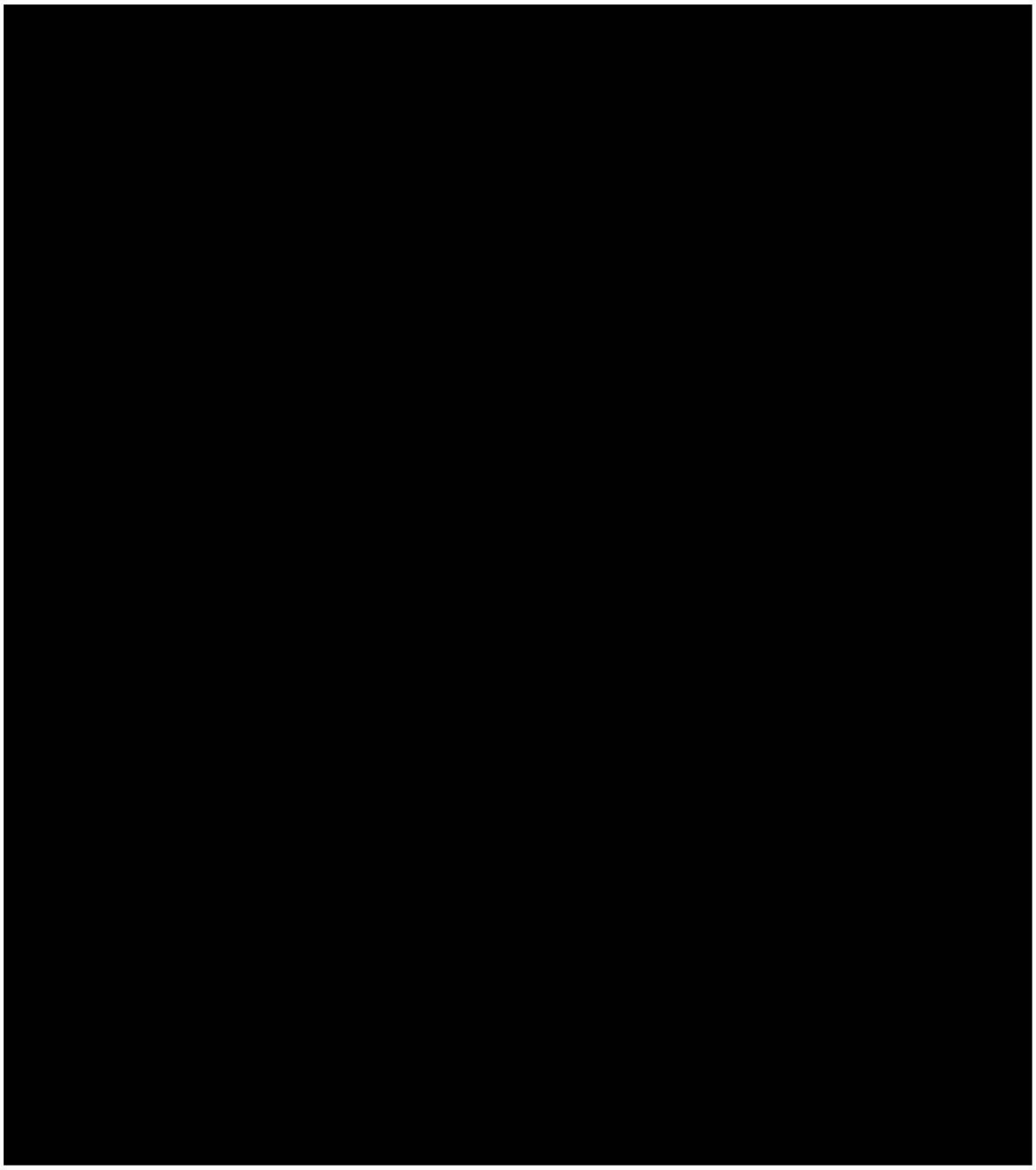
[redacted]

[redacted]

[redacted]

[redacted]



[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Section 6.2.2 Percutaneous absorption *(in vitro* test)

Section A6.2(2) **Percutaneous absorption *(in vitro* test)**
Annex Point IIA6.2 ***In vitro* absorption through human epidermis**
IUCLID 5/8

			Official use only
		13 REFERENCE	
1.1	**Reference**	[redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Sumitomo Chemical Co., Ltd.	
1.2.2	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I/IA.	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	This study was conducted according to the following Regulatory guidelines and guidance documents: 1) OECD (2004a). Organisation for Economic Co-operation and Development. Test Guideline 428: Skin Absorption: *In Vitro* Method. Organisation for Economic Co-operation and Development, Paris. 2) OECD (2004b). Organisation for Economic Co-operation and Development. Guidance Document No. 28: The Conduct of Skin Absorption Studies. Organisation for Economic Co-operation and Development, Paris. 3) European Commission (2004). Guidance Document on Dermal Absorption. Sanco/222/2000 rev. 7 (19th March 2004).	
2.2	**GLP**	[redacted]	
2.3	**Deviations**	[redacted]	
		3 MATERIALS AND METHODS	
3.1	**Test material**	[redacted] d-Phenothrin[redacted]	
3.1.1	Lot/Batch number	[redacted]	
3.1.2	Specification	As given in section 2.	
3.1.2.1	Description	[redacted]	
3.1.2.2	Purity	[redacted]	
3.1.2.3	Stability	[redacted]	
3.1.2.4	Radiolabelling	Not applicable.	X
3.2	**Study conduct**		

Section A6.2(2)
Annex Point IIA6.2
IUCLID 5/8

Percutaneous absorption *(in vitro* test)
***In vitro* absorption through human epidermis**

X

3.2.1 Dose preparation

The dose was prepared, conforming with instructions supplied by the Sponsor, to give a 1% w/v [redacted] nominal concentration in ethanol. The dose preparation solution was not analysed for concentration or stability.

[redacted]

3.2.2 Analytical techniques

<u>High performance liquid chromatography conditions</u>

An initial analytical method development study and a preliminary study concluded that the analytical method shown below was the most suitable for use in this study.

Column:	Waters µBondupak phenyl; 10 µ; 150 mm x 3.9 mm
Mobile phase:	Methanol : water (80 : 20 v/v)
Flow rate:	1.25 ml/min
Detector wavelength:	230 nm
Injection volume:	25 µl

The preliminary study using pig epidermis also concluded that a 1:1 dilution of each mass balance sample obtained, with water, was necessary prior to analysis to achieve suitable chromatographic quality. The reproducibility and recovery of the test material was unaffected.
An associated preliminary study also indicated that, as a precaution, taking all time course samples into amber vials and storing all samples in the fridge, including mass balance samples, minimized any effects of light or temperature on test substance breakdown. These procedures were therefore employed in this study.
From examination of the data, the limit of quantification (LOQ) using the above procedure was set at 0.03 µg/ml.

3.2.3 Human skin preparation

Extraneous tissue was removed from human whole skin samples [redacted]

3.2.4 Assemby of diffused cells

The type of glass diffusion cell used in this study has an exposed [redacted]

3.2.5 Measurement of membrane integrity

Membrane integrity was determined by measurement [redacted]

3.2.6 Measurement of test substance absorption

No entry field

Section A6.2(2)
Annex Point IIA6.2
IUCLID 5/8

Percutaneous absorption *(in vitro* test)
***In vitro* absorption through human epidermis**

3.2.6.1	Pre-treatment of cells and dosing	[redacted] X [redacted] X [redacted]
3.2.6.2	Sampling of receptor fluid	At recorded intervals (1, 2, 3, 4, 6, 8, 10, 12, 16, 20 and 24 hours) 500µl samples of receptor fluid were taken using an autosampler. [redacted] fluid in the receptor chamber was discarded and the chamber rinsed with [redacted]
3.2.7	Measurement of mass balance	The donor chamber was carefully removed, washed with ethanol (10ml) [redacted]

Section A6.2(2)
Annex Point IIA6.2
IUCLID 5/8

Percutaneous absorption *(in vitro* test)
***In vitro* absorption through human epidermis**

[redacted]

3.2.8 Definition of absorbed Sumithrin

4 RESULTS AND DISCUSSION

4.1 Percutaneous absorption

The results obtained in this study are summarised [redacted] where data are presented both in terms of absorption rate and in terms of amount and percent of the dose applied during periods representing typical working days (6, 8 and 10h) and at 24h.

[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

Section A6.2(2)
Annex Point IIA6.2
IUCLID 5/8

Percutaneous absorption *(in vitro* test)
***In vitro* absorption through human epidermis**

5.1 Materials and methods

The study was performed to GLP and OECD Test Guideline 428.

The absorption of Sumithrin from a nominal 1% w/v Sumithrin formulation, (actual content 10g Sumithrin/l) has been measured in vitro through human epidermis.

[redacted]

5.2 Results and discussion

[redacted]

Section A6.2(2) Annex Point IIA6.2 IUCLID 5/8	**Percutaneous absorption *(in vitro* test)** ***In vitro* absorption through human epidermis**
5.3.1 Reliability	1
5.3.2 Deficiencies	No

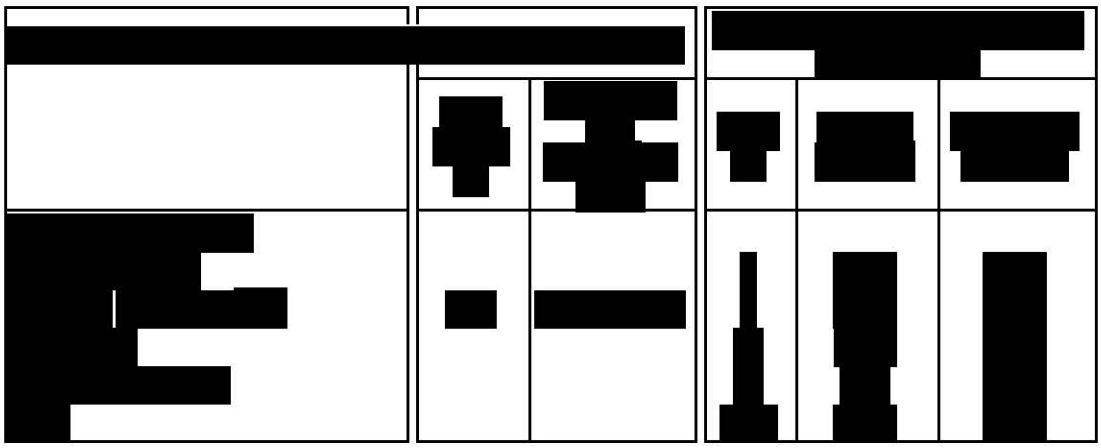
	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted] The skin absorption of the substance should be recorded as 4.5% of applied dose [redacted].
	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	None
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*

Section A6.2(2)
Annex Point IIA6.2
IUCLID 5/8

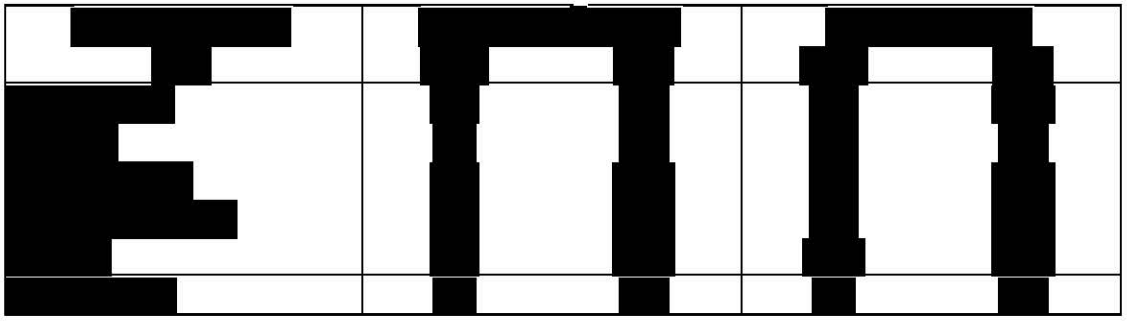
Percutaneous absorption *(in vitro* test)
***In vitro* absorption through human epidermis**

Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

[redacted]



[redacted]



[redacted]

[redacted]

Section 6.3.1 Subacute oral toxicity

Annex Point IIA6.4 **Subacute dietary toxicity study in mice**

IUCLID 5.4/1

			Official use only
		14 REFERENCE	
1.1	**Reference**	[redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Sumitomo Chemicals Co., Ltd.	
1.2.2	Companies with letter of access	Sumitomo Chemical (UK) PLC.	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I/IA.	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	This is a dose range finding study. The study report makes no claims on guideline compliance.	
2.2	**GLP**	[redacted]	x
2.3	**Deviations**	This study has been checked for compliance with OECD 407 (adopted 27 July 1995). The following deviations were noted: haematology and clinical chemistry parameters investigated, and organs weighed and examined histopathologically do not correspond with guideline.	
		3 MATERIALS AND METHODS	
3.1	**Test material**	[redacted] d-Phenothrin.	
3.1.1	Lot/Batch number	[redacted].	
3.1.2	Specification	[redacted]	
3.1.2.1	Description	[redacted].	
3.1.2.2	Purity	[redacted]	
3.1.2.3	Stability	Not reported. However, test diets were analysed (see 3.3.4.2).	
3.2	**Test Animals**	*Non-entry field*	
3.2.1	Species	Mouse	
3.2.2	Strain	[redacted]	
3.2.3	Source	[redacted].	
3.2.4	Sex	Male and female.	
3.2.5	Age/weight at study initiation	[redacted]	

Section 6.3.1 Subacute oral toxicity

Annex Point IIA6.4 **Subacute dietary toxicity study in mice**

IUCLID 5.4/1

3.2.6	Number of animals per group	[redacted]
3.2.7	Control animals	Yes
3.3	**Administration/ Exposure**	Oral
3.3.1	Duration of treatment	5 weeks
3.3.2	Frequency of exposure	Daily
3.3.3	Postexposure period	None
3.3.4	**Oral**	
3.3.4.1	Type	Dietary
3.3.4.2	Concentration	

Group	1	2	3	4	5
Dose Level (ppm)	[redacted]				
Achieved dose [1] (mg/kg bw/d) – Males	0	56.7	189.5	565.7	1957.6
Achieved dose [1] (mg/kg bw/d) – Females	0	71.6	230.9	710.5	2339.4

[redacted]

3.3.4.3	Vehicle	None
3.3.4.4	Concentration in vehicle	Not relevant.
3.3.4.5	Total volume applied	Not applicable.
3.3.4.6	Controls	Yes, controls received plain diet.
3.4	**Examinations**	
3.4.1	Observations	
3.4.1.1	Clinical signs	Mice were inspected twice daily for evidence of reaction to treatment or ill-health. In addition, all animals were handled and palpated once weekly throughout. The outcome of this examination was recorded for every animal. Any deviations from normal were recorded in respect of nature, date of onset, duration and progress.
3.4.1.2	Mortality	Each cage was inspected for the presence of moribund animals twice daily.
3.4.2	Body weight	Each animal was weighed prior to the randomisation and allocation procedures, on the day treatment commenced (Day 0) and at weekly

Section 6.3.1 Subacute oral toxicity

Annex Point IIA6.4 **Subacute dietary toxicity study in mice**

IUCLID 5.4/1

		intervals thereafter.	
3.4.3	Food consumption	Food consumption The weight of food consumed by each mouse was calculated weekly from measurements of food offered and food remaining. Group mean values were calculated from the total amount consumed by each group. Efficiency of food conversion Group mean food conversion ratios were calculated at weekly intervals as the amount of food consumed per unit gain of bodyweight. Achieved dosage of Sumithrin The group mean achieved dosages, expressed as mg/kg bodyweight/day, were calculated at the same intervals as bodyweights, from the group mean bodyweight and food consumption data, and nominal concentrations of Sumithrin in the diet.	
3.4.4	Water consumption	Water consumption was assessed daily by visual inspection of the water bottles at approximately 10 am. Precise measurement was performed during a five day period in Weeks 1 and 5 for all surviving animals.	
3.4.5	Ophthalmoscopic examination	Not performed.	
3.4.6	Haematology	[redacted]	x
3.4.7	Clinical Chemistry		x
3.4.8	Urinalysis		
3.5	**Sacrifice and pathology**		
3.5.1	Organ Weights	[redacted]	x
[redacted]			x
3.5.3	Other examinations	None	
3.5.4	Statistics	Parameters were analysed with recognised statistical techniques.	
3.6	**Further remarks**	None	

Section 6.3.1 Subacute oral toxicity

Annex Point IIA6.4 **Subacute dietary toxicity study in mice**

IUCLID 5.4/1

4 RESULTS AND DISCUSSION

4.1 Observations

4.1.1 Clinical signs: No signs of response to treatment were seen at any time during the study.

4.1.2 Mortality: [redacted]

4.2 Body weight gain: The growth of male and female mice receiving Sumithrin was similar to that of control animals.

4.3 Food consumption and compound intake: [redacted]

4.4 Ophthalmoscopic examination: Not performed.

4.5 Blood and urine analysis

4.5.1 Haematology: [redacted]

4.5.2 Clinical chemistry: [redacted]

4.5.3 Urinalysis: Not investigated.

4.6 Sacrifice and pathology

4.6.1 Organ weights: [redacted]

Section 6.3.1 Subacute oral toxicity

Annex Point IIA6.4 **Subacute dietary toxicity study in mice**

IUCLID 5.4/1

4.6.2 Gross and histopathology

[redacted]

4.7 Other

Water consumption

Water consumption amongst mice receiving 10000 ppm Sumithrin was higher than that of their respective controls during the first week of treatment. However there was no difference between mice receiving this concentration and their respective controls during Week 5. Water consumption amongst the remaining groups was unaffected by treatment.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

This study was conducted according to GLP. The report makes no claims on guideline compliance.
Sumithrin was administered in the diet for five weeks, to groups of [redacted] male and [redacted] female [redacted] mice at dietary concentrations of 300, 1000, 3000 or 10000 ppm. A similarly constituted group received untreated diet and served as controls.

5.2 Results and discussion

[redacted]

Section 6.3.1 Subacute oral toxicity

Annex Point IIA6.4 **Subacute dietary toxicity study in mice**

IUCLID 5.4/1

5.3 Conclusion

[redacted]

[redacted]

5.3.3 Other

5.3.4 Reliability

5.3.5 Deficiencies No

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*Give date of action*

Section 6.3.1 Subacute oral toxicity

Annex Point IIA6.4 **Subacute dietary toxicity study in mice**

IUCLID 5.4/1

Materials and Methods	[redacted]
	[redacted]
	[redacted]
	The applicants account is otherwise acceptable.
Conclusion	[redacted] (56.7 and 71.6 mg/kg bw/day in males and females respectively).
	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	

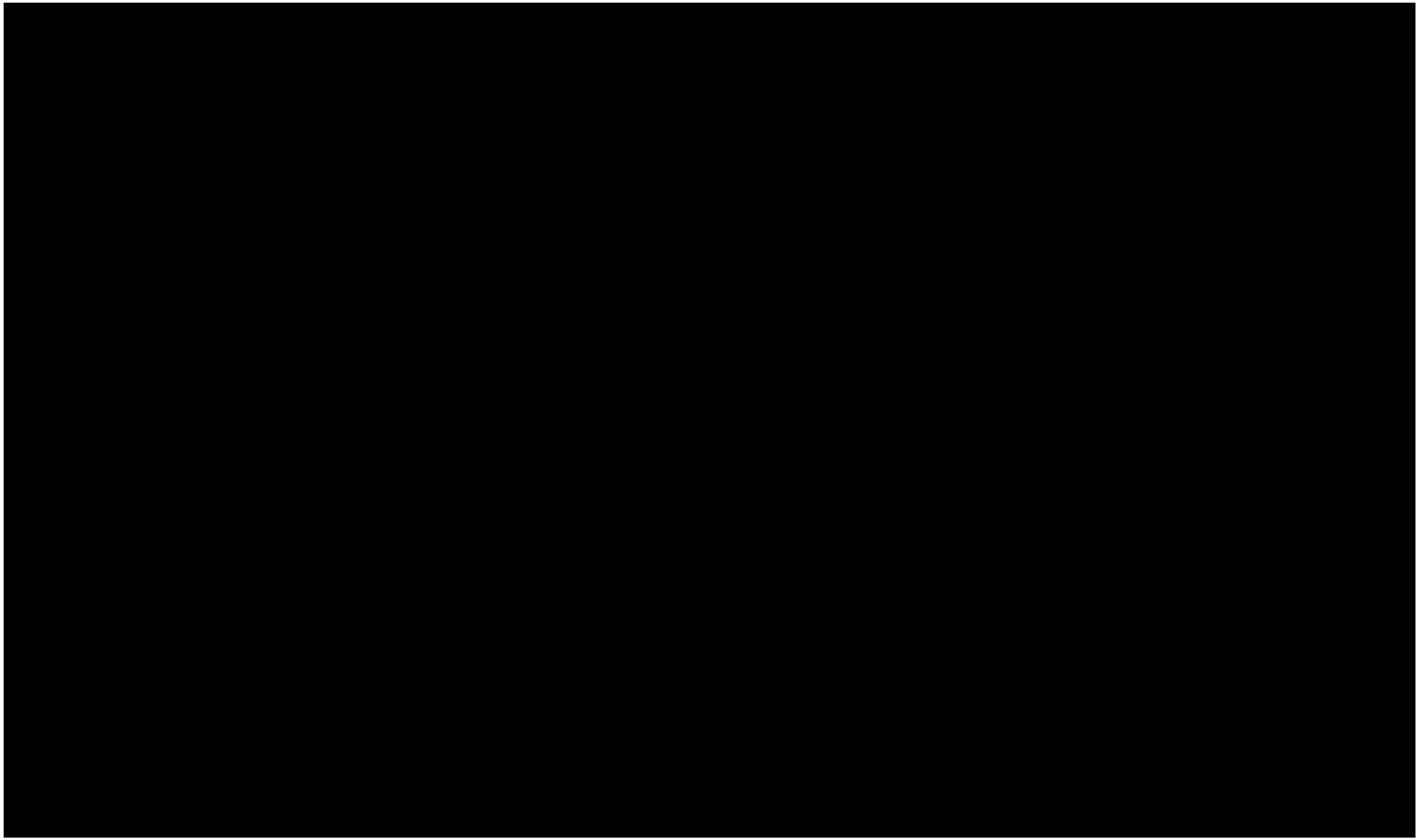
Section 6.3.1 Subacute oral toxicity

Annex Point IIA6.4 **Subacute dietary toxicity study in mice**

IUCLID 5.4/1

	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

[redacted]



[redacted]

Section 6.6.2 Repeated dose toxicity (dermal)

Section IIIA 6.3.2 **Annex Point IIA, VI.6.3**	**Repeated dose toxicity (dermal)**
	[redacted]
Other existing data [ ]	**Technically not feasible [ ]** **Scientifically unjustified [X]**
Limited exposure [ ]	**Other justification [ ]**
Detailed justification:	No studies are available investigating repeat dose toxicity via the dermal route. As d-phenothrin has shown very low acute dermal toxicity it is considered appropriate to extrapolate from oral repeat dose toxicity data when assessing risk from dermal exposure.
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*
	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*Give date of action*
Evaluation of applicant's justification	[redacted]
Conclusion	[redacted] Acceptable.
Remarks	None
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*

Section IIIA 6.3.2 Annex Point IIA, VI.6.3	Repeated dose toxicity (dermal)
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section 6.3.3 Subacute inhalation toxicity

Section A6.3.3	**Subacute inhalation toxicity**
Annex Point IIA6.3	**Subacute inhalation toxicity study in rats**
IUCLID 5.4/7	

			Official use only
		15 REFERENCE	
1.1	**Reference**	[redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Sumitomo Chemicals Co., Ltd.	
1.2.2	Companies with letter of access	Sumitomo Chemical (UK) PLC.	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	The study was conducted prior to GLP, no guideline was available at the time the study was conducted.	
2.2	**GLP**	[redacted]	
2.3	**Deviations**	The study meets many of the criteria of OECD Test Guideline 412 (adopted 12 May 1981). [redacted]	[redacted]
		3 MATERIALS AND METHODS	
3.1	**Test material**	[redacted] d-Phenothrin [redacted]	[redacted]
3.1.1	Lot/Batch number	[redacted]	
3.1.2	Specification	[redacted]	[redacted]
3.1.2.1	Description	Not described.	
3.1.2.2	Purity	[redacted]	
3.1.2.3	Stability	Not described.	
3.2	**Test Animals**	*Non-entry field*	
3.2.1	Species	Rat	
3.2.2	Strain	[redacted]	
3.2.3	Source	[redacted]	
3.2.4	Sex	Male and female.	
3.2.5	Age/weight at study	[redacted]	

Section A6.3.3 **Subacute inhalation toxicity**
Annex Point IIA6.3 **Subacute inhalation toxicity study in rats**
IUCLID 5.4/7

	initiation	[redacted]
3.2.6	Number of animals per group	[redacted]
3.2.7	Control animals	Yes, vehicle control and negative control
3.3	**Administration/ Exposure**	Inhalation
3.3.1	Duration of treatment	4 weeks.
3.3.2	Frequency of exposure	5 consecutive days per week.
3.3.3	Postexposure period	3 weeks.
3.3.4	**Inhalation**	
3.3.4.1	Type	Inhalation, whole body exposure.
3.3.4.2	Concentration	Measured concentrations: 41, 63, 210 mg/m^3.
3.3.4.3	Particle size	Not investigated
3.3.4.4	Type or preparation of particles	-
3.3.4.5	Vehicle	Deo base (deodorized kerosene).
3.3.4.6	Concentration in vehicle	1, 2, 10 (units not specified).
3.3.4.7	Duration of exposure	4 hours/day.
3.3.4.8	Controls	Vehicle controls received vehicle only. Negative controls did not receive vehicle however it is not clear if they were subjected to the test conditions.
3.4	**Examinations**	
3.4.1	Observations	
3.4.1.1	Clinical signs	Any toxic symptoms were recorded daily.
3.4.1.2	Mortality	Animals were examined once each day.
3.4.2	Body weight	Body weight was determined every 2-4 days during exposure and weekly thereafter.
3.4.3	Food consumption	Not measured.
3.4.4	Water consumption	Not measured.
3.4.5	Ophthalmoscopic examination	Not performed.
3.4.6	Haematology	[redacted]
3.4.7	Clinical Chemistry	

Section A6.3.3 **Subacute inhalation toxicity**
Annex Point IIA6.3 **Subacute inhalation toxicity study in rats**
IUCLID 5.4/7

		[redacted]
3.4.8	Urinalysis	Not performed.
3.5	**Sacrifice and pathology**	
3.5.1	Organ Weights	[redacted] Recovery animals The weights of the following organs were recorded: lung, liver, kidney, spleen, testis/ovary.
3.5.2	Gross and histopathology	[redacted]
3.5.3	Other examinations	None
3.5.4	Statistics	The data of body weight, haematology, biochemistry, and organ weight and its ratio to body weight were analysed statistically. The mean values of treated groups and the negative control group were compared with the vehicle control by using a Student's t test.
3.6	**Further remarks**	Dose level selection [redacted] Comment In this summary, only methods, results and conclusion of subacute inhalation toxicity in the rat with [redacted] are reported.

4 RESULTS AND DISCUSSION

4.1	**Observations**	
4.1.1	Clinical signs	No toxic symptoms were found in any animal.
4.1.2	Mortality	No deaths occurred during the study.
4.2	**Body weight gain**	[redacted]
4.3	**Food consumption and compound intake**	Not measured.
4.4	**Ophthalmoscopic examination**	Not examined.
4.5	**Blood and urine**	

Section A6.3.3 **Subacute inhalation toxicity**
Annex Point IIA6.3 **Subacute inhalation toxicity study in rats**
IUCLID 5.4/7

	analysis	
4.5.1	Haematology	[redacted]
4.5.2	Clinical chemistry	[redacted]
4.5.3	Urinalysis	Not investigated.
4.6	**Sacrifice and pathology**	
4.6.1	Organ weights	[redacted]
4.6.2	Gross and histopathology	
4.7	**Other**	

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted]

Groups of 15 male and 15 female [redacted] rats were exposed to the mist [redacted] at aerial concentrations of 0, 41, 63 and 210 mg/m^3, for 4 weeks, 4 hours daily and 5 consecutive days per week. Also, one group of the animals (15 of each sex of both animal species) was simultaneously used as the negative control.

[redacted]

Section A6.3.3 **Subacute inhalation toxicity**

Annex Point IIA6.3 **Subacute inhalation toxicity study in rats**

IUCLID 5.4/7

5.2	**Results and discussion**	[redacted]
5.3	**Conclusion**	[redacted] was of extremely low toxicity in rats upon subacute inhalation exposure.
5.3.1	LO(A)EL	> 210 mg/m^3
5.3.2	NO(A)EL	> 210 mg/m^3
5.3.3	Other	None
5.3.4	Reliability	2
5.3.5	Deficiencies	[redacted]

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*Give date of action*

Section A6.3.3 **Subacute inhalation toxicity**

Annex Point IIA6.3 **Subacute inhalation toxicity study in rats**

IUCLID 5.4/7

Materials and Methods	*State if the applicants version is acceptable or indicate relevant discrepancies referring to the (sub) heading numbers and to applicant's summary and conclusion.* [redacted]
Results and discussion	[redacted]
Conclusion	NO(A)EL: > 210 mg/m^3 Other conclusions: [redacted]
Reliability	[redacted]

Section A6.3.3 **Subacute inhalation toxicity**

Annex Point IIA6.3 **Subacute inhalation toxicity study in rats**

IUCLID 5.4/7

Acceptability	[redacted]
Remarks	
	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section 6.4.1(1) Subchronic oral toxicity

Section A6.4.1(1)	**Subchronic oral toxicity**
Annex Point IIA6.4	**Subchronic dietary toxicity study in rats**
IUCLID 5.4/2	

			Official use only
		16 REFERENCE	
1.1	**Reference**	[redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Sumitomo Chemicals Co., Ltd.	
1.2.2	Companies with letter of access	Sumitomo Chemical (UK) PLC.	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I/IA.	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	[redacted] The study essentially meets the requirements of OECD Test Guideline 408 (adopted 21 September 1998).	
2.2	**GLP**	[redacted]	x
2.3	**Deviations**	[redacted]	
		3 MATERIALS AND METHODS	
3.1	**Test material**	[redacted] d-Phenothrin.	
3.1.1	Lot/Batch number	[redacted]	
3.1.2	Specification	[redacted]	
3.1.2.1	Description	[redacted]	
3.1.2.2	Purity	[redacted]	
3.1.2.3	Stability	[redacted]	
3.2	**Test Animals**	*Non-entry field*	
3.2.1	Species	Rat	
3.2.2	Strain	[redacted]	
3.2.3	Source	[redacted]	

Section A6.4.1(1) **Subchronic oral toxicity**
Annex Point IIA6.4 **Subchronic dietary toxicity study in rats**
IUCLID 5.4/2

3.2.4	Sex	Male and female.
3.2.5	Age/weight at study initiation	[redacted]
3.2.6	Number of animals per group	[redacted]
3.2.7	Control animals	Yes
3.3	**Administration/ Exposure**	Oral
3.3.1	Duration of treatment	13 weeks.
3.3.2	Frequency of exposure	Daily
3.3.3	Postexposure period	None
3.3.4	**Oral**	
3.3.4.1	Type	Dietary
3.3.4.2	Concentration	

Group [redacted]	1 [redacted]	2 [redacted]	3 [redacted]	4 [redacted]	5 [redacted]
Achieved dose (mg/kg bw/d) – Males	0	21	70	216	706
Achieved dose (mg/kg bw/d) – Females	0	23	75	227	714

Accuracy, homogeneity and stability
The various analyses performed indicated that the homogeneity, stability and achieved concentrations of the dietary admixtures were satisfactory.

3.3.4.3	Vehicle	None
3.3.4.4	Concentration in vehicle	Not relevant.
3.3.4.5	Total volume applied	Not applicable.
3.3.4.6	Controls	Yes, controls received plain diet.
3.4	**Examinations**	
3.4.1	Observations	
3.4.1.1	Clinical signs	Rats were inspected twice daily during the treatment period for evidence of reaction to treatment or ill-health. In addition, all rats were handled and scrutinised once weekly.
3.4.1.2	Mortality	Each cage was scrutinised twice daily for moribund animals.
3.4.2	Body weight	Each rat was weighed on the day that treatment commenced and at weekly intervals thereafter. Group mean values were calculated at the same intervals.
3.4.3	Food consumption	The quantity of food eaten by each rat was calculated weekly.

Section A6.4.1(1) **Subchronic oral toxicity**
Annex Point IIA6.4 **Subchronic dietary toxicity study in rats**
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		Food conversion ratios were calculated at weekly intervals as the amount of food consumed per unit of bodyweight gain. Achieved dosages were calculated weekly and expressed as mg/kg bw/day.
3.4.4	Water consumption	Water consumption was assessed by daily visual observation of the water bottles. The water consumption of all cages in each group was measured over a 3 day period in each of Weeks 5/6 and 10/11.
3.4.5	Ophthalmoscopic examination	Not performed.
3.4.6	Haematology	Yes. After 5 and 11 weeks of treatment blood samples were obtained [redacted]
3.4.7	Clinical Chemistry	Yes. After 5 and 11 weeks of treatment blood samples were obtained [redacted]
3.4.8	Urinalysis	
3.5	**Sacrifice and pathology**	
3.5.1	Organ Weights	[redacted]
3.5.2	Gross and histopathology	[redacted]

Section A6.4.1(1) **Subchronic oral toxicity**
Annex Point IIA6.4 **Subchronic dietary toxicity study in rats**
IUCLID 5.4/2

[redacted]

3.5.3	Other examinations	None
3.5.4	Statistics	Parameters were analysed with recognised statistical techniques.
3.6	**Further remarks**	None

4 RESULTS AND DISCUSSION

4.1	**Observations**	
4.1.1	Clinical signs	There were no signs of reaction to treatment.
4.1.2	Mortality	No deaths occurred during the study.
4.2	**Body weight gain**	[redacted]
4.3	**Food consumption and compound intake**	[redacted]
4.4	**Ophthalmoscopic examination**	Not performed.
4.5	**Blood and urine analysis**	
4.5.1	Haematology	[redacted]
4.5.2	Clinical chemistry	[redacted]

Section A6.4.1(1) **Subchronic oral toxicity**
Annex Point IIA6.4 **Subchronic dietary toxicity study in rats**
IUCLID 5.4/2

4.5.3 Urinalysis — No treatment-related inter-group differences were recorded.

4.6 Sacrifice and pathology

4.6.1 Organ weights

4.6.2 Gross and histopathology

Section A6.4.1(1) **Subchronic oral toxicity**
Annex Point IIA6.4 **Subchronic dietary toxicity study in rats**
IUCLID 5.4/2

The changes noted were incidental, minor in character [redacted]

4.7 Other

Water consumption

The water consumption of the control and treated rats was similar.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted]

5.2 Results and discussion

[redacted]

Section A6.4.1(1) **Subchronic oral toxicity**
Annex Point IIA6.4 **Subchronic dietary toxicity study in rats**
IUCLID 5.4/2

		weeks produced mild intoxication, with the liver as the target organ.
5.3	**Conclusion**	
5.3.2	NO(A)EL	70 and 75 mg/kg bw/d in males and females, respectively).
5.3.3	Other	
5.3.4	Reliability	
5.3.5	Deficiencies	

Evaluation by Competent Authorities
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
EVALUATION BY RAPPORTEUR MEMBER STATE

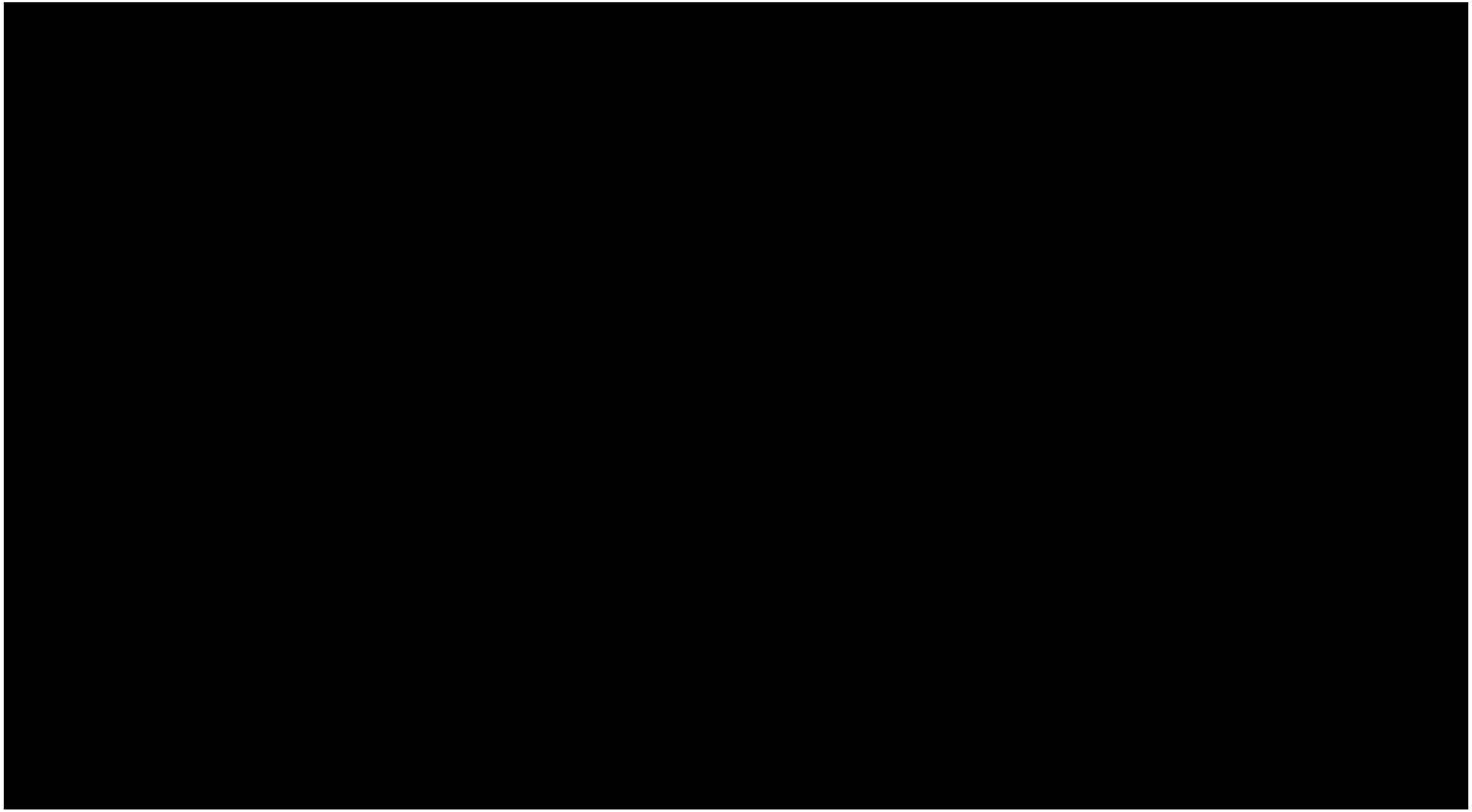
Section A6.4.1(1) **Subchronic oral toxicity**

Annex Point IIA6.4 **Subchronic dietary toxicity study in rats**

IUCLID 5.4/2

Reliability	[redacted]
	[redacted]
Remarks	

	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	



[redacted]

[redacted]

[redacted]

[redacted]

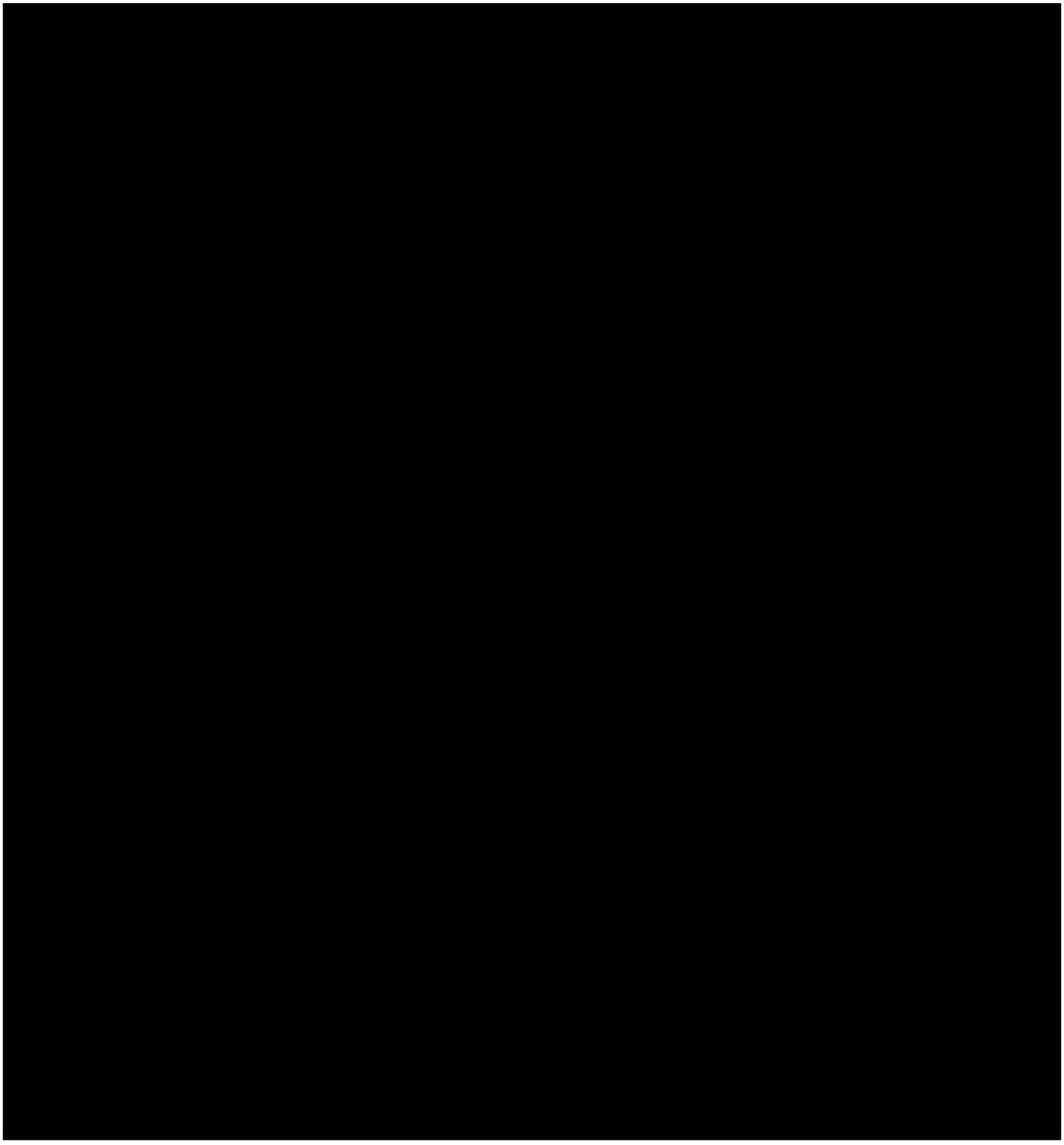
[redacted]

[redacted]

[redacted]

[redacted]

[redacted]



[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Section 6.4.1(2) Subchronic oral toxicity

Section A6.4.1(2) **Subchronic oral toxicity**

Annex Point IIA6.4 **Six months dietary toxicity study in rats**

IUCLID 5.4/3

			Official use only
		17 REFERENCE	
1.1	**Reference**	[redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Sumitomo Chemicals Co., Ltd.	
1.2.2	Companies with letter of access	Sumitomo Chemical (UK) PLC.	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I/IA.	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	The test report makes no claims on guideline compliance.	
2.2	**GLP**	[redacted]	[redacted]
2.3	**Deviations**	[redacted]	
		3 MATERIALS AND METHODS	
3.1	**Test material**	[redacted] d-Phenothrin.	
3.1.1	Lot/Batch number	[redacted]	
3.1.2	Specification	[redacted]	
3.1.2.1	Description	[redacted]	
3.1.2.2	Purity	[redacted]	
3.1.2.3	Stability	[redacted]	
3.2	**Test Animals**	*Non-entry field*	
3.2.1	Species	Rat	
3.2.2	Strain	[redacted]	
3.2.3	Source	[redacted]	

Section A6.4.1(2) **Subchronic oral toxicity**
Annex Point IIA6.4 **Six months dietary toxicity study in rats**
IUCLID 5.4/3

3.2.4	Sex	Male and female.
3.2.5	Age/weight at study initiation	5 weeks Mean body weights of Main study animals on day 0: 129.1 to 130.4 g (males); 110.0 to 112.2 g (females)
3.2.6	Number of animals per group	[redacted]
3.2.7	Control animals	Yes
3.3	**Administration/ Exposure**	Oral
3.3.1	Duration of treatment	6 months (Main study) 3 months (Satellite study)
3.3.2	Frequency of exposure	Daily
3.3.3	Postexposure period	None
3.3.4	**Oral**	
3.3.4.1	Type	Dietary
3.3.4.2	Concentration	[redacted]
3.3.4.3	Vehicle	Accuracy, homogeneity and stability [redacted]
3.3.4.4	Concentration in vehicle	See 3.3.4.3.
3.3.4.5	Total volume applied	See 3.3.4.3.
3.3.4.6	Controls	It is assumed from the report that controls also received the diet preparations adjusted for corn oil content of 2 %.
3.4	**Examinations**	
3.4.1	Observations	
3.4.1.1	Clinical signs	All the animals were observed for any abnormal behaviour and death twice a day and palpated every two weeks.
3.4.1.2	Mortality	See 3.4.1.1.
3.4.2	Body weight	[redacted]

[redacted]		[redacted]	[redacted]	[redacted]
Achieved dose (mg/kg bw/d) – Males (Main study)	-	55.4	162.6	563.0
Achieved dose (mg/kg bw/d) – Females (Main study)	-	63.6	189.0	635.0

Section A6.4.1(2) **Subchronic oral toxicity**
Annex Point IIA6.4 **Six months dietary toxicity study in rats**
IUCLID 5.4/3

		[redacted]
3.4.3	Food consumption	The food intake of each cage in the main group was measured weekly for three consecutive days.
3.4.4	Water consumption	The water intake of each cage in the main group were measured weekly for three consecutive days.
3.4.5	Ophthalmoscopic examination	[redacted]
3.4.6	Haematology	
3.4.7	Clinical Chemistry	
3.4.8	Urinalysis	
3.5	**Sacrifice and pathology**	
3.5.1	Organ Weights	[redacted]
3.5.2	Gross and histopathology	The following tissues were examined microscopically for all main study [redacted]
3.5.3	Other examinations	None
3.5.4	Statistics	The mean value of body weight, food and water intakes, haematological and biochemical values and organ weight were statistically analyzed using Student's t-test.
3.6	**Further remarks**	None

4 RESULTS AND DISCUSSION

4.1	**Observations**	
4.1.1	Clinical signs	No abnormal clinical signs due to the test compound were found.

Section A6.4.1(2) **Subchronic oral toxicity**
Annex Point IIA6.4 **Six months dietary toxicity study in rats**
IUCLID 5.4/3

4.1.2	Mortality	No deaths occurred during the study.
4.2	**Body weight gain**	[redacted]
4.3	**Food consumption and compound intake**	
4.4	**Ophthalmoscopic examination**	
4.5	**Blood and urine analysis**	
4.5.1	Haematology	[redacted]
4.5.2	Clinical chemistry	[redacted]

[redacted]

[redacted]

4.5.3 Urinalysis

[redacted]

4.6 Sacrifice and pathology

4.6.1 Organ weights

[redacted]

Section A6.4.1(2)
Annex Point IIA6.4
IUCLID 5.4/3

Subchronic oral toxicity
Six months dietary toxicity study in rats

[redacted]

4.6.2 Gross and histopathology

Macroscopic pathology

[redacted]

4.7 Other

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted]

Section A6.4.1(2)
Annex Point IIA6.4
IUCLID 5.4/3

Subchronic oral toxicity
Six months dietary toxicity study in rats

[redacted]

5.3 Conclusion

[redacted]

5.3.2 NO(A)EL [redacted] 55.4 and 63.6 mg/kg bw/d in males and females, respectively).

5.3.3 Other [redacted]

5.3.4 Reliability [redacted]

5.3.5 Deficiencies [redacted]

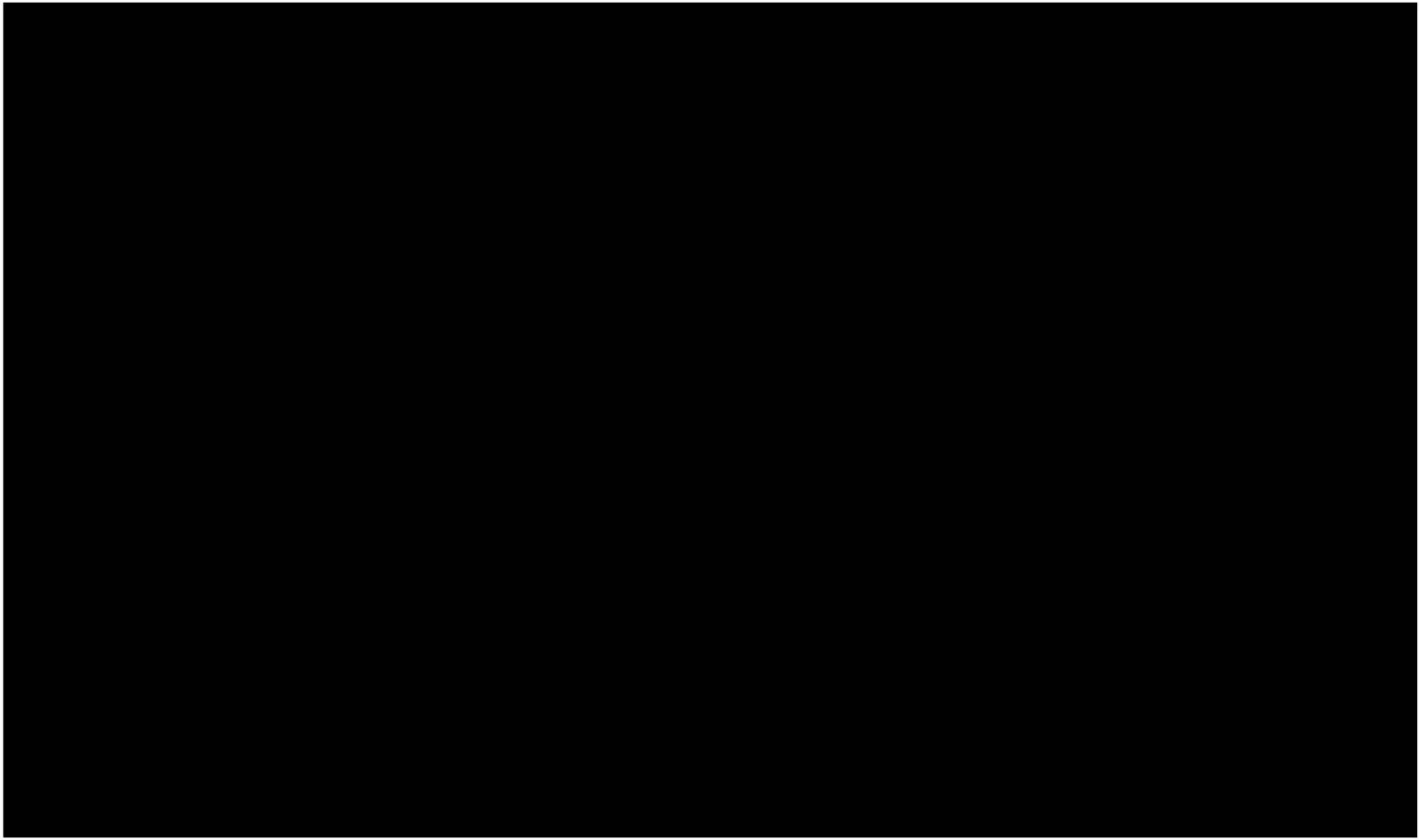
	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*Give date of action*
Materials and Methods	*State if the applicants version is acceptable or indicate relevant discrepancies referring to the (sub) heading numbers and to applicant's summary and conclusion.* [redacted]

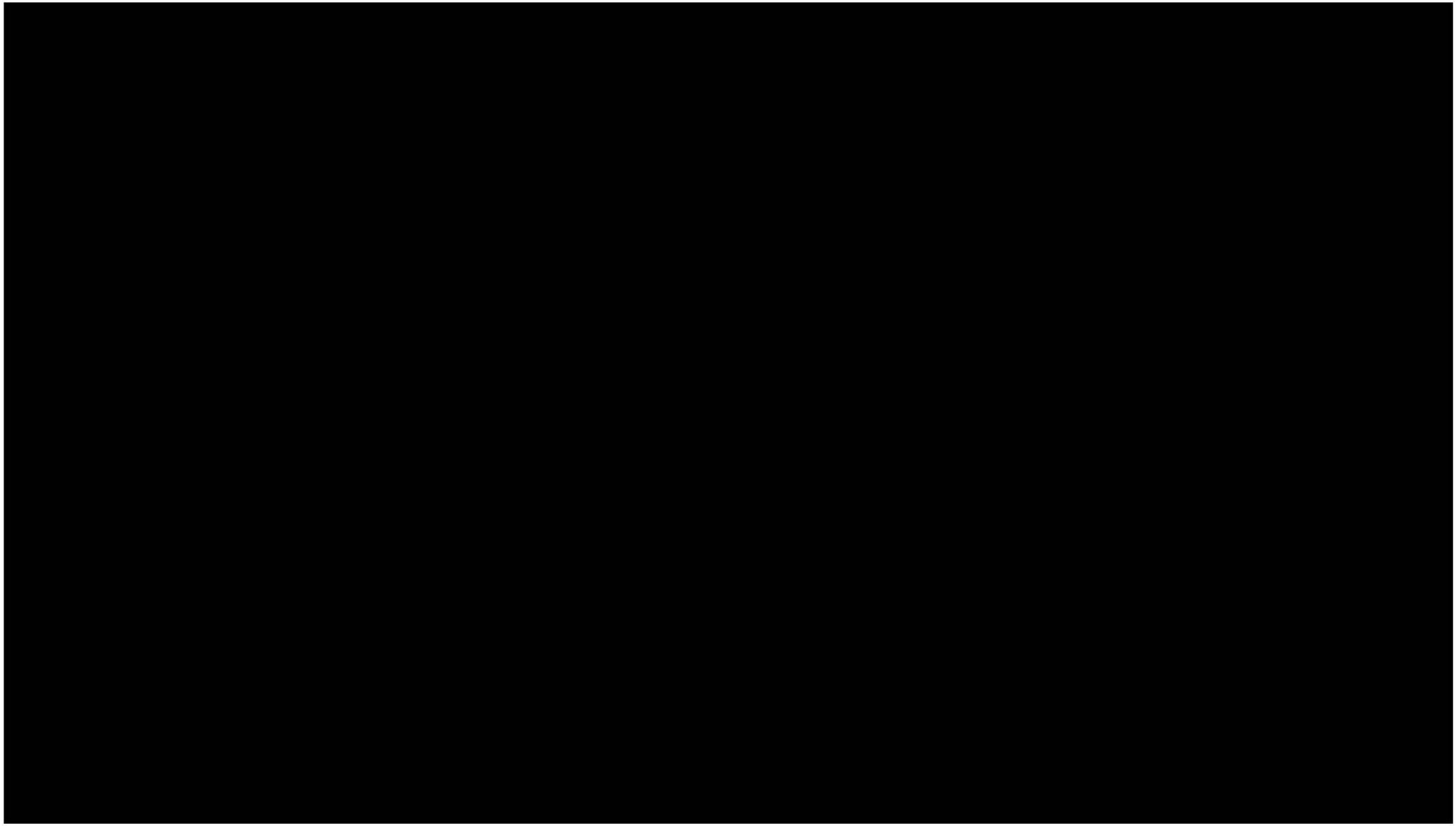
Section A6.4.1(2) **Subchronic oral toxicity**

Annex Point IIA6.4 **Six months dietary toxicity study in rats**

IUCLID 5.4/3

Results and discussion	[redacted]
	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	





[redacted]

Section 6.4.1 Subchronic oral toxicity dog

Section A6.4.1(3) Subchronic oral toxicity

Annex Point IIA6.4 Subchronic dietary toxicity study in dogs

IUCLID 5.4/5

			Official use only
		18 REFERENCE	
1.1	**Reference**	[redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Sumitomo Chemicals Co., Ltd.	
1.2.2	Companies with letter of access	Sumitomo Chemical (UK) PLC.	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I/IA.	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	[redacted]	
2.2	**GLP**	[redacted]	[redacted]
2.3	**Deviations**	[redacted]	
		3 MATERIALS AND METHODS	
3.1	**Test material**	[redacted] d-Phenothrin.	
3.1.1	Lot/Batch number	[redacted]	
3.1.2	Specification	[redacted]	
3.1.2.1	Description	[redacted]	
3.1.2.2	Purity	See point 3.1.1	
3.1.2.3	Stability	Not reported. However, test diets were analysed (see 3.3.4.2).	
3.2	**Test Animals**	*Non-entry field*	
3.2.1	Species	Dog	
3.2.2	Strain	[redacted]	
3.2.3	Source	[redacted]	
3.2.4	Sex	Male and female.	
3.2.5	Age/weight at study	[redacted]	

Section A6.4.1(3) **Subchronic oral toxicity**
Annex Point IIA6.4 **Subchronic dietary toxicity study in dogs**
IUCLID 5.4/5

	initiation	[redacted]
3.2.6	Number of animals per group	[redacted]
3.2.7	Control animals	Yes
3.3	**Administration/ Exposure**	Oral
3.3.1	Duration of treatment	26 weeks.
3.3.2	Frequency of exposure	Daily
3.3.3	Postexposure period	None
3.3.4	**Oral**	
3.3.4.1	Type	Dietary
3.3.4.2	Concentration	

Group [redacted]	1	2	3	4
Achieved dose (mg a.i. /kg bw/d) – Males [2]	0	3.02	9.27	30.87
Achieved dose (mg a. i. /kg bw/d) – Females [2]	0	3.14	9.30	32.90

[redacted]

3.3.4.3	Vehicle	None
3.3.4.4	Concentration in vehicle	Not relevant.
3.3.4.5	Total volume applied	Not applicable.
3.3.4.6	Controls	Yes, controls received plain diet.
3.4	**Examinations**	
3.4.1	Observations	
3.4.1.1	Clinical signs	All of the dogs were observed once daily for appearance, behaviour, elimination, and signs of toxic and pharmacologic effects.
3.4.1.2	Mortality	All dogs were observed twice daily for mortality and moribundity.
3.4.2	Body weight	Individual body weights were recorded weekly.
3.4.3	Food consumption	Individual food consumption was recorded daily.
3.4.4	Water consumption	Not measured.

Section A6.4.1(3) **Subchronic oral toxicity**
Annex Point IIA6.4 **Subchronic dietary toxicity study in dogs**
IUCLID 5.4/5

3.4.5	Ophthalmoscopic examination	[redacted]
3.4.6	Haematology	
3.4.7	Clinical Chemistry	
3.4.8	Urinalysis	
3.5	**Sacrifice and pathology**	
3.5.1	Organ Weights	[redacted]
3.5.2	Gross and histopathology	The following tissues were examined microscopically for all animals: [redacted]
3.5.3	Other examinations	None
3.5.4	Statistics	All parameters were analysed with recognised statistical techniques.
3.6	**Further remarks**	None

4 RESULTS AND DISCUSSION

4.1	**Observations**	
4.1.1	Clinical signs	There were no compound-related clinical signs noted during the study.
4.1.2	Mortality	[redacted]
4.2	**Body weight gain**	

Section A6.4.1(3) **Subchronic oral toxicity**

Annex Point IIA6.4 **Subchronic dietary toxicity study in dogs**

IUCLID 5.4/5

4.3 Food consumption and compound intake

4.4 Ophthalmoscopic examination

4.5 Blood and urine analysis

4.5.1 Haematology

4.5.2 Clinical chemistry

4.5.3 Urinalysis

4.6 Sacrifice and pathology

4.6.1 Organ weights

4.6.2 Gross and histopathology

Section A6.4.1(3) **Subchronic oral toxicity**
Annex Point IIA6.4 **Subchronic dietary toxicity study in dogs**
IUCLID 5.4/5

[redacted]

4.7 Other

None

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

This study was conducted according to GLP.

[redacted]

5.2 Results and discussion

[redacted]

5.3 Conclusion

[redacted]

Section A6.4.1(3) **Subchronic oral toxicity**

Annex Point IIA6.4 **Subchronic dietary toxicity study in dogs**

IUCLID 5.4/5

[redacted]		
5.3.2	NO(A)EL	[redacted] 9.27 and 9.30 mg/kg bw/d in males and females,
[redacted]		[redacted]
5.3.4	Reliability	[redacted]
[redacted]		[redacted]

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*Give date of action*
Materials and Methods	[redacted]
	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*

Section A6.4.1(3)	**Subchronic oral toxicity**
Annex Point IIA6.4	**Subchronic dietary toxicity study in dogs**
IUCLID 5.4/5	

Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

[redacted]

[redacted]