions to horizontal surfaces of both 10 % (default - tier 1 assessment) and 3 % (Applicant's data - tier 2 assessment) have been assumed.

The PEC data have all been presented within the 'Risk Characterisation' Section below.

2.2.2.5 Risk Characterisation

The risk assessment is based upon the PEC:PNEC ratio for the compartments of concern. These are presented in the Table 2.6 below:

Table 2.6 Risk Characterisation (PEC:PNEC) values for metofluthrin as a result of using SumiOne® Liquid vapouriser

Compartment	Assessment level	PEC	PNEC	PEC:PNEC
STP	**Tier 1**	2.54×10^{-5}	0.5	5.09×10^{-5}
	Tier 2	7.63×10^{-6}		1.53×10^{-5}
Surface waters	**Tier 1**	2.52×10^{-6}	1.2×10^{-6}	2.1*
	Tier 2	7.56×10^{-7}		0.63
Sediment	**Tier 1**	3.41×10^{-4}	0.0034	0.1
	Tier 2	1.02×10^{-4}		0.03
Soil ($local_{soil}$)	**Tier 1 only**	2.60×10^{-5}	1.31×10^{-4}	0.20 [a]
Biota ($PNEC_{avian}$)	**Tier 1**	3.02×10^{-4}	1.87	1.61×10^{-5}
	Tier 2	9.07×10^{-5}		4.85×10^{-5}
Biota ($PNEC_{mammal,\ food\ ch}$)	**Tier 1**	3.02×10^{-4}	13.33	2.26×10^{-5}
	Tier 2	9.07×10^{-5}		6.7×10^{-6}

Tier 1 = 10 % default deposition value,
Tier 2 = 3 % refinement deposition value
+ lowest PNEC based on limit of solubility for main isomer
* unacceptable risk
wwt – wet weight
dwt – dry weight
[a] assuming a soil DT_{50} of 97 d (for TFPA) to cover potential exposure of metabolites, the PEC:PNEC increases to 0.88 and it is therefore considered that the risk assessment is acceptable

These data suggest that the use of metofluthrin in the product SumiOne® Liquid vapouriser would be acceptable after adjustment for reduced deposition to horizontal surfaces from the ESD default of 10 % to 3 % as shown by the Applicants data (necessary to refine the surface water risk assessment). It is also acknowledged that these PEC data are 'initial' values and no degradation has been taken into account (with the exception of the soil PEC values where reliable information on the degradation rates was available and used in the assessment). They are therefore likely to represent a conservative estimate of actual environmental exposures in the opinion of the UK CA. Therefore, the risk quotients presented in the above table do present a worst-case scenario as available data suggest that a degree of photodegradation (DT_{50} < 6 h) in air is likely to occur during daylight prior to cleaning. In conclusion, this limited use pattern should not present any unacceptable environmental risks.

2.2.3. List of endpoints

In order to facilitate the work of Member States (MS) 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. DECISION

3.1. Background to the Decision

Following potential worst-case short-term dermal primary exposure to metofluthrin through the use of the representative product, there is no cause for concern.

Also, the application of metofluthrin via the representative product is unlikely to present an unacceptable risk to infants, children and adults via secondary oral, dermal and inhalation exposure, although recommendations for statements to be included on the product label are suggested (see Section 3.3 below).

The scenario used for the environmental risk assessment is based on treatment against flying insects (such as mosquitoes) using the SumiOne® Liquid vapouriser followed by wet cleaning presenting a potential exposure to surface waters via STP. The risk assessment of this use pattern has shown that metofluthrin would not pose an unacceptable risk to surface waters. Therefore, the use of the SumiOne® Liquid vapouriser (containing 0.69 % w/w metofluthrin) in rooms where 'wet cleaning' is likely, requires no restriction as no concerns with regards to environmental compartments are triggered according to the assumptions made.

The exposure from one vapouriser per household has been assessed (see Doc IIB Section 3.3.3). However, use of more than one product per home could result in a concern for the environment (assuming daily cleaning at the end of the 12 hour use period can 'in reality' be envisaged). Therefore, use of more than one metofluthrin product per home (i.e. multiple vapourisers or a vapouriser plus other metofluthrin-based insecticidal products) would require a risk assessment which may lead to restrictions in order to mitigate risk (e.g. label phrases to restrict the use to only one metofluthrin containing product per household.)

The physico-chemical properties of the active substance and biocidal products have been evaluated and are deemed acceptable for the appropriate use, storage and transportation of the active substance and biocidal products.

The data on the active substance and associated biocidal product have demonstrated sufficient efficacy for inclusion into Annex I to be recommended. However, further efficacy data will be required on specific products (including SumiOne® Liquid Vapouriser) to support product authorisation at the Member State level.

3.2. Decision regarding Inclusion in Annex I

Metofluthrin shall be included in Annex I to Directive 98/8/EC as an active substance for use in product-type **18** (insecticide), subject to the following specific provisions:

Identity:

RTZ Isomer

IUPAC Name: 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl-(1R,3R)-2,2-dimethyl-3-[(Z)-prop-1-enyl]cyclopropanecarboxylate

CAS No: 240494-71-7

Purity: 75.4 – 89.1 % w/w

Metofluthrin as the sum of all isomers as follows

IUPAC Name: 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (EZ)-(1RS,3RS;1SR,3SR)-2,2-dimethyl-3-prop-1-enylcyclopropanecarboxylate

CAS No: 240494-70-6

Purity: 93 – 98.8 % w/w

Proposed product type:

- 18 (Insecticides, acaricides and products to control other arthropods)

Proposal for conditions of particular uses:

The proposed use is for a plug-in electrical Liquid Vapouriser, containing 0.69 % w/w of metofluthrin. This is designed for amateur use and is to be used indoors. In order to mitigate against excessive environmental exposure, the product should be marketed in a single pack only. However, removal of these restrictions can be agreed at MS level with the support of additional degradation data to refine the risk assessments.

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

The UK CA recommends that the following statements should appear on the product label once product authorisation is granted:

- 'DO NOT TOUCH WICK'
- 'WASH HANDS AFTER HANDLING'
- 'KEEP OUT OF REACH OF CHILDREN'
- 'To prevent contamination of food, DO NOT use the unit in kitchens, or other food storage or preparation areas'

The UK CA also notes that products must be labelled appropriately to ensure safe storage, handling, use and disposal in accordance with national arrangements.

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 metofluthrin onto Annex I to Directive 98/8/EC.

Analytical methods for body fluids and tissues will be required if metofluthrin is classified as Toxic.

The use of metofluthrin in any product other than SumiOne® Liquid Vapouriser should be considered carefully at Member State level, as additional uses of this substance in insecticidal products may result in an unacceptable risk to surface waters and sediment. Therefore, before authorisation for any products additional to SumiOne® Liquid Vapouriser containing metofluthrin (at any concentration) can be agreed; additional data to address the biodegradation and identification of major metabolites of this substance in sediment-water systems may be submitted and evaluated. This is necessary because despite the current risk assessment assumptions being worst-case (i.e. simultaneous use and daily cleaning with 100% cleaning efficiency before any photodegradation has taken place), any increase in the predicted aquatic concentrations could result in an unacceptable risk.

Before product authorisation can be granted for any metofluthrin-based product (including SumiOne® Liquid Vapouriser), adequate efficacy data (including field or simulated-use data that demonstrates how the product will be used in practice) should be submitted to Member States.

It should also be noted that floor deposition rate data relating to prallethrin were used in the refined environmental risk assessment of metofluthrin. The applicability of studies on deposition rates for refining the environmental exposure assessment is still under discussion at TM level. The results of the discussion on floor deposition rates and their impact on the environmental risk assessment must be considered during product authorisation of metofluthrin containing products including SumiOne® Liquid Vapouriser.

3.5. Updating this Assessment Report

This assessment 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 metofluthrin in Annex I to the Directive.

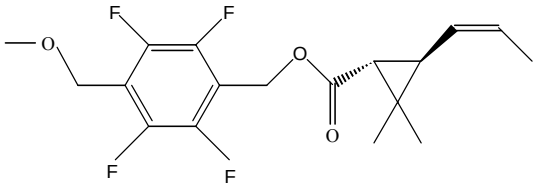
4. APPENDIX I: LIST OF ENDPOINTS

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

Active substance (ISO Common Name)	Metofluthrin
Function (*e.g.* fungicide)	Insecticide (PT 18)

Rapporteur Member State	United Kingdom

Identity

Chemical name (IUPAC)	RTZ isomer: 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl-(1R,3R)-2,2-dimethyl-3-[(Z)-prop-1-enyl]cyclopropanecarboxylate (All isomers: 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (EZ)-(1RS,3RS;1SR,3SR)-2,2-dimethyl-3-prop-1-enylcyclopropanecarboxylate)
Chemical name (CA)	RTZ isomer: Cyclopropanecarboxylic acid, 2,2-dimethyl-3-(1Z)-1-propen-1-yl-[2,3,5,6-tetrafluoro-4-(methoxymethyl)phenyl]methyl ester, (1R,3R)- (All isomers: Cyclopropanecarboxylic acid, 2,2-dimethyl-3-(1-propen-1-yl)-[2,3,5,6-tetrafluoro-4-(methoxymethyl)phenyl]methyl ester)
CAS No	RTZ isomer: 240494-71-7 (All isomers:240494-70-6)
EC No	Not applicable
Other substance No.	Also known as S-1264 or SumiOne®
Minimum purity of the active substance as manufactured (g/kg or g/l)	RTZ isomer: 754 g/kg (All isomers: 930 g/kg)
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	No impurities of concern
Molecular formula	$C_{18}H_{20}F_4O_3$
Molecular mass	360.35g
Structural formula	

Physical and chemical properties

Melting point	-54°C (purity 87 % RTZ/99.8% all isomers)
Boiling point	334ºC (purity 87 % RTZ/99.8% all isomers)
Temperature of decomposition	-
Appearance	Pale yellow Liquid (purity 82.2% RTZ/96.6% all isomers)
Relative density	1.21 at 20ºC (purity 82.2% RTZ/96.6% all isomers)
Surface tension	39.8 ± 3.0 mN/m [estimated, Chemsketch 5.0]. No test data, however limited exposure to aquatic environmental compartments. Furthermore the low water solubility (< 1 mg/l) of metofluthrin means that the surface tension does not need to be determined.
Vapour pressure	20°C: 9.47 E-04 Pa 25ºC: 1.96 E-03 Pa
Henry's law constant	S-1264RTE: 0.509 Pa.m3mol-1 and S-1264RTZ: 0.681 Pa.m3mol-1 at pH 7 and 20°C
Solubility in water	S-1264 RTE (E isomer) Purity: 99.2% result: 0.67 mg/L at 20ºC and pH 7.2
	S-1264 RTZ (Z isomer) Purity: 98.5% result: 0.50 mg/L at 20ºC and pH 7.5
	The effects of pH on solubility in water have not been assessed as S-1264 does not dissociate in the pH range 1 to 13
Solubility in organic solvents	Solvent / mg/l Acetone 303400 Methanol 312200 Ethyl acetate 307600 Toluene 326900 n-Hexane 328700 Dichloromethane 318900 n-Octanol 325100 Isopropyl alcohol 313200
	The Z:E isomer ratio was 92.3 % showing that S-1264 remained in its original Z:E ratio
Stability in organic solvents used in biocidal products including relevant breakdown products	Z:E isomer ratio 92.3 %, showing that the active substance remained in its original Z:E ratio
Partition coefficient (log P_{ow})	S-1264 RTZ (Z isomer): 5.0 at 25 ± 2°C
	S-1264 RTE (E isomer): 5.0 at 25 ± 2°C
Hydrolytic stability (DT_{50}) (state pH and temperature)	pH 4: >1year at 25°C
	pH 7: >1 year at 25°C
	pH 9: 30.7 - 33.5 days at 25°C
Dissociation constant	No dissociation activity detected from pH 1 to pH 13.

UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	Peak maximum 273 nm with an extinction co-efficient of 1750 M^{-1} cm^{-1}.
Photostability (DT_{50}) (aqueous, sunlight, state pH)	Photolysis in water: DT_{50} 2.2 - 2.6 days for 40 and 50 °N latitude, pH 4
Quantum yield of direct phototransformation in water at Σ > 290 nm	Reaction quantum yield (ϕ^c_E): 0.125
Flammability	Autoflammability: 365°C No flash point observed. Flash point >110ºC
Explosive properties	Thermal explodability: negative Impact (mechanical) explodability: negative

Classification and proposed labelling

with regard to physical/chemical data	No classification
with regard to toxicological data	T, Xn; R25[6], R20, R48/20
with regard to fate and behaviour data	N; R53
with regard to ecotoxicological data	N; R50

[6] The Applicant does not agree with the proposal to classify metofluthrin with T; R25. A justification for their position is provided at Annex I of Document IIA.

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	Capillary GC-FID
Impurities in technical active substance (principle of method)	Chiral HPLC-UV (270 nm) Capillary GC-FID Reverse phase HPLC-UV (270 nm) MS and NMR spectroscopy

Analytical methods for residues

Soil (principle of method and LOQ)	Due to negligible exposure to the terrestrial environmental compartment, and considering the limitations of current analytical technology, the need for an analytical method to determine residues in soil is considered to be scientifically unjustified.
Air (principle of method and LOQ)	GC–ECD
Water (principle of method and LOQ)	capillary GC-ECD (column DB-5) capillary GC-ECD (column RTX 1701)
Body fluids and tissues (principle of method and LOQ)	The TNsG on data requirements state analytical methods are only required if a substance is toxic or highly toxic. It is possible that metofluthrin will be classified as toxic, however, until such a time as this classification is confirmed a method for the determination of the active substance in animal and human body fluids and tissues is not required.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Due to negligible potential residue levels in food and zero exposure to feedstuffs, the need for an analytical method to determine residues in food and feeding stuffs is considered to be scientifically unjustified.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Due to negligible potential residue levels in food and zero exposure to feedstuffs, the need for an analytical method to determine residues in food of animal origin is considered to be scientifically unjustified.

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	Rat: RTZ and RTE isomers of metofluthrin are well absorbed (up to 100 %) following both single and repeated administration. Following single administration peak plasma levels of RTZ and RTE isomers of metofluthrin and/or their metabolites are achieved within 8 hours.
Rate and extent of dermal absorption:	Data are available from an *in vivo* dermal absorption study in rats. From these data a conservative dermal absorption value of 53 % is derived.
Rate and extent of inhalation absorption:	There are no toxicokinetic studies by the inhalation route, but as RTZ and RTE isomers of metofluthrin are well absorbed from the gastrointestinal tract it is predicted that it will be well absorbed from the respiratory tract. This is supported by single and repeated inhalation exposure toxicodynamic studies that provide evidence for systemic effects. Overall, it is assumed that uptake of metofluthrin vapour across the respiratory tract is 100%.
Distribution:	Once absorbed, metofluthrin and/or its metabolites are widely distributed; principal concentrations being found in the liver and kidney.
Potential for accumulation:	Metofluthrin and/or its metabolites are not expected to bioaccumulate.
Rate and extent of excretion:	Elimination is rapid and essentially complete within 48 h via both urine and faeces.
Toxicologically significant metabolite(s)	None

Acute toxicity

LD_{50} oral	> 2000 mg/kg (no corn oil) Mortalities were observed in 7/20 and 0/10 animals (in an acute neurotoxicity study and sighting study, respectively) when administered at a dose level of 100 mg/kg in corn oil.
Rat LD_{50} dermal	> 2000 mg/kg
Rat LC_{50} inhalation	1 – 2 mg/l
Skin irritation	Not classified.
Eye irritation	Not classified.
Skin sensitization (test method used and result)	Not classified (Maximisation test).

Repeated dose toxicity

Species/ target / critical effect	The most prominent findings, from the oral repeated

	dose studies were neurotoxicity in rats and dogs, hepatotoxicity in rats and mice and indications of nephrotoxicity in rats. Following repeated inhalation exposure of rats for 28 days to an aerosol of metofluthrin, mortality and tremors (suggestive of neurotoxicity) were observed at 0.2 mg/l, the highest concentration tested. Following dermal exposure, mortality and neurotoxicity were observed at the top dose level (1000 mg/kg/d) in a 13 week rat study.
Lowest relevant oral NOAEL / LOAEL	$NOAEL_{acute/medium-term}$: 10 mg/kg/d (90 day/1 year dog study) $NOAEL_{long-term}$: 8 mg/kg/d (2 year rat study)
Lowest relevant dermal NOAEL / LOAEL	300 mg/kg/d (90 day rat study)
Lowest relevant inhalation NOAEL / LOAEL	0.1 mg/l (28 day rat study)

Genotoxicity	Metofluthrin produced negative results *in vitro*, in an Ames test and a mammalian cell gene mutation test. A negative result was reported in a mouse bone marrow micronucleus test.

Carcinogenicity

Species/type of tumour	Rat: Liver carcinomas and adenomas (not considered relevant to humans based on mode of action being similar to that of phenobarbitone) Mouse: No tumours
Lowest dose with tumours	Rat :38 mg/kg/d Mouse: > 209 mg/kg/d

Reproductive toxicity

Species/ Reproduction target / critical effect	No treatment-related effects on fertility.
Lowest relevant reproductive NOAEL / LOAEL	NOAEL (F1): 20 mg/kg/d (rat)
Species/Developmental target / critical effect	No treatment-related effects on development.
Lowest relevant developmental NOAEL / LOAEL	NOAEL (parental): 15 mg/kg/d (rat) NOAEL (parental): 25 mg/kg/d (rabbit)

Neurotoxicity / Delayed neurotoxicity

Acute neurotoxicity study in rats	NOAEL (neurotoxicity): 50 mg/kg/d
13-weeks neurotoxicity study in rats	NOAEL (neurotoxicity): 60 mg/kg/d
12-month chronic neurotoxicity study in rats	Not available.

Other toxicological studies

....	None submitted

Medical data

....	None submitted

Summary[7]	Value	Study	Safety factor
Oral AEL (acute)	0.1 mg/kg/d	1 year dog study	100
Oral AEL (medium-term)	0.1 mg/kg/d	1 year dog study	100
Oral AEL (long-term)	0.08 mg/kg/d	2 year study	100
Systemic Dermal AEL (acute)	1.59 mg/kg/d	13-week rat study	100
Systemic Dermal AEL (medium-term)	1.59 mg/kg/d	13-week rat study	100
Systemic Dermal AEL (long-term)	0.8 mg/kg/d	13-week rat study	200
Systemic Inhalation AEC (acute)	0.15 mg/kg/d	28 day rat study	100
Systemic Inhalation AEC (medium-term)	0.05 mg/kg/d	28 day rat study	300
Systemic Inhalation AEC (long-term)	0.025 mg/kg/d	28 day rat study	600

[7] Please note that dermal and inhalation external values have been transformed into systemic NOAELs using appropriate absorption values.

Acceptable exposure scenarios (including method of calculation)

Professional users	Not required as product is for non-professional use
Production of active substance:	N/A (active substance is manufactured outside of the EU)
Formulation of biocidal product	N/A (biocidal product is formulated outside of the EU)
Intended uses	SumiOne® Liquid Vapouriser is packaged in a 45 ml HDPE or PET screw-top bottle for use in a preparatory electrically heated vapourising unit for use as an indoor space treatment to knockdown and kill mosquitoes.

Primary exposure

Exposure routes: dermal.

Method of calculation: MOE and AEL.

1. Acute/dermal exposure

NOAEL = 159 mg kg^{-1} d^{-1} (90-day dermal study in the rat)

Scenario	MOE	Exposure/AEL
Adult: skin contamination with Liquid product during removal of bottle from, and its insertion into, vapouriser unit	750	0.1333

Secondary exposure

Exposure routes: oral, dermal and inhalation.

Method of calculation: MOE, AEL and reverse reference scenario.

1. Acute/dermal exposure

NOAEL = 159 mg kg^{-1} d^{-1} (90-d dermal study in the rat)

Scenario	MOE	Exposure/AEL
Infant: skin contact with Liquid product	250	0.4

2. Medium-term dermal exposure

NOAEL = 159 mg kg^{-1} d^{-1} (90-d dermal study in the rat)

Scenario	Infant		Child		Adult	
Infant: skin contact with floor/carpet upon which a.s. from ait has condensed	781	0.1280	N/A	N/A	N/A	N/A
Exposure to volatilised a.s. which deposits onto the body	93529	0.0011	176667	0.0006	176667	0.0006

3. Acute/oral exposure

NOAEL = 10 mg kg^{-1} d^{-1} (1-year oral study in the dog)

Scenario	Reverse Reference Scenario
Amount of SumiOne® Liquid an infant would need to drink to achieve NOAEL	18.75 ml (equivalent to 41.7 % of the contents of one bottle of SumiOne® Liquid)

4. Medium-term/oral exposure

NOAEL = 10 mg kg^{-1} d^{-1} (1-year oral study in the dog)

Scenario	Reverse Reference Scenario					
	Infant		Child		Adult	
	sandwiches	apples	sandwiches	apples	sandwiches	apples
Number of sandwiches or apples (following 24 hours exposure) to be eaten to achieve NOAEL	635	122	2184	421	3810	735

5. Medium-term/inhalation exposure

NOAEL = 15 mg kg^{-1} d^{-1} (28-d repeat dose inhalation study in the rat)

Scenario	Infant		Child		Adult	
	MOE	AEL	MOE	AEL	MOE	AEL
Exposure for 24 hours to metofluthrin volatilised by vapouriser	7500	0.04	8333	0.036	13636	0.022

Non-professional users

Exposure route: dermal.

Method of calculation: MOE and AEL.

Scenario	Values used in the assessment	
	MOE	AEL
Removal and insertion of bottle into vapouriser unit by adult	750	1.59 (acute)

Indirect exposure as a result of use

See Secondary exposure above.

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water

Hydrolysis of active substance and relevant metabolites (DT50) (state pH and temperature)	pH 5: > 1year at 25 °C and 12°C
	pH 7: > 1 year at 25 °C and 12°C
	pH 9: 30.7 - 33.5 days at 25 °C ≡ 86.9 – 94.8 at 12°C
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	Photolysis in water: DT_{50} 2.2 - 2.6 days for 40 °N and 50 °N latitude, pH 4 Photo oxidation in air: DT_{50} 1.4 - 6 h
Readily biodegradable (yes/no)	No
Biodegradation in seawater	Due to limited exposure to the marine environmental compartment, the need to conduct studies on biodegradation in seawater is considered to be scientifically unjustified
Non-extractable residues	-
Distribution in water / sediment systems (active substance)	Due to limited exposure to aquatic environmental compartments, the need to conduct studies on the rate and route of degradation in aquatic systems (including identification of metabolites and degradation products) is considered to be scientifically unjustified for SumiOne® Liquid Vapouriser (changes to the formulation or different products may trigger the need to address this endpoint with an appropriate study).
Distribution in water / sediment systems (metabolites)	See above.

Route and rate of degradation in soil

Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} (25 °C, aerobic): 2.3 - 3.5 days (mean 2.7 days). Two soils, 8 measurements each. [Metofluthrin (Z and E isomers) was shown to degrade in soil with half-lives of 2.3 - 3.5 d (at 25 ºC) and was ultimately mineralized to CO_2 under the conditions tested. However, since metofluthrin is not present in equal quantities of Z and E isomers but in a ratio of 9:1, the UK CA considered that using a combined mean from both data sets would not present a realistic DT_{50}. Therefore, following agreement at the TMIII09 the geometric mean of the Z isomer data, which is 2.6 d at 25 ˚C or 7.4 d converted to 12 ˚C (using equation 25 of TGD) is proposed for the risk assessment.]
Non-extractable residues	The available data suggests that metofluthrin would not persist or accumulate in the soil compartment and that non-extractable residues would be < 25 % (test duration 60/120 d).
Mineralization (aerobic)	Cumulative amounts of $^{14}CO_2$ evolved during incubation period were 47.8 – 88.6 % of the applied ^{14}C (59 - 120 days)

Field studies (state location, range or median with number of measurements)	Due to limited exposure to the terrestrial environmental compartment, the need to conduct field studies on the rate and route of degradation in soil is considered to be scientifically unjustified.
Anaerobic degradation	Due to limited exposure to the terrestrial environmental compartment, the need to conduct studies on anaerobic degradation in soil is considered to be scientifically unjustified.
Soil photolysis	Due to limited exposure to the terrestrial environmental compartment, the need to conduct a soil photolysis study is considered to be scientifically unjustified.
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	MFOA-D 65.2 - 76.0 % [DT50 12.5 – 23.8 days] TFPA 21.8 - 57.1 % [DT50 6.2 – 76.9 days] M7 6.5 – 21.9 % [DT50 0.5 – 0.8 days]
Soil accumulation and plateau concentration	Negligible exposure to the terrestrial environmental compartment.

Adsorption/desorption

Ka , Kd Ka_{oc} , Kd_{oc}	Ka: 54.6 – 119; Kd: 67.3 - 265 Ka_{oc}: 2729 – 11855; Kd_{oc}: 4289 – 18428 Mean: 6184 l kg^{-1} 10497 l kg^{-1}
pH dependence (yes / no) (if yes type of dependence)	No

Fate and behaviour in air

Direct photolysis in air	Not determined
Quantum yield of direct photolysis	Not determined
Photo-oxidative degradation in air	Estimated photo-oxidation in air: 5.230 to 5.832 hours over a 24 h day assuming an OH radical concentration of 5 x 10^5 molecules cm^{-3}
Volatilization	See Document II-B, Section 3.3.2, Vapour pressures.

Monitoring data, if available

Soil (indicate location and type of study)	No monitoring data available
Surface water (indicate location and type of study)	No monitoring data available
Ground water (indicate location and type of study)	No monitoring data available
Air (indicate location and type of study)	No monitoring data available

Chapter 5: Effects on Non-target Species

Toxicity data for aquatic species (most sensitive species of each group)

Species	Time-scale	Endpoint	Toxicity
Fish			
Oncorhynchus mykiss	96 h	LC_{50}	1.2 µg l^{-1}
Invertebrates			
Daphnia magna	48 h	EC_{50}	4.7 µg l^{-1}
Chironomus riparius	28 d	NOEC	340 µg kg^{-1} wwt
Algae			
Pseudokirchneriella subcapitata	72 h	E_bC_{50} E_rC_{50}	0.16 mg l^{-1} 0.37 mg l^{-1}
Microorganisms			
Activated sewage sludge respiration inhibition	3 h culture 10 min O_2 depletion	EC_{10} EC_{50}	> 1000 mg l^{-1} > 1000 mg l^{-1}

Effects on earthworms or other soil non-target organisms

Acute toxicity to …….	Negligible exposure of the outdoor environment including soil from the uses proposed therefore these data are not required. $PNEC_{soil}$ estimated using the equilibrium partitioning method.
Reproductive toxicity to……..	Negligible exposure of the outdoor environment including soil from the uses proposed therefore these data are not required. $PNEC_{soil}$ estimated using the equilibrium partitioning method.

Effects on soil micro-organisms

Nitrogen mineralization	Negligible exposure of the outdoor environment including soil from the uses proposed therefore these data are not required. $PNEC_{soil}$ estimated using the equilibrium partitioning method.
Carbon mineralization	Negligible exposure of the outdoor environment including soil from the uses proposed therefore these data are not required. $PNEC_{soil}$ estimated using the equilibrium partitioning method.

Effects on terrestrial vertebrates

Acute toxicity to mammals	Acute oral and dermal LD_{50} > 2000 mg kg^{-1} bw (rat)
Acute toxicity to birds	Acute oral LD_{50} > 2250 mg a.s. kg^{-1} bw (*Colinus virginianus*)
Dietary toxicity to birds	5-day dietary LC_{50} > 5620 mg a.s. kg^{-1} (*Colinus*

	virginianus and *Anas platyrhynchos)*
Reproductive toxicity to birds	Negligible exposure of the outdoor environment from the uses proposed therefore these data are not required.

Effects on honeybees

Acute oral toxicity	Negligible exposure of the outdoor environment from the uses proposed therefore these data are not required.
Acute contact toxicity	Negligible exposure of the outdoor environment from the uses proposed therefore these data are not required.

Effects on other beneficial arthropods

Acute oral toxicity	Negligible exposure of the outdoor environment from the uses proposed therefore these data are not required.
Acute contact toxicity	Negligible exposure of the outdoor environment from the uses proposed therefore these data are not required.
Acute toxicity to ……..	Negligible exposure of the outdoor environment from the uses proposed therefore these data are not required.

Bioconcentration

Bioconcentration factor (BCF)	BCF for metofluthrin is 110 and 120 at 0.5 and 0.05 µg a.s. l^{-1}
Depuration time(DT_{50}) (DT_{90})	Not determined. As there will be negligible exposure of the outdoor environment these data are not required.
Level of metabolites (%) in organisms accounting for > 10 % of residues	Not determined. As there will be negligible exposure of the outdoor environment these data are not required.

Chapter 6: Other End Points

Not applicable.

5. APPENDIX II: LIST OF INTENDED USES

Object and/or situation	Member State or Country	Product name	Organisms controlled	Formulation		Application			Applied amount per treatment			Remarks:
(a)			(c)	Type (b)	Conc. of as (e)	method kind (f-g)	number min max (h)	interval between applications (min)	g as/L min max	water L/m^2 min max	mg as/m^3 min max	(i)
Flying insects	EU	S-1264 Liquid	Mosquitoes	LV	5.33 g/l	Heated vapouriser Space treatment	Max: 12h use per day	-	N/A	N/A	0.0217 (in-use)	In-use concentration calculated from measured emission rate (0.28 mgAS/h) for heated vapouriser in 16 m^3 room, with standard ventilation (0.5/h). Effective for 60 days @ 12h use per day

6. 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.

Metofluthrin – Reference list by section point

Section No /Reference No. in Doc IIIA	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A2.6	Suzuki, M.	2004	Description of beginning materials and manufacturing process for S-1264 Report No. QAP-0033 [Sumitomo Ref: QAP 0033] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A2.7	Shono, F.	2004	Specification of S-1264 technical grade Report No. QAP-0004 [Sumitomo Ref: QAP 0004] Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A2.8/01	Shono, F.	2004	Specification of S-1264 technical grade Report No. QAP-0004 [Sumitomo Ref: QAP 0004] Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A2.8/02	Inoue, H.	2002a	Preliminary analysis of S-1264 technical grade Report No. QAP-0016 [Sumitomo Ref: QAP 0016] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.1.1	Lentz N. R	2004a	Determination of Freezing Point, Solvent Solubility, Absorption Spectra and Autoflammability of S-1264. Report No. 016369-1 [Sumitomo Ref: QAP 0030] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.1.2	Sweetapple G.G. and Lentz N. R.	2003a	Determination of UV/Visible Absorption and Boiling Point of S-1264. Report No. 015681-1 [Sumitomo Ref: QAP 0022] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.1.3	Sweetapple G.G. and Lentz N. R.	2003b	Determination of Physical-Chemical Properties of S-1264. Report No 015682-1, [Sumitomo Ref: QAP 0020] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.2	DiFrancesco D. And Lentz N. R.	2004	Determination of Vapour Pressure - S-1264. Report No 015632. [Sumitomo Ref: QAP 0028] GLP, Unpublished	Y (New/	Sumitomo Chemical Co. Ltd

Section No /Reference No. in Doc IIIA	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
				First)	
A3.2.1	Lentz, R.	2004b	Calculation of the Henry's Law Constant of S-1264. Report No 015632-2, [Sumitomo Ref: QAP-0029] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.3.1	Sweetapple G.G. and Lentz N. R.	2003b	Determination of Physical-Chemical Properties of S-1264. Report No 015682-1, [Sumitomo Ref: QAP 0020] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.3.2	Sweetapple G.G. and Lentz N. R.	2003b	Determination of Physical-Chemical Properties of S-1264. Report No 015682-1, [Sumitomo Ref: QAP 0020] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.3.3	Sweetapple G.G. and Lentz N. R.	2003b	Determination of Physical-Chemical Properties of S-1264. Report No 015682-1, [Sumitomo Ref: QAP 0020] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.4/01	Sweetapple G.G. and Lentz N. R.	2003a	Determination of UV/Visible Absorption and Boiling Point of S-1264. Report No. 015681-1 [Sumitomo Ref: QAP 0022] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.4/02	Lentz N. R	2004a	Determination of Freezing Point, Solvent Solubility, Absorption Spectra and Autoflammability of S-1264. Report No. 016369-1 [Sumitomo Ref: QAP 0030] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.4/03	Shono F.	2003	IR Spectrum of S-1264 Technical Material. Report No QAP-0014 [Sumitomo Ref: QAP 0014] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.5	Walsh K.J. and Lentz N. R	2003a	Determination of Water Solubility - S-1264. Report No. 015634-1, [Sumitomo Ref: QAP 0019] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.6	Beckwith R.C. and Lentz N. R.	2003	Determination of Dissociation Constant (pKa) - S-1264, 09.09.2003. Report No. 015635. [Sumitomo Ref: QAP 0021] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.7	Lentz N. R	2004a	Determination of Freezing Point, Solvent Solubility, Absorption Spectra and Autoflammability of S-1264. Report No. 016369-1 [Sumitomo Ref: QAP 0030] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd

Section No /Reference No. in Doc IIIA	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A3.8	Lentz N. R	2004a	Determination of Freezing Point, Solvent Solubility, Absorption Spectra and Autoflammability of S-1264. Report No. 016369-1 [Sumitomo Ref: QAP 0030] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.9	Walsh K.J. and Lentz N. R.	2003b	Determination of *n*-Octanol/Water Partition Coefficient – S-1264. Report No. 015633-1, [Sumitomo Ref: QAP 0023] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.10	Inoue H.	2004b	Stability of S-1264 Technical Grade to Normal and Elevated temperatures, Metals and Metal Ions. Report No. 0007. [Sumitomo Ref: QAP 0024]. GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.11	Lentz N. R	2004a	Determination of Freezing Point, Solvent Solubility, Absorption Spectra and Autoflammability of S-1264. Report No. 016369-1 [Sumitomo Ref: QAP 0030] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.12	Sweetapple G.G. and Lentz N. R.	2003b	Determination of Physical-Chemical Properties of S-1264. Report No 015682-1, [Sumitomo Ref: QAP 0020] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.14	Sweetapple G.G. and Lentz N. R.	2003b	Determination of Physical-Chemical Properties of S-1264. Report No 015682-1, [Sumitomo Ref: QAP 0020] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.15	Sweetapple G.G. and Lentz N. R.	2003b	Determination of Physical-Chemical Properties of S-1264. Report No 015682-1, [Sumitomo Ref: QAP 0020] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.16	Sweetapple G.G. and Lentz N. R.	2003b	Determination of Physical-Chemical Properties of S-1264. Report No 015682-1, [Sumitomo Ref: QAP 0020] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A3.17	Inoue H.	2004c	Storage Stability of S-1264 Technical Grade. Report No. 0001. [Sumitomo Ref: QAP 0025]. GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A4.1.1	Inoue, H	2002a	Preliminary Analysis of S-1264 Technical Grade. Report No. 3771. [Sumitomo Ref: QAP-0016] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A4.1.1	Inoue, H.	2002b	Enforcement Analytical Methods of S-1264 Technical Grade. Report No. 3679 [Sumitomo Ref: QAA-0009]	Y (New/	Sumitomo Chemical Co. Ltd

Section No /Reference No. in Doc IIIA	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			[Validation] GLP, Unpublished	First)	
A4.1.2	Inoue, H	2002a	Preliminary Analysis of S-1264 Technical Grade. Report No. 3771. [Sumitomo Ref: QAP-0016] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A4.1.2	Inoue, H	2005	Analytical method for isomer ratio of S-1264 Technical Grade. Report No. QAA-0026 [Sumitomo Ref: QAA-0026] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A4.1.2	Inoue, H.	2002b	Enforcement Analytical Methods of S-1264 Technical Grade. Report No. 3679 [Sumitomo Ref: QAA-0009] [Validation] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A4.2.2/01	Matsunaga, T.	2002a	Analytical test of the active ingredient concentration in the air under normal use of S-1264 liquid. Report No. 20020055 [Sumitomo ref: QAF-0020]. Non-GLP, unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A4.2.2/02	Matsunaga, T.	2002b	A Study on Determination of Amount of Active Ingredient Vaporized from S-1264 Liquid. Report No. 20020055 [Sumitomo ref: QAF-0019] Non-GLP, unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A4.2.2/03	Wimbush, J.	2006	Definitive Protocol - SumiOne® (metofluthrin): Validation of an Analytical Method for the Determination of Residues in Air. Study Number 2282/026. Dated 19/12/05	Y (New/ First)	Sumitomo Chemical Co. Ltd
A4.2.3	Wolf, S.	2003	Validation of a multi-residue method for the determination of S-1264 in surface water. Report No. 848612. [Sumitomo Ref: QAA-0023] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A5.3/01	Anon.	2000a	Efficacy evaluation of S-1264 paper strip in 28 m^3 chamber in comparison with a fan vaporizer and a vaporizer liquid. Report No and date: not given Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A5.3/02	Anon.	2000b	Efficacy evaluation of S-1264 paper strip in 28 m^3 chamber in comparison with transfluthrin for 480 hrs. Report No.: not given Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A5.3/03	Muto, A.	2002a	Basic efficacy evaluation of "S-1264 Liquid" against adult common house mosquitoes. Report No.: not given Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd

Section No /Reference No. in Doc IIIA	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A5.3/04	Muto, A.	2002b	Efficacy of "S-1264 Liquid" against adult mosquitoes in a living room. Report No.: not given Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A5.3/05	Serit, M.	2003	Efficacy of mosquito coils containing 0.005% w/w S-1264 and 0.0075% w/w S-1264 compared with SIRIM standard mosquito coil containing 0.2% w/w Pynamin Forte evaluated using Glass Chamber test method (LS-BT-T14) following Malaysian Standard (MS 23: Part 2: 1986) against mosquitoes Aedes aegypti and Culex quinquefasciatus. Report No TS-03101. Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A5.3/06	Shono, Y.	2002a	Basic efficacy evaluation of S-1264 vaporizer liquid formulation under laboratory conditions (Part 2). Report No not given. Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A5.3/07	Shono, Y.	2002b	Basic efficacy evaluation of S-1264 vaporizer liquid formulation under laboratory conditions (Part 1); Setting of optimum S-1264 content. Report No not given. Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A5.3/08	Shono, Y	2002c	Efficacy evaluation of S-1264 vaporizer liquid under semi-field condition. Report No not given Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A5.3/09	Sugano, M.	2005	Comparison of lethal efficacy of SumiOne® side chain isomers. Report No.: QAE-0024 Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A5.7.1/01	Anon	1992	Vector Resistance to Pesticides. Fifteenth Report of the WHO Expert Committee on Vector Biology and Control, TRS 818, 1992 Non-GLP, published	N	Public
A5.7.1/02	Anon	2000	Guidelines for preventing and managing insecticide resistance in the peach-potato aphid, *Myzus persicae* Insecticide Resistance Action Group, February 2000 Non-GLP, published	N	Public
A5.7.1/03	Brogdon & McAllister	1998	Insecticide Resistance and Vector Control Emerging Infectious Diseases; Vol. 4 No. 4, December 1998. http://www.cdc.gov/ncidod/EID/vol4no4/brogdon.htm Non-GLP, published	N	Public
A5.7.1/04	Staetz	2004	Insecticide Mode of Action Classification: A Key to Insecticide Resistance Management (v.3.3.2) Insecticide Resistance Action Committee (IRAC International), 2004 Non-GLP, published	N	Public
A5.7.1/05	Hopley, J.	2005	Letter subject: Resistance – metofluthrin	Y	Sumitomo Chemical

Section No /Reference No. in Doc IIIA	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			No report number Non GLP, unpublished	(New/ First)	Co. Ltd
A6.1.1	Kunimatsu, T.	2002a	Acute oral toxicity of S-1264 in rats. Report No. 3670 [Sumitomo Ref: QAT-0004] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.1.2	Kunimatsu, T.	2002b	Acute dermal toxicity of S-1264 in rats. Report No. 3671 [Sumitomo Ref: QAT-0005] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.1.3	Yoshihito, D.	2002	Acute inhalation toxicity study of S-1264 in rats. Report No. 3666 [Sumitomo Ref: QAT-0028] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.1.4	Nakamura, Y.	2001a	Skin and eye irritation of S-1264 in rabbits. Report No. 3634 [Sumitomo Ref: QAT-0014] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.1.5	Nakamura, Y.	2002b	Skin sensitization test of S-1264 in guinea pigs (Maximization Test). Report No. 3684 [Sumitomo Ref: QAT-0017] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.2/01	Sugimoto, K. *et al.*	2002a	The disposition and metabolism of [carbonyl]-^{14}C S-1264RTZ in rats. Report No. PK0141. [Sumitomo Ref: QAM 001] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.2/02	Sugimoto, K. *et al.*	2002b	The disposition and metabolism of [carbonyl]-^{14}C S-1264RTE in rats. Report No. PK0143. [Sumitomo Ref: QAM 002] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.2/03	Sugimoto, K. *et al.*	2002c	The disposition and metabolism of [methoxymethylbenzyl-α-^{14}C] S-1264RTZ in rats. Report No. PK0142. [Sumitomo Ref: QAM 003] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.2/04	Sugimoto K *et al.*	2004a	The Disposition and Metabolism of [carbonyl]-^{14}C S-1264RTZ (1R-trans-Z) in Rats. Report no. P020096. [Sumitomo Ref: QAM 004**]** GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.2/05	Sugimoto K *et al.*	2004b	The Disposition and Metabolism of [methoxymethylbenzyl-α-^{14}C] S-1264RTZ (1R-trans-Z) After Repeated Administration to Rats". Report no. P020095. [Sumitomo Ref: QAM 005] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd

Section No /Reference No. in Doc IIIA	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A6.2/06	Tomigahra, Y.	2004	Percutaneous absorption of S-1264 in rats. Report No. X0088 [Sumitomo Ref: QAM-0022] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.3.1	Kunimatsu, T.	2002c	One Month Oral Toxicity Study in Rats. Report No. 3641. [Sumitomo Ref: QAT-0029] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.3.3	Deguchi, Y.	2002	Four-week repeated inhalation study of S-1264 in rats. Report No. 3704 [Sumitomo Ref: QAT-0031] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.4.1/01	Sommer, E.W., Knuppe, C., Gretener, P. & Weber, K.	2003	S-1264: 13-Week Repeated Dose Oral Toxicity (Feeding) Study in the Wistar Rat. Report No: 841950 [Sumitomo Ref. QAT-0051] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.4.1/02	Uchida, H.	2002	90-Day Oral Toxicity Study with S-1264 in Beagle Dogs followed by 42-day recovery Study. Report No. 20142 [Sumitomo Ref. QAT-0018] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.4.1/03	Sommer, E.W., Knuppe, C., Gretene, P. & Weber, K.	2004	S-1264: 13-Week Repeated Dose Oral Toxicity (Feeding) Study in the CD-1 Mouse. Report No. 841949 [Sumitomo Ref QAT-0058] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.4.2/01	Furukawa, H.	2004	A 90-day repeated dose dermal toxicity study of S-1264 in rats. Report No: P030373, [Sumitomo Ref. QAT-0064] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.4.2/02	Bando, K.	2004	The dose finding study for absence of clinical signs by single dermal administration of S-1264 in rats. Report No. 3888 [Sumitomo Ref. QAT-0056] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.5/01	Kunimatsu, T.	2002d	Six-month Oral Toxicity Study of S-1264 in Rats. Report No. 3663 [Sumitomo Ref: QAT-0030] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.5/02	Uchida H.	2004	12-Month Repeated Dose Oral Toxicity Study of S-1264 in Beagle Dogs. Report no P020637 [Sumitomo Ref: QAT-0061] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.5/03	Schmid H., *et al.*	2005a	S-1264: Combined chronic toxicity/oncogenicity (feeding) study in the rat. Report No. 846244 [Sumitomo Ref: QAT-0078]	Y (New/	Sumitomo Chemical Co. Ltd

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			GLP, Unpublished	First)	
A6.5/04	Schmid H., *et al.*	2005b	S-1264: Combined chronic toxicity/oncogenicity (feeding) study in the CD-1 mouse. Report No. 847663 [Sumitomo Ref: QAT-0079] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.6.1	Odawara, K.	2002a	Reverse mutation test of S-1264 in bacterial systems. Report No. 3673 [Sumitomo Ref: QAT-0026] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.6.2	Odawara, K.	2002b	In vitro chromosomal aberration test on S-1264 in Chinese hamster lung cells (CHL/IU). Report No. 3633 [Sumitomo Ref: QAT-0022] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.6.3	Durward, R.	2005	S-1264: CHO HPRT forward mutation assay. Report No.: 483/0047 [Sumitomo Ref.: QAT-0080] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.6.4	Odawara, K.	2002c	Micronucleus Test on S-1264 in Mice. Report No. 3685 [Sumitomo Ref: QAT-0032] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.7/01	Schmid H., *et al.*	2005c	S-1264: Combined chronic toxicity/oncogenicity (feeding) study in the rat. Report No. 846244 [Sumitomo Ref: QAT-0078] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.7/02	Schmid H., *et al.*	2005d	S-1264: Combined chronic toxicity/oncogenicity (feeding) study in the CD-1 mouse. Report No. 847663 [Sumitomo Ref: QAT-0079] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.8.1/01	Hara, H.	2002a	Study for Effects on Embryofoetal development of S-1264 administered Orally to Rats. Report, No. ST01085 [Sumitomo Ref: QAT-0003] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.8.1/02	Horie, N.	2002	Study for Effects on Embryofoetal Development of S-1264 administered Orally to Rabbits. Report No. 3644 [Sumitomo Ref: QAT-0019]. GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.8.1/03	Hoberman, A. M.	2005	Oral (diet) two-generation (one litter per generation) reproduction study of S-1264 in rats. Report no.: 1119-031 [Sumitomo Ref: QAT-0076]. GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd

Section No /Reference No. in Doc IIIA	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A6.8.2/01	Hara, H.	2002b	Study of fertility and early embryonic development to implantation of S-1264 administered orally to rats. Report, No. ST01083 [Sumitomo Ref: QAT-0011] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.8.2/02	Hara, H.	2002c	Study for effects on pre- and postnatal development, including maternal function of S-1264 administered orally to rats. Report, No. ST01084 [Sumitomo Ref: QAT-0020] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.9/01	York, R.G.	2004a	Oral (Gavage) Acute Neurotoxicity Study of S-1264 in Rats. Report no. 1119-032. [Sumitomo Ref: QAT-0059] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.9/02	York, R.G.	2004b	Oral (Diet) Subchronic Neurotoxicity Study of S-1264 in Rats. Report no. 1119-033 [Sumitomo Ref: QAT-0060] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.10	Deguchi, Y.	2005	Study for mode of action of S-1264 for liver tumour promotion in rats. Report No. S1226 [Sumitomo Ref: QAT-0077] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A6.12	Hopley, J.	2005	Letter re: Medical surveillance – metofluthrin. Report no.: not given Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A7.1.1.1.1	Ponte, M.	2004a	Hydrolysis of [^{14}C]S-1264 at pH 4, 7 and 9. Report number 1192W-001. [Sumitomo Ref: QAM-0017]. GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A7.1.1.1.2	Ponte, M.	2004b	Aqueous Photolysis of [14-C]S-1264 in pH 4 Buffer by Artificial Light. Report No. 1238W-1. [Sumitomo Ref: QAM-0019]. GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A7.1.1.2.1	Matsumoto, K.	2000	Biodegradation test of S-1264 by microorganisms etc Report No. 1212. [Sumitomo Ref: QAM-0021] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A7.1.3-01	Ponte, M.	2004c	Soil Adsorption/Desorption of [^{14}C]S-1264 by the Batch Equilibrium Method. Report No. 1191W-1 [Sumitomo Ref: QAM-0018] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A7.1.3-02	Walsh, K.J. and Lentz, N.R.	2003c	Estimation of the Adsorption Coefficient (K_{oc}) on Soil and on Sewage Sludge using High Performance Liquid Chromatography (HPLC) - S-1264.	Y (New/	Sumitomo Chemical Co. Ltd

Section No /Reference No. in Doc IIIA	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			Report No. 016238-1 [Sumitomo Ref: QAM-0016] GLP, Unpublished	First)	
A7.2.1	Kodaka, R., Sugano, T., Yoshimura, J., Katagi, T. & Takimoto, Y.	2003	Aerobic Soil Metabolism Study of [^{14}C]S-1264. Report No. EF-2003-003, [Sumitomo Ref: QAM-0014] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A7.3.1	Nishiyama, M, Katagi, T and Takimoto, Y.	2004	Stability in air of S-1264. Report No. EF-2004-032. [Sumitomo Ref: QAP-0032] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A7.4.1.1-01	Lima, W.	2004	S-1264 – Acute Toxicity to Rainbow Trout (Oncorhynchus mykiss) Under Flow-Through Conditions. Report No. 13048.6398. [Sumitomo Ref: QAW-0007]. GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A7.4.1.1-02	Gries, T.	2002	[methoxymethylbenzyl-alpha-^{14}C]S-1264: Acute toxicity test with common carp (Cyprinus carpio) under flow-through conditions. Report No. 1043.010.174. [Sumitomo ref: QAW-0002]. GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A7.4.1.2	Putt, A.E.	2004	S-1264 – Acute Toxicity to Water Fleas (*Daphnia magna*) Under Flow-Through Conditions. Report No. 13048.6397. [Sumitomo ref: QAW-0006]. GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A7.4.1.3	Hoberg, J.R.	2004	S-1264- Toxicity to the Freshwater Green Alga, *Pseudokirchneriella subcapitata*. Report No. 13048.6441. [Sumitomo Ref: QAW-0009] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A7.4.1.4	McLaughlin, S.P.	2004	S-1264 – Activated Sludge Respiration Inhibition Report No. 13048.6442. [Sumitomo Ref: QAW-0008]. GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A7.4.3.3.1	Yakata, N.	2002	Bioaccumulation Test of S-1264 Carp. Report No. 43789. [Sumitomo Ref: QAM-0020] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A7.4.3.5.1	Picard, C. R.	2009	S-1264 Technical Grade – Toxicity Test with Sediment-Dwelling Midges (Chironomus riparius) Using Spiked Sediment including Food Under Static Conditions. Report No. 13048.6598. [Sumitomo Ref: QAW-0016] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A7.5.3.1.1	Gallagher, S.P., Grimes, J. and Beavers, J.B.	2003c	S-1264: An acute oral toxicity study with the Northern Bobwhite. Report No. 166-172, [Sumitomo reference: QAW-0005].	Y (New/	Sumitomo Chemical Co. Ltd

Section No /Reference No. in Doc IIIA	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			GLP, Unpublished	First)	
A7.5.3.1.2/ 01	Gallagher, S. P., Grimes, J. Martin, K.H. and Beavers, J.B.	2003a	S-1264: A dietary LC50 study with the Mallard Report No. 166-171, [Sumitomo ref: QAW 0004]. GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A7.5.3.1.2/ 02	Gallagher, S. P., Grimes, J., Martin, K.H. and Beavers, J.B.	2003b	S-1264: A dietary LC50 study with the Northern Bobwhite. Report No. 166-170. [Sumitomo ref: QAW 0003]. GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
A8	Anon	2005	MSDS for Sumi-One TG Non-GLP, published	N	Sumitomo Chemical Co. Ltd
A9	Anon	2005	MSDS for Sumi-One TG Non-GLP, published	N	Sumitomo Chemical Co. Ltd

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Section No /Reference No. in Doc IIIB	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
B3.1	Shono, F.	2004a	Stability test of S-1264 Liquid. Report No. NPF01046, [Sumitomo Ref: QAF 0009] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B3.2	Sweetapple G.G. and Lentz N. R.	2003	Determination of Physical-Chemical Properties of S-1264. Report No 015682-1, [Sumitomo Ref: QAP 0020] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B3.2	Anon	2005	MSDS for Norpar 15 . Non-GLP, published	N	Sumitomo Chemical Co. Ltd
B3.4	Sweetapple G.G. and Lentz N. R.	2003	Determination of Physical-Chemical Properties of S-1264. Report No 015682-1, [Sumitomo Ref: QAP 0020] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B3.4	Anon	2005	MSDS for Norpar 15 Non-GLP, published	N	Sumitomo Chemical Co. Ltd
B3.7	Shono, F.	2004a	Stability test of S-1264 Liquid. Report No. NPF01046, [Sumitomo Ref: QAF 0009] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B3.7	Shono, F	2004b	Stability test of S-1264 Liquid. Report No. NPF01046, [Sumitomo Ref: QAF 0012] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B4.1	Shono, F.	2004c	Analytical methods for the determination of active substance in S-1264 Liquid. Report No. B6502, [Sumitomo Ref: QAA 0024] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B4.1	Shono, F	2004a	Stability test of S-1264 Liquid. Report No. NPF01046, [Sumitomo Ref: QAF 0009] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B5.10-01	Anon.	2000a	Efficacy evaluation of S-1264 paper strip in 28 m^3 chamber in comparison with a fan vaporizer and a vaporizer liquid. Report No and date: not given Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B5.10-02	Anon.	2000b	Efficacy evaluation of S-1264 paper strip in 28 m^3 chamber in comparison with transfluthrin for 480 hrs. Report No.: not given Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd

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B5.10-03	Muto, A	2002a	Basic efficacy evaluation of "S-1264 Liquid" against adult common house mosquitoes. Report No.: not given Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B5.10-04	Muto, A	2002b	Efficacy of "S-1264 Liquid" against adult mosquitoes in a living room. Report No.: not given Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B5.10-05	Serit, M	2003	Efficacy of mosquito coils containing 0.005% w/w S-1264 and 0.0075% w/w S-1264 compared with SIRIM standard mosquito coil containing 0.2% w/w Pynamin Forte evaluated using Glass Chamber test method (LS-BT-T14) following Malaysian Standard (MS 23: Part 2: 1986) against mosquitoes Aedes aegypti and Culex quinquefasciatus. Report No TS-03101. Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B5.10-06	Shono, Y	2002a	Basic efficacy evaluation of S-1264 vaporizer liquid formulation under laboratory conditions (Part 2). Report No not given. Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B5.10-07	Shono, Y	2002b	Basic efficacy evaluation of S-1264 vaporizer liquid formulation under laboratory conditions (Part 1); Setting of optimum S-1264 content. Report No not given. Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B5.10-08	Shono, Y	2002c	Efficacy evaluation of of S-1264 vaporizer liquid under semi-field condition. Report No not given Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B5.10-09	Sumitomo Chemical Co. Ltd	2005	Draft label for SumiOne® Liquid Vapouriser Non-GLP, Unpublished	N	Sumitomo Chemical Co. Ltd
B5.10-10	Yee, C. S.	2009a	Bio-efficacy evaluation of a SumiOne® LV vs. a European commercial standard in large chamber (30 m^3) against *Aedes aegypti* mosquitoes. Report No.: TS-09151., 13.07.2009. Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B5.10-11	Yee, C. S.	2009b	Bio-efficacy evaluation of a SumiOne® LV vs a European commercial standard in large chamber (30 m^3) against *Culex quinquefasciatus* mosquitoes. Report No.: TS-09152., 13.07.2009. Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B5.10-12	Lee, L. L.	2009a	Evaluation of SumiOne® LV vs. European Commercial Standard. Report No. TS-09150R1 28.07.2009. Non-GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd

Section No /Reference No. in Doc IIIB	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
B5.11	Hopley, J	2005	Letter subject: Resistance – metofluthrin No report number Non GLP, unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B6.1.1	Kunimatsu T.	2002a	Single Does Oral Toxicity Study of S-1264 Liquid in Rats. Report No. 3681. [Sumitomo Ref: QAT-0006] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B6.1.2	Kunimatsu, T.	2002b	Single Dose Dermal Toxicity Study of S-1264 Liquid in Rats. Report No. 3682, [Sumitomo Ref: QAT-0007] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B6.1.3/01	Omori, M.	2002a	Single Inhalation Toxicity Study of S-1264 Liquid in Rats. Report SBL 27-07, [Sumitomo Ref: QAT-0023] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B6.1.3/02	Omori, M.	2002b	Four Week Repeated Inhalation Toxicity of S-1264 Liquid in Rats. Report SBL-27-09 GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B6.2	Nakamura, Y.	2001	Skin and eye irritation tests of S-1264 Liquid in rabbits. Report No. 3635, [Sumitomo Ref: QAT-0015] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B6.3	Nakamura, Y	2002	Skin sensitization test of S-1264 Liquid in guinea pigs. Report No. 3691. [Sumitomo Ref: QAT-0008] GLP, Unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B6.4-01	McDougal, J., Pollard, D., Weisman, W., Garrett, C., and Miller, T	2000	Assessment of skin absorption and penetration of JP-8 jet fuel and its components. Tox. Sci. 55:247-255. Non-GLP, Published	No	n.a.
B6.4-02	Woollen BH, Marsh JR, Laird WJD, et al.	1992	The metabolism of cypermethrin in man: Differences in urinary metabolite profiles following oral and dermal administration. Xenobiotica 22(8):983-991. Non-GLP, Published	No	n.a.
B6.4-03	Eadsforth CV, Bragt PC, van Sittert NJ	1988	Human dose-excretion studies with pyrethroid insecticides cypermethrin and alphacypermethrin: relevance for biological monitoring. Xenobiotica 18(5): 603-14 Non-GLP, Published	No	n.a.
B6.4-04	Ross, JH, Driver, JH, Cochran, RC, Thongsinthus	2001	Could pesticide toxicology studies be more relevant to occupational risk assessment?. Ann. Occup. Hyg. 45(1001):S5-S17 Non-GLP, Published	No	n.a.

Section No /Reference No. in Doc IIIB	Author(s)	Year	Title Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
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B6.6-01	Matsunaga, T.	2002a	Analytical test of the active ingredient concentration in the air under normal use of S-1264 liquid. Report No. 20020055 [Sumitomo re: QAF-0020]. Non-GLP, unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B6.6-02	Matsunaga, T.	2002b	A Study on Determination of Amount of Active Ingredient Vaporized from S-1264 Liquid Report No. 20020055 [Sumitomo re: QAF-0019]	Y (New/ First)	Sumitomo Chemical Co. Ltd
B6.6-04	Matsumoto, O.	2005	A Study on Determination of Residual Amount of Liquid after Use-Up of S-1264 Liquid Vaporizer. [Sumitomo Ref: QAF-0018] Non-GLP, unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B6.6-05	Matoba, Y., Takimoto, Y.	1996	Indoor distribution of Etoc®. Evaporated by an Electric Vaporizer. Report No. FFF-0123. [Sumitomo Ref: FFF-0123] Non-GLP, unpublished	Y (New/ First)	Sumitomo Chemical Co. Ltd
B8-01	Anon	2005	MSDS for Norpar 15 Non-GLP, published	N	Sumitomo Chemical Co. Ltd
B8-02	Anon	2005	MSDS for SumiOne® Liquid Vapouriser Non-GLP, published	N	Sumitomo Chemical Co. Ltd
B9-01	Anon	2005	MSDS for SumiOne® Liquid Vapouriser Non-GLP, published	N	Sumitomo Chemical Co. Ltd