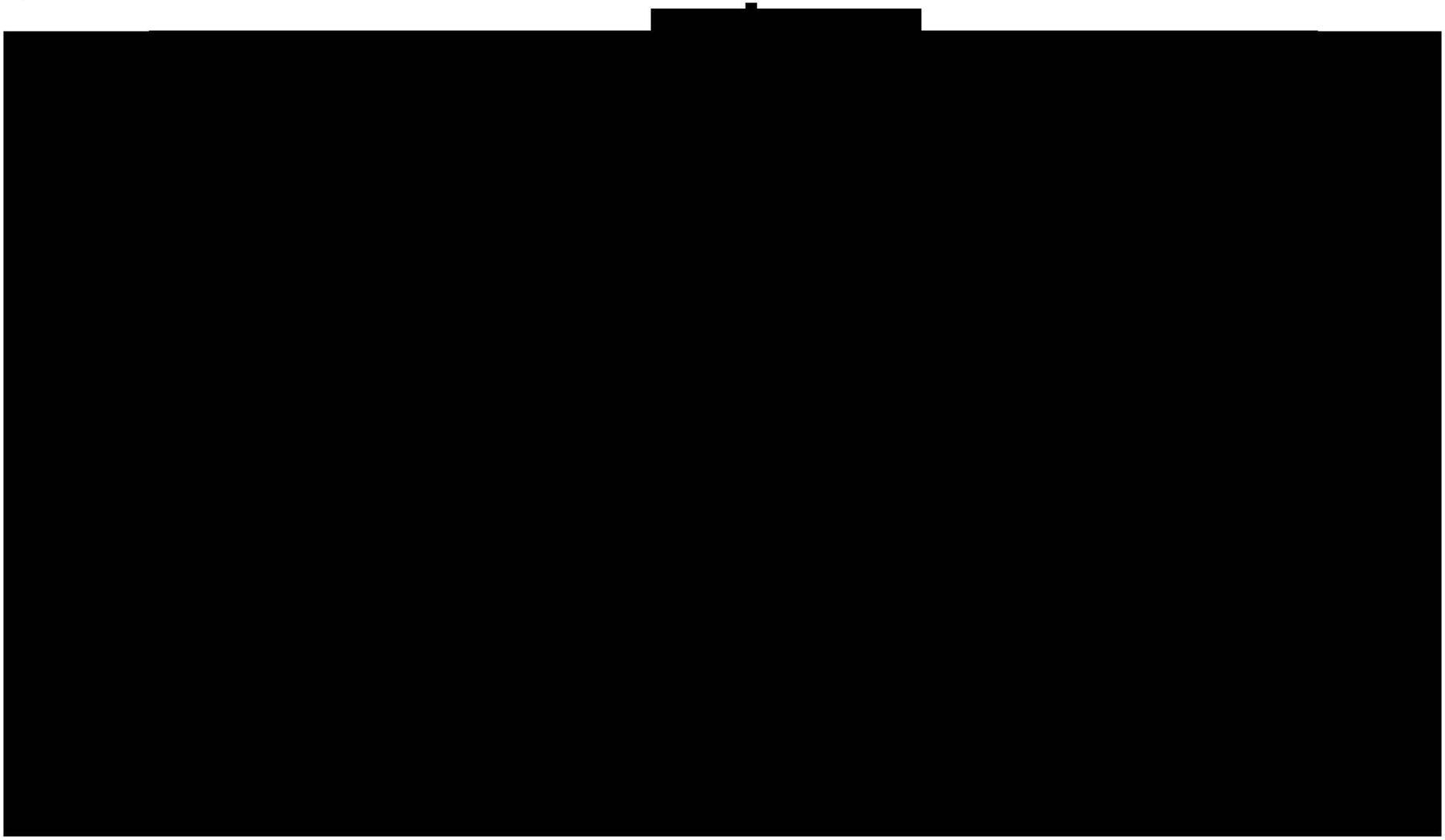
[redacted]



[redacted]

[redacted]

[redacted]

			Official use only
		19 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 413 (adopted 12 May 1981).	x
2.2	GLP	[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]	
3.2.4	Sex	Male and female.	
3.2.5	Age/weight at study initiation	[redacted]	
3.2.6	Number of animals	[redacted]	

Section A6.4.3		Subchronic inhalation toxicity
Annex Point IIA6.4		Subchronic inhalation toxicity study in rats
IUCLID 5.4/9		
	per group	
3.2.7	Control animals	Yes
3.3	Administration/ Exposure	Inhalation
3.3.1	Duration of treatment	90 days.
3.3.2	Frequency of exposure	[redacted]
3.3.3	Postexposure period	None
3.3.4	Inhalation	
3.3.4.1	Type	Inhalation, whole body exposure.
3.3.4.2	Concentration	[redacted]
3.3.4.3	Particle size	See point 3.3.4.2.
3.3.4.4	Type or preparation of particles	-
3.3.4.5	Vehicle	None
3.3.4.6	Concentration in vehicle	Not relevant.
3.3.4.7	Duration of exposure	[redacted]
3.3.4.8	Controls	Yes, control rats received air only.
3.4	Examinations	
3.4.1	Observations	

Section A6.4.3		Subchronic inhalation toxicity
Annex Point IIA6.4		Subchronic inhalation toxicity study in rats
IUCLID 5.4/9		
3.4.1.1	Clinical signs	During exposure [redacted]
3.4.1.2	Mortality	Animals were examined twice each day.
3.4.2	Body weight	[redacted]
3.4.3	Food consumption	The quantity of food consumed by each cage of rats was recorded weekly commencing one week prior to the start of exposures until the end of the study.
3.4.4	Water consumption	Not measured.
3.4.5	Ophthalmoscopic examination	The eyes of all rats were examined prior to allocation and during Week 13 using a Keeler indirect ophthalmoscope.
3.4.6	Haematology	[redacted]
3.4.7	Clinical Chemistry	[redacted]
3.4.8	Urinalysis	Not performed.
3.5	Sacrifice and pathology	
3.5.1	Organ Weights	[redacted]
3.5.2	Gross and histopathology	[redacted]

Section A6.4.3 Subchronic inhalation toxicity

Annex Point IIA6.4 Subchronic inhalation toxicity study in rats

IUCLID 5.4/9

[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 [redacted]

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 [redacted]

4.5 Blood and urine analysis

4.5.1 Haematology [redacted]

Section A6.4.3 Subchronic inhalation toxicity

Annex Point IIA6.4 Subchronic inhalation toxicity study in rats

IUCLID 5.4/9

4.5.2 Clinical chemistry

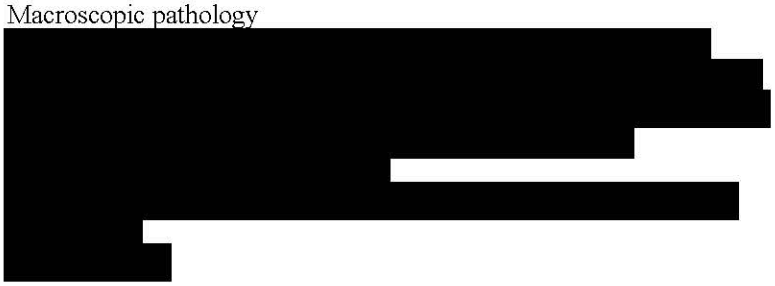
4.5.3 Urinalysis Not investigated.

4.6 Sacrifice and pathology

4.6.1 Organ weights

4.6.2 Gross and histopathology

Macroscopic pathology



Section A6.4.3 Subchronic inhalation toxicity

Annex Point IIA6.4 Subchronic inhalation toxicity study in rats

IUCLID 5.4/9

[redacted]

4.7 Other None.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods The study was conducted to GLP. [redacted]

5.2 Results and discussion [redacted]

Section A6.4.3 [redacted] toxicity

Annex Point IIA6.4 Subchronic inhalation toxicity study in rats

IUCLID 5.4/9

- [redacted]

5.3 Conclusion [redacted]

5.3.1 LO(A)EL [redacted]

5.3.2 NO(A)EL 0.104 mg/l

5.3.3 Other None

5.3.4 Reliability [redacted]

5.3.5 Deficiencies [redacted]

[redacted]

EVALUATION BY RAPPORTEUR MEMBER STATE

Date [redacted]

[redacted]

Section A6.4.3	Subchronic inhalation toxicity
Annex Point IIA6.4	Subchronic inhalation toxicity study in rats
IUCLID 5.4/9	
Reliability	[redacted]
	[redacted]
	[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 6.5 Chronic toxicity

Annex Point IIA6.5 **52-week dietary chronic toxicity study in dogs**

IUCLID 5.4/6

			Official use only
		20 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 requirements under the above guideline are essentially equivalent to OECD Test Guideline 452 (adopted 12 May 1981).	
2.2	**GLP**	[redacted]	
2.3	**Deviations**	No	
		3 MATERIALS AND METHODS	
3.1	**Test material**	[redacted] (equivalent to 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.	
3.2	**Test Animals**	*Non-entry field*	

Section 6.5 Chronic toxicity

Annex Point IIA6.5 **52-week dietary chronic toxicity study in dogs**

IUCLID 5.4/6

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 initiation	[redacted]
3.2.6	Number of animals per group	[redacted]als.
3.2.7	Control animals	Yes
3.3	**Administration/ Exposure**	Oral
3.3.1	Duration of treatment	52 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	2.7	8.2	27.7	80.2
Achieved dose (mg/kg bw/d) - Females	0	2.6	7.1	26.8	79.8

[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	

Section 6.5 Chronic toxicity

Annex Point IIA6.5 **52-week dietary chronic toxicity study in dogs**

IUCLID 5.4/6

3.4.1.1	Clinical signs	All animals were examined once daily for obvious indications of a toxic effect. Physical examinations were performed weekly.	
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.	
3.4.5	Ophthalmoscopic examination	Indirect ophthalmologic examinations were performed on all dogs prior to the initiation of treatment and at termination using a mydriatic.	
3.4.6	Haematology	[redacted]	
3.4.7	Clinical Chemisty	[redacted]	x
3.4.8	Urinalysis	Yes. [redacted]	
3.5	**Sacrifice and pathology**		
3.5.1	Organ Weights	[redacted]	x
3.5.2	Gross and histopathology	[redacted]	x
3.5.3	Other examinations	None	
3.5.4	Statistics	All parameters were analysed with recognised statistical techniques.	
3.6	**Further remarks**	None	

Section 6.5 Chronic toxicity

Annex Point IIA6.5 **52-week dietary chronic toxicity study in dogs**

IUCLID 5.4/6

4 RESULTS AND DISCUSSION

4.1 Observations

4.1.1 Clinical signs

[redacted]

4.1.2 Mortality

No deaths occurred during the study.

4.2 Body weight gain

[redacted]

4.3 Food consumption and compound intake

No significant differences were noted between treated group values and respective control values for food consumption.
Mean food efficiency values were similar between treated and control groups for both sexes.

4.4 Ophtalmoscopic examination

There were no treatment related effects.

4.5 Blood and urine analysis

4.5.1 Haematology

[redacted]

4.5.2 Clinical chemistry

[redacted]

Section 6.5 Chronic toxicity

Annex Point IIA6.5 **52-week dietary chronic toxicity study in dogs**

IUCLID 5.4/6

[redacted]

4.5.3 Urinalysis [redacted]

4.6 Sacrifice and pathology

4.6.1 Organ weights Increased mean absolute and relative liver weights were noted [redacted]

4.6.2 Gross and histopathology [redacted]

Section 6.5 Chronic toxicity

Annex Point IIA6.5 **52-week dietary chronic toxicity study in dogs**

IUCLID 5.4/6

4.7	**Other**	None

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	[redacted]
[redacted]		
[redacted]		

Section 6.5 Chronic toxicity

Annex Point IIA6.5 **52-week dietary chronic toxicity study in dogs**

IUCLID 5.4/6

5.3.2	NO(A)EL	Males - NOEL = [redacted] 8.2 mg/kg bw/d). Females - NOEL = [redacted] 26.8 mg/kg bw/d).
5.3.3	Other	None
5.3.4	Reliability	1
5.3.5	Deficiencies	No

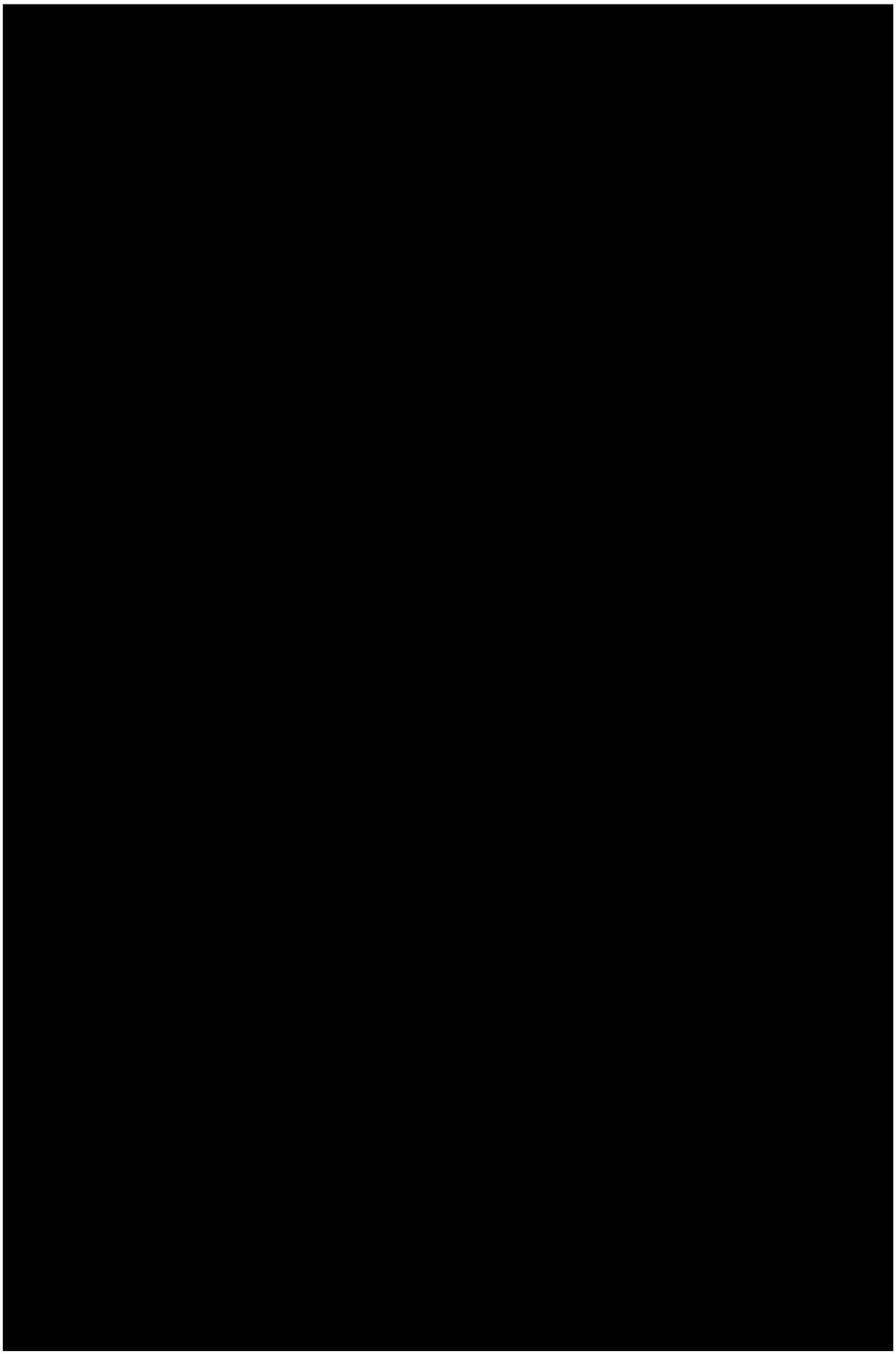
Evaluation by Competent Authorities
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
[redacted]
Remarks

COMMENTS FROM ... *(specify)*
Date *Give date of comments submitted*

Section 6.5 Chronic toxicity	
Annex Point IIA6.5	**52-week dietary chronic toxicity study in dogs**
IUCLID 5.4/6	

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 6.6.1 Genotoxicity in vitro

Annex Point IIA6.6.1 **In vitro gene mutation study in bacteria**

IUCLID 5.5/1

			Official use only
		21 REFERENCE	
1.1	**Reference**	[redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Sumitomo Chemical 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**	Performed according to the methods described by Ames et. al and Yahagi et. al: B. N. Ames, T. McCann and E. Yamasaki; Mutation Res., 31, 347, (1975), T. Yahagi, M.Degawa, Y.Seino, T. Matsushima, N.Nagao, T. Sugimura and Y. Hashimoto; Cancer letters, 1, 91, (1975).	
2.2	**GLP**	[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	Not provided.	
3.1.2.2	Purity	[redacted]	
3.1.2.3	Stability	Not specified.	
3.2	**Study Type**	Bacterial reverse mutation test.	
3.2.1	Organism/cell type	Salmonella typhimurium TA98, TA100, TA1535, TA1537 and TA1538. Escherichia coli WP-2 uvrA.	
3.2.2	Deficiencies / Proficiencies	Histidine requiring Salmonella typhimurium mutant strains. Tryptophan requiring Escherichia coli WP-2 uvrA.	

Section 6.6.1 Genotoxicity in vitro

Annex Point IIA6.6.1 **In vitro gene mutation study in bacteria**

IUCLID 5.5/1

3.2.3	Metabolic activation system	[redacted]
3.2.4	Positive control	
3.3	**Administration / Exposure; Application of test substance**	*Non-entry field*
3.3.1	Concentrations	Main tests: 0, 10, 50, 100, 500, 1000 and 5000 µg/plate.

Section 6.6.1 Genotoxicity in vitro

Annex Point IIA6.6.1 **In vitro gene mutation study in bacteria**

IUCLID 5.5/1

3.3.2	Way of application	[redacted]
3.3.3	Pre-incubation time	See point 3.3.2
3.3.4	Other modifications	None.
3.4	**Examinations**	
3.4.1	Number of cells evaluated	[redacted]
		22 RESULTS AND DISCUSSION
3.5	**Genotoxicity**	*Non-entry field*
3.5.1	without metabolic activation	No
3.5.2	with metabolic activation	No
3.6	**Cytotoxicity**	[redacted]
		4 APPLICANT'S SUMMARY AND CONCLUSION
4.1	**Materials and methods**	[redacted]

Section 6.6.1 Genotoxicity in vitro

Annex Point IIA6.6.1 **In vitro gene mutation study in bacteria**

IUCLID 5.5/1

4.2	**Results and discussion**	The number of the revertants at each dose level did not increase [redacted]
4.3	**Conclusion**	Sumithrin did not induce significant number of revertants as compared with the vehicle control for each strain. So, it was concluded that Sumithrin was not mutagenic under the test condition.
4.3.1	Reliability	[redacted]

Evaluation by Competent Authorities	
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
[redacted]	
Reliability	1
Acceptability	Acceptable
Remarks	

Section 6.6.1 Genotoxicity in vitro

Annex Point IIA6.6.1 **In vitro gene mutation study in bacteria**

IUCLID 5.5/1

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

Section 6.6.2 Genotoxicity in vitro

Annex Point IIA6.6.2 **In-vitro cytogenicity study in mammalian cells**

IUCLID 5.5/5

			Official use only
		23 REFERENCE	
1.1	**Reference**	[redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Sumitomo Chemical 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 study report makes no claims on guideline compliance. The study appears to meet the requirements of OECD 473 (adopted 21 July 1997).	
2.2	**GLP**	[redacted]	
2.3	**Deviations**	[redacted]	
		3 MATERIALS AND METHODS	
3.1	**Test material**	[redacted] d-Phenothrin.	
3.1.1	Lot/Batch number	[redacted]	
3.1.2.1	Description	[redacted]	
3.1.2.2	Purity	[redacted]	
3.1.2.3	Stability	Not specified.	
3.2	**Study Type**	In vitro mammalian chromosome aberration test.	
3.2.1	Organism/cell type	Chinese Hamster Ovary cell (CHO-WBL)	
3.2.2	Deficiencies / Proficiencies	–	
3.2.3	Metabolic activation system	S9 reaction mixture (S9 15 µl/ml, NADP 1.5 mg/ml, and isocitric acid 2.7 mg/ml). The S9 fraction was derived from the liver of male Sprague-Dawley rats which had previously been treated with Aroclor 1254.	

Section 6.6.2 Genotoxicity in vitro

Annex Point IIA6.6.2 **In-vitro cytogenicity study in mammalian cells**

IUCLID 5.5/5

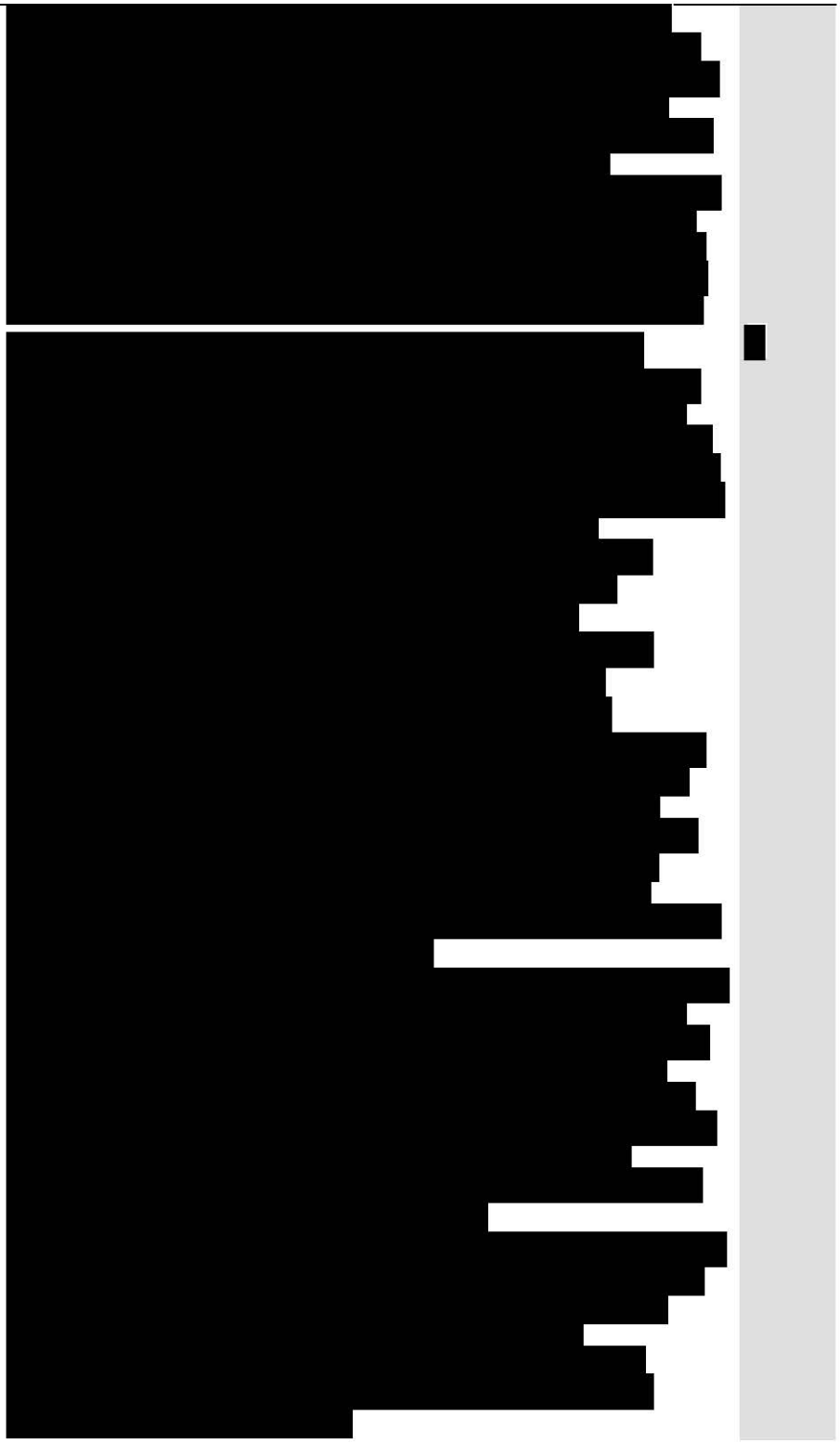
3.2.4	Positive control	[redacted]
3.3	**Administration / Exposure; Application of test substance**	*Non-entry field*
3.3.1	Concentrations	Without S9-mix: 35.3 to 252 µg/ml culture medium. With S9-mix (20 or 30 hour harvest): 126 to 505 µg/ml culture medium.
3.3.2	Way of application	The test article was dissolved in dimethyl sulfoxide
3.3.3	Pre-incubation time	In the non-activation assay, 20 hour harvest was conducted. In the activation assay, 20 and 30 hour harvests were conducted
3.3.4	Other modifications	None
3.4	**Examinations**	
3.4.1	Number of cells evaluated	One hundred cells from each duplicate culture at four dose levels of the test article and from each of the negative and solvent control cultures were analyzed for the different types of chromosomal aberrations.
		24 RESULTS AND DISCUSSION
3.5	**Genotoxicity**	*Non-entry field*
3.5.1	without metabolic activation	No
3.5.2	with metabolic activation	No
3.6	**Cytotoxicity**	Cytotoxic concentrations were investigated. See point 5.1 and 5.2. [redacted]
		4 APPLICANT'S SUMMARY AND CONCLUSION
4.1	**Materials and methods**	[redacted]

Section 6.6.2 Genotoxicity in vitro

Annex Point IIA6.6.2 **In-vitro cytogenicity study in mammalian cells**

IUCLID 5.5/5

4.2 Results and discussion



Section 6.6.2 Genotoxicity in vitro

Annex Point IIA6.6.2 **In-vitro cytogenicity study in mammalian cells**

IUCLID 5.5/5

		[redacted]
4.3	**Conclusion**	The test article, Sumithrin T.G., is considered negative for inducing chromosomal aberrations in Chinese hamster ovary cells under both nonactivation and activation conditions of these assays.
4.3.1	Reliability	[redacted]
4.3.2	Deficiencies	

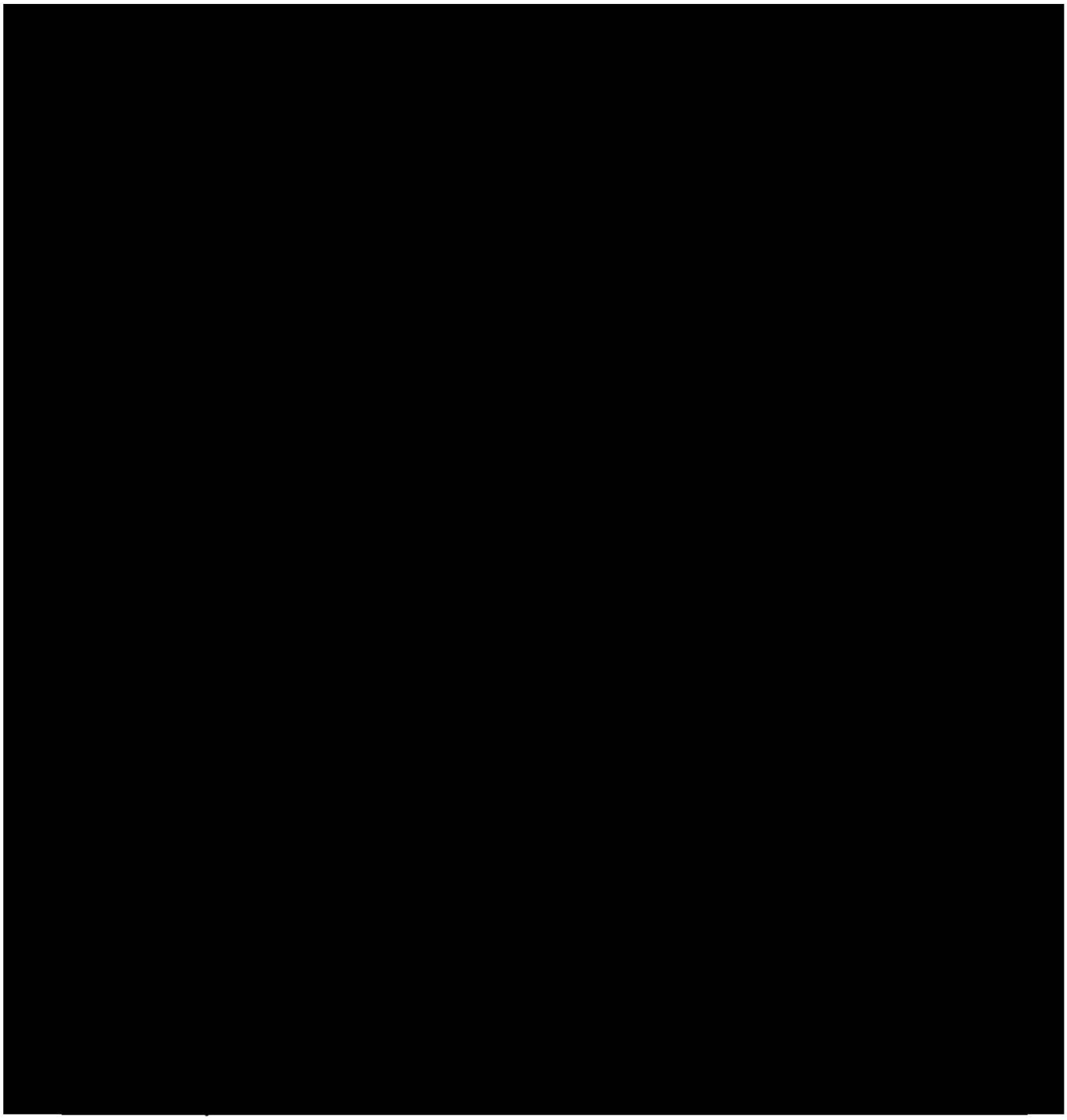
Evaluation by Competent Authorities
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
[redacted]
[redacted]

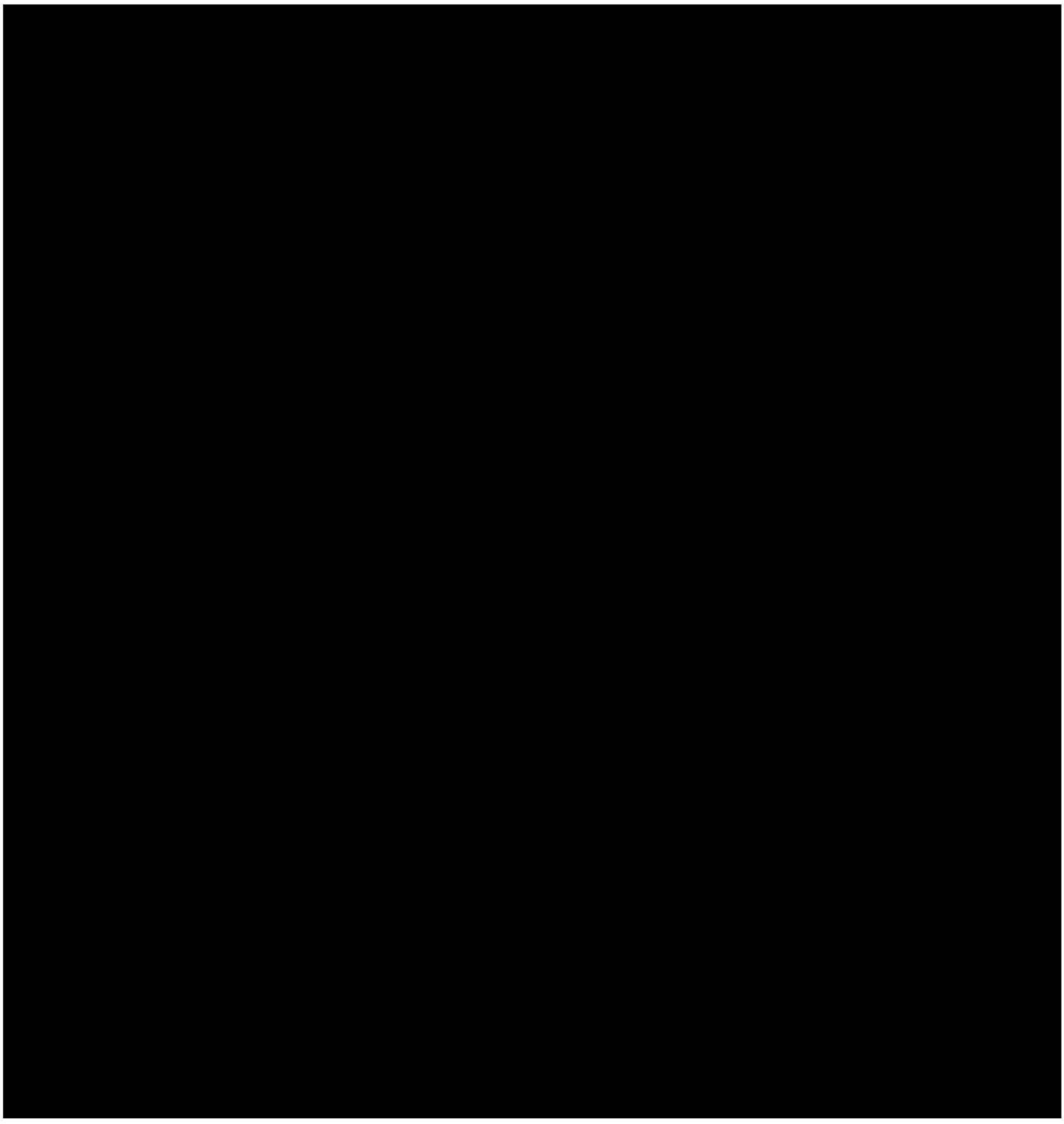
Section 6.6.2 Genotoxicity in vitro

Annex Point IIA6.6.2 **In-vitro cytogenicity study in mammalian cells**

IUCLID 5.5/5

Remarks





[redacted]

Section 6.6.4(1)
Genotoxicity in vivo

Annex Point IIA6.6.4 **In vivo chromosomal aberration test in mice**

IUCLID 5.6/1

			Official use only
		25 REFERENCE	
1.1	**Reference**	[redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Sumitomo Chemical 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 report makes no claims on guideline compliance. Deviations from OECD Test Guideline 475 are listed under point 2.3.	
2.2	**GLP**	[redacted]	
2.3	**Deviations**	The reporting of this study was incomplete. A number of 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	Not described.	
3.1.2.2	Purity	[redacted]	
3.1.2.3	Stability	[redacted]	
3.1.2.4	Maximum tolerable dose	The acute toxicity in mice following intraperitoneal administration of Sumithrin® [redacted] has been investigated in a separate study	

Section 6.6.4(1)
Genotoxicity in vivo

Annex Point IIA6.6.4 **In vivo chromosomal aberration test in mice**

IUCLID 5.6/1

		[redacted] The LD_{50} was found to be greater than 10,000 mg/kg bw. No toxicity data was reported in the current study.
3.2	**Test Animals**	
3.2.1	Species	Mouse
3.2.2	Strain	[redacted]
3.2.3	Source	[redacted]
3.2.4	Sex	Male
3.2.5	Age/weight at study initiation	[redacted]
3.2.6	Number of animals per group	[redacted]
3.2.7	Control animals	Yes, [redacted]
3.3	**Administration/ Exposure**	Intraperitoneal
3.3.1	Number of applications	Single dose.
3.3.2	Interval between applications	Not applicable
3.3.3	Postexposure period	6, 24, 48 h.
3.3.4	Type	intraperitoneal
3.3.5	Concentration	2500, 5000 or 10000 mg/kg bw.
3.3.6	Vehicle	None
3.3.7	Concentration in vehicle	Not applicable.
3.3.8	Total volume applied	Not applicable.
3.3.9	Controls	No vehicle (untreated).
3.4	**Examinations**	
3.4.1	Clinical signs	Not reported.
3.4.2	Tissue	bone marrow
	Number of animals:	All rats ([redacted])
	Number of cells:	50 metaphase spreads from each animal were scored.

Section 6.6.4(1)
Genotoxicity in vivo

Annex Point IIA6.6.4 **In vivo chromosomal aberration test in mice**

IUCLID 5.6/1

		Time points: 6, 24, 48h after dosing. Type of cells Bone marrow cells. Parameters: Chromatid and chromosome gaps, Chromatid and chromosome breaks, Exchanges, Fragmentation and pulverisation of chromosomes.
3.5	**Further remarks**	None
		26 RESULTS AND DISCUSSION
3.6	**Clinical signs**	Toxicity was not reported in this study.
3.7	**Haematology / Tissue examination**	The frequencies of chromosomal aberrations are summarised in Table A6_6_4(1)-1.
		[redacted]
3.8	**Genotoxicity**	No
3.9	**Other**	None
		4 APPLICANT'S SUMMARY AND CONCLUSION
4.1	**Materials and methods**	[redacted]

Section 6.6.4(1)
Genotoxicity in vivo

Annex Point IIA6.6.4 **In vivo chromosomal aberration test in mice**

IUCLID 5.6/1

		[redacted]
4.2	**Results and discussion**	[redacted]
4.3	**Conclusion**	From the above data, it is concluded that Sumithrin® has no clastogenic effect under the test conditions.
4.3.1	Reliability	[redacted]
4.3.2	Deficiencies	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	1/03/2007
Materials and Methods	[redacted]
[redacted]	[redacted]
Reliability	[redacted]
Acceptability	
Remarks	[redacted]
	COMMENTS FROM ...

Section 6.6.4(1)
Genotoxicity in vivo

Annex Point IIA6.6.4 **In vivo chromosomal aberration test in mice**

IUCLID 5.6/1

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 6.6.4(2)
Genotoxicity in vivo
Section

Annex Point IIA6.6.4/2

IUCLID 5.6/2 **Host mediated assay in mice**

			Official use only
		27 REFERENCE	
1.1	**Reference**	[redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Sumitomo Chemical 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**	No OECD or EC guideline available for this assay. The experiment was performed according to the following method: M. S. Legator and H. V. Mailing; Chemical Mutagen, vol 2, pp 569-589 Prenum Press (1971).	
2.2	**GLP**	[redacted]	
2.3	**Deviations**	[redacted]	
		3 MATERIALS AND METHODS	
3.1	**Test material**	Sumithrin®, equivalent to 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		
3.1.2.3	Stability		
3.1.2.4	Maximum tolerable dose	The report indicates that the (oral) LD_{50} of Sumithrin® exceeds 10,000 mg/kg bw.	
3.2	**Test Animals**	Non-entry field	
3.2.1	Species	Mouse	
3.2.2	Strain	[redacted]	
3.2.3	Source		
3.2.4	Sex		

Section 6.6.4(2)
Genotoxicity in vivo
Section

Annex Point IIA6.6.4/2

IUCLID 5.6/2		**Host mediated assay in mice**
3.2.5	Age/weight at study initiation	[redacted]
3.2.6	Number of animals per group	[redacted]
3.2.7	Control animals	Yes, negative and positive.
3.3	**Administration/ Exposure**	Oral
3.3.1	Number of applications	2
3.3.2	Interval between applications	24 h
3.3.3	Postexposure period	3 h
3.3.4	Type	Oral Gavage
3.3.5	Concentration	2500, 5000 mg/kg bw
3.3.6	Vehicle	Corn oil
3.3.7	Concentration in vehicle	Not specified.
3.3.8	Total volume applied	Not specified.
3.3.9	Controls	Negative control (vehicle only) Positive control (dimethylnitrosamine)
3.4	**Examinations**	
3.4.1	Clinical signs	Not described.
3.4.2	Tissue	Indicator bacteria: histidine requiring *Salmonella typhimurium* G46 (his^-), Host animals: ICR Mice. Number of animals: 6 animals/group Number of cells: 3×10^9 bacterial cells inoculated. Time points: Indicator organisms recovered after 3 h, colonies were counted after 1-2 day incubation. Type of cells: *Salmonella typhimurium* G46 (his^-) inoculated into the peritoneum of each animal (immediately following exposure to the test compound). Parameters: Revertants and survivals of recovered cells form each mouse were counted.
3.5	**Further remarks**	None

Section 6.6.4(2)
Genotoxicity in vivo
Section

Annex Point IIA6.6.4/2

IUCLID 5.6/2 **Host mediated assay in mice**

28 RESULTS AND DISCUSSION

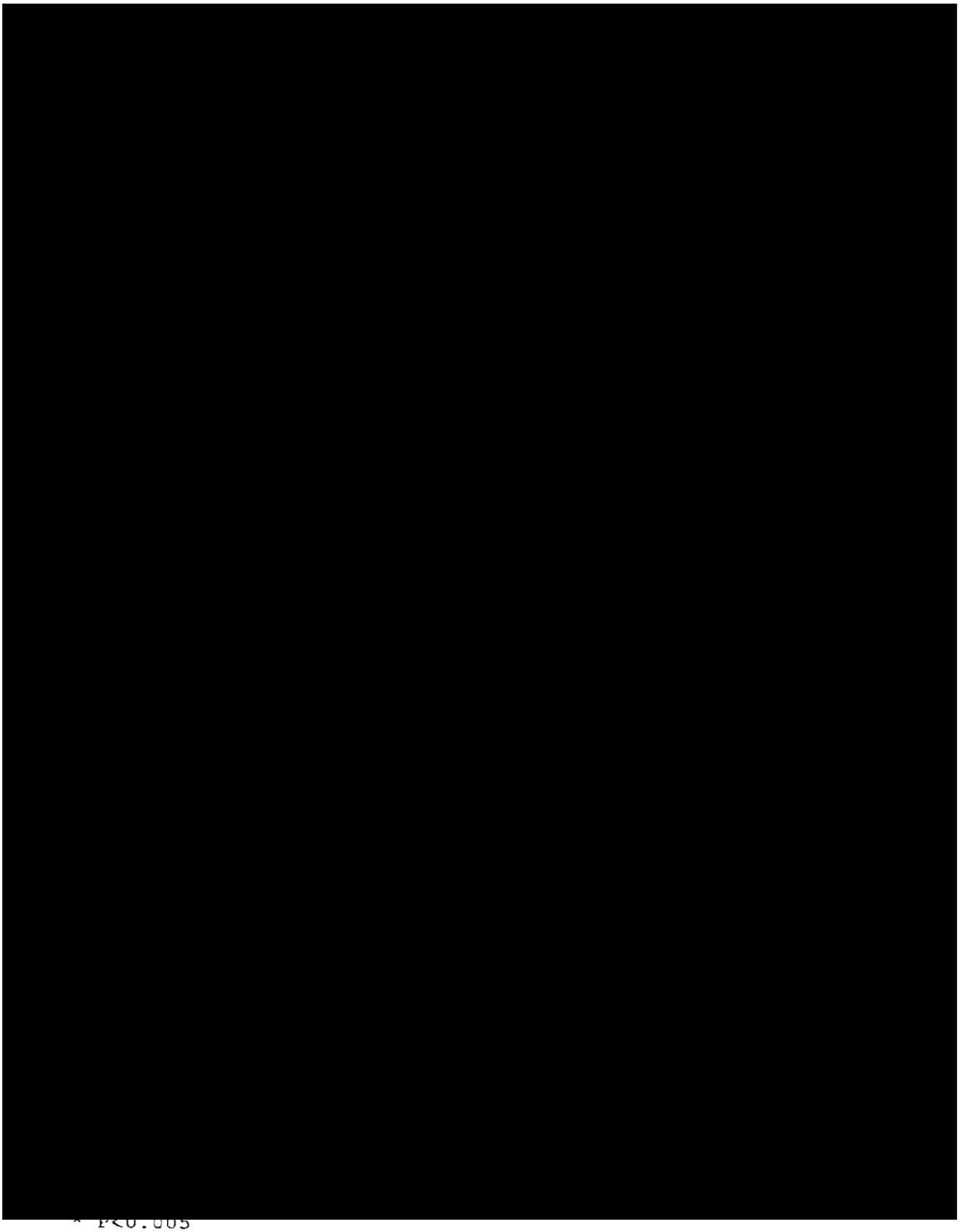
3.6	**Clinical signs**	No data presented.
3.7	**Haematology / Tissue examination**	[redacted]
3.8	**Genotoxicity**	No
3.9	**Other**	None
4.1	**Materials and methods**	[redacted]
4.2	**Results and discussion**	There was no increase in mutation frequency of Sumithrin®-treated groups as compared with the vehicle control group. It was concluded that Sumithrin® was not mutagenic under the test conditions.
4.3	**Conclusion**	Sumithrin® was not mutagenic in the host mediated assay in mice.
4.3.1	Reliability	[redacted]
4.3.2	Deficiencies	[redacted]

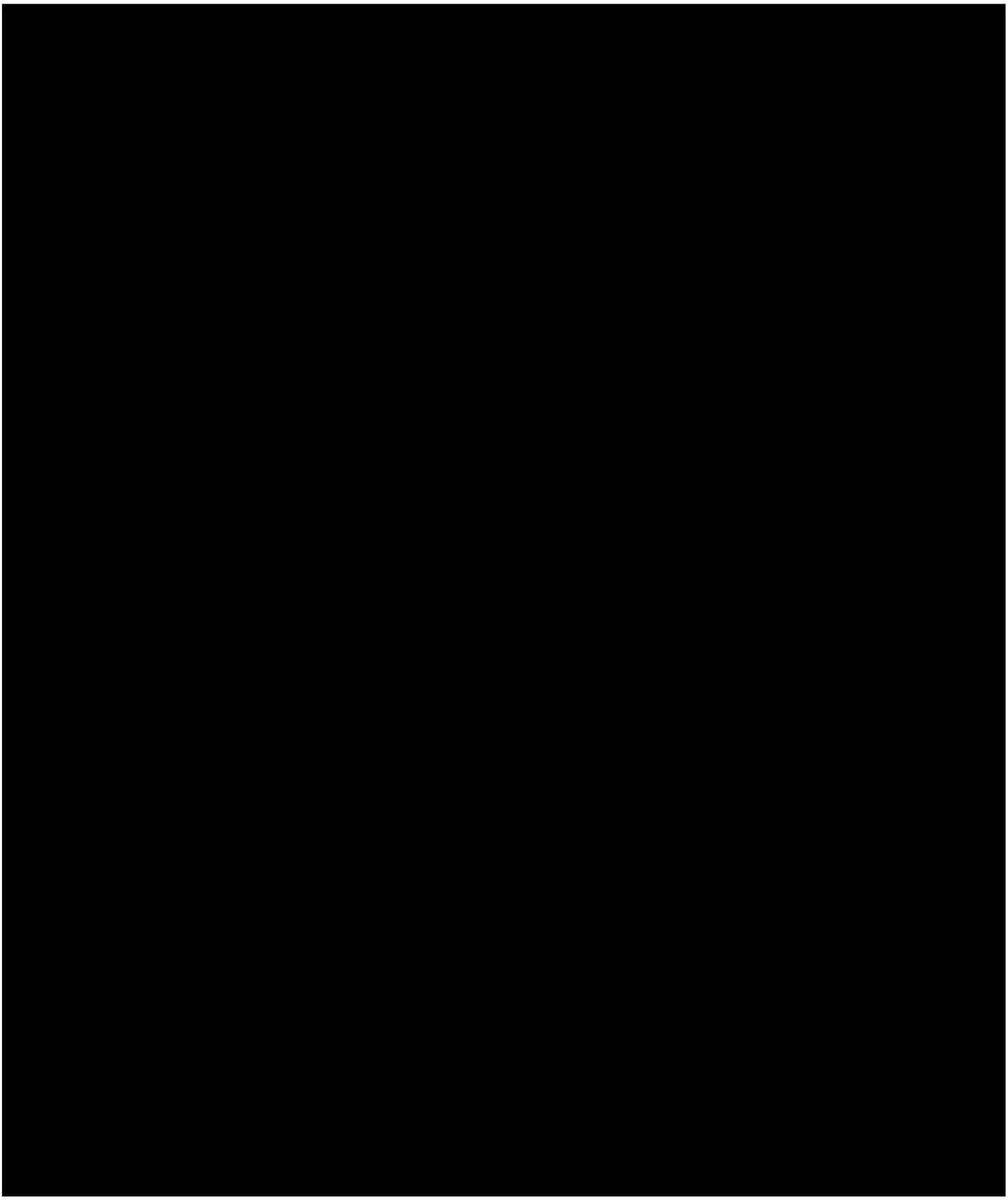
Section 6.6.4(2)
Genotoxicity in vivo
Section

Annex Point IIA6.6.4/2

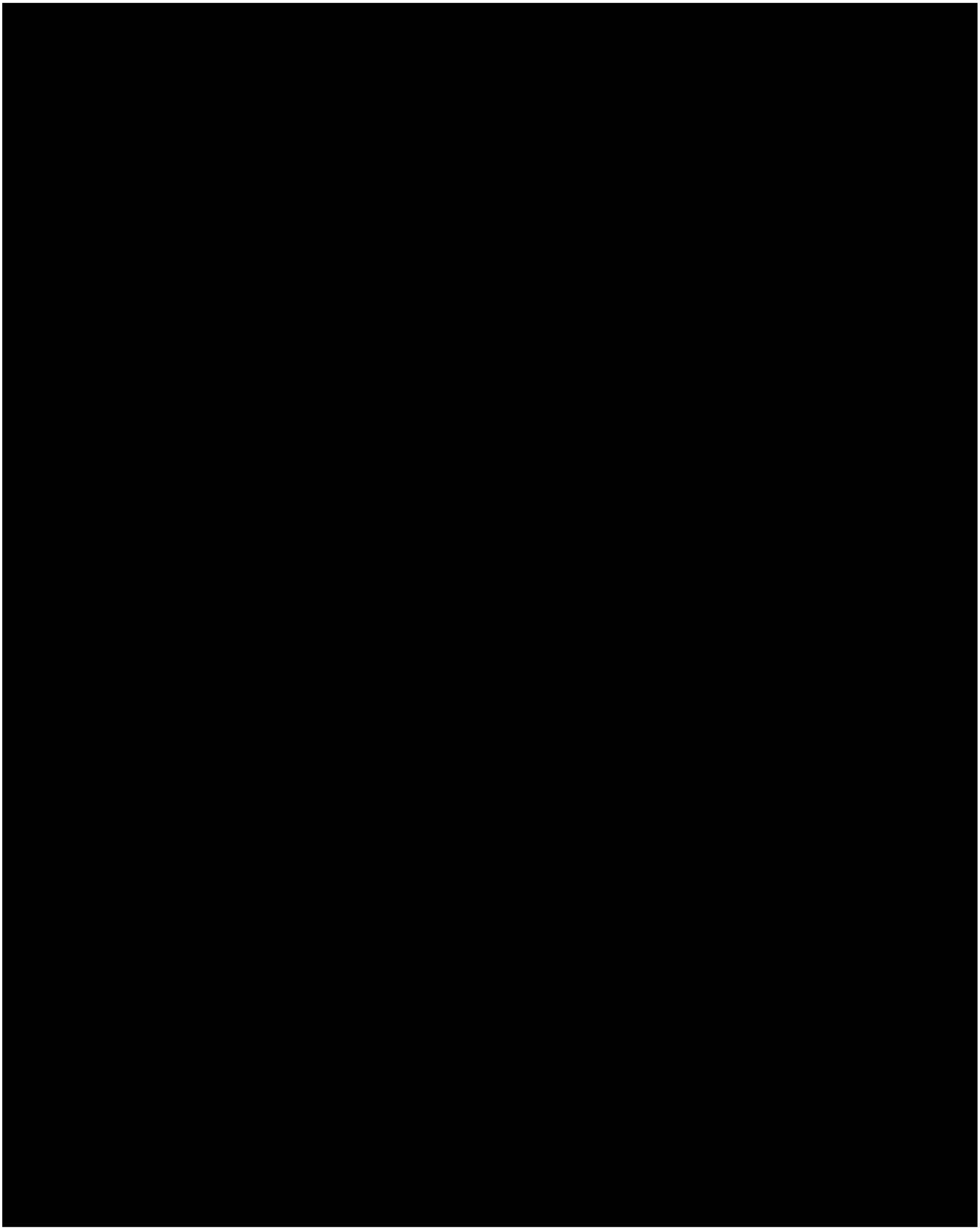
IUCLID 5.6/2 **Host mediated assay in mice**

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Materials and Methods	
Results and discussion	
Conclusion	
Reliability	[redacted]
Acceptability	
Remarks	[redacted]
	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*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

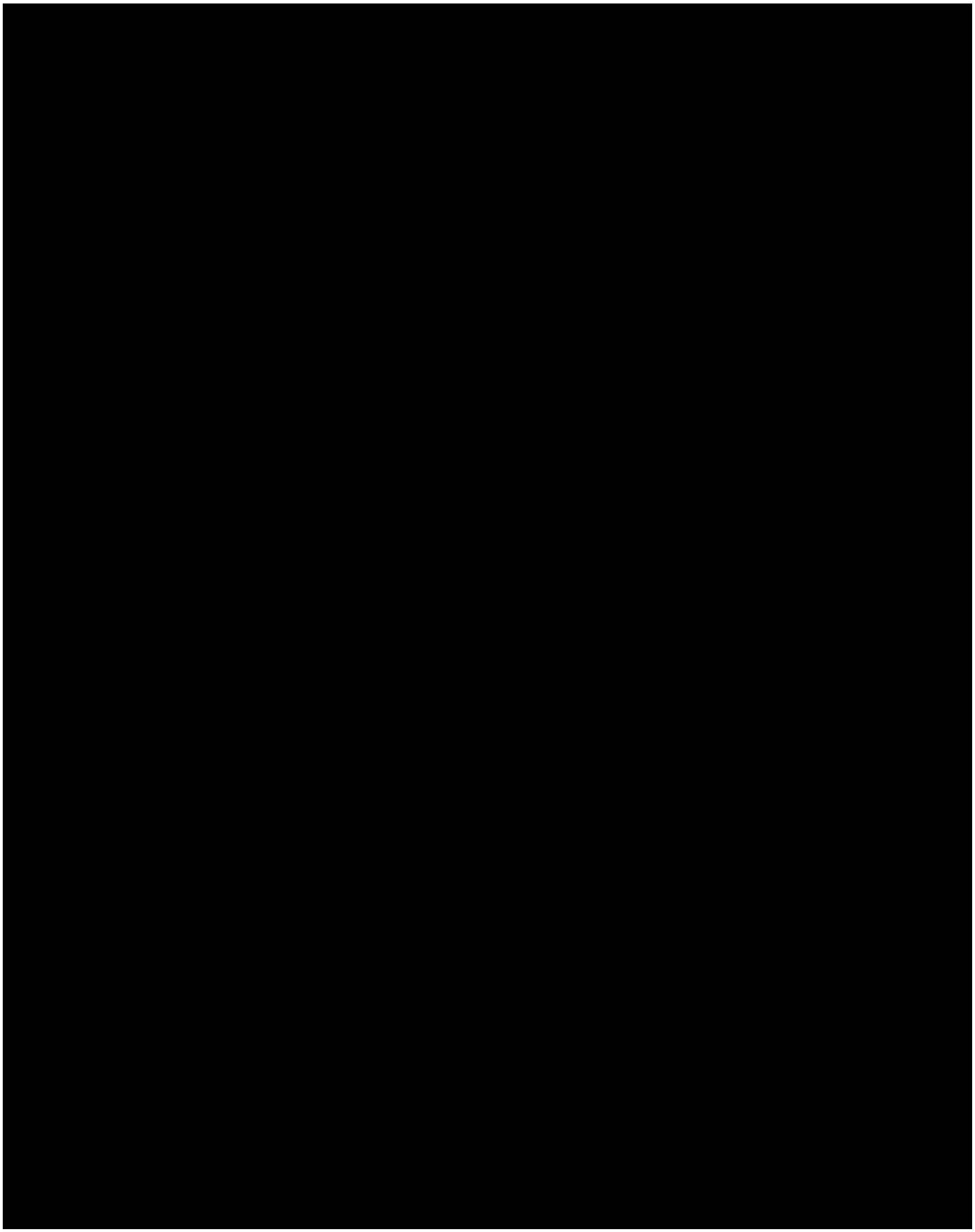




Section 6.6.5. Justification VI.6.VI.6.5 Annex Point [redacted]
Remarks



Section IIIA 6.6.6. Justification Annex Point IIA, VI.6.VI.6.6	**If positive in 6.6.4 then a test to assess possible germ cell effects may be required**
Remarks	



Section IIIA 6.6.7 **Justification**	**If the results are negative for the three tests 6.6.1, 6.6.2 and 6.6.3, then further testing is normally only required if metabolites of concern are formed in mammals**
Remarks	

Section 6.7(1)
Carcinogenicity -Rat
Annex Point IIA6.7
IUCLID 5.7/1

2 year dietary combined toxicity/ carcinogenicity study in rats

			Official use only
		29 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**	[redacted] OECD Test Guideline 453 (adopted 12 May 1981).	
2.2	**GLP**	[redacted]	x
2.3	**Deviations**		
		3 MATERIALS AND METHODS	
3.1	**Test material**	[redacted] d-Phenothrin).	
3.1.1	Lot/Batch number	[redacted]	
3.1.2	Specification		

Section 6.7(1)
Carcinogenicity -Rat

2 year dietary combined toxicity/ carcinogenicity study in rats

Annex Point IIA6.7

IUCLID 5.7/1

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]
3.2.4	Sex	[redacted]
3.2.5	Age/weight at study initiation	[redacted]
3.2.6	Number of animals per group	[redacted]s:

Group	Dose Level (ppm)
Replicate A	
1	0
2	300
3	1000
4	3000
Replicate B	
1	0
2	300
3	1000
4	3000

[redacted]

Section 6.7(1)
Carcinogenicity -Rat
Annex Point IIA6.7
IUCLID 5.7/1

2 year dietary combined toxicity/ carcinogenicity study in rats

3.2.6.1	at interim sacrifice	[redacted]	
3.2.6.2	at terminal sacrifice		
3.2.7	Control animals	Yes. See point 3.2.6.	
3.3	**Administration/ Exposure**	Oral	
3.3.1	Duration of treatment	52 or 105 weeks (males)/ 118 weeks (females). Treatment of females was prolonged due to high survival (at least 64-96% at week 104).	
3.3.2	Interim sacrifice(s)	After 52 weeks.	
3.3.3	Final sacrifice	After 105/118 weeks.	
3.3.4	Frequency of exposure	Daily	
3.3.5	Postexposure period	None	
3.3.6	Type	Oral Via the diet.	
3.3.7	Concentration	[redacted] Achieved dosage in mg/kg bw/day are presented in the report (Table 6)	x

Dose ppm	Group mean achieved dosage (mg/kg bw/day)	Range of values (mg/kg bw/day)
	Males	
[redacted]	14.2	37 - 11
	47.5	115 - 35
	142.7	342 - 113
	Females	
[redacted]0	16.7	35.5 - 13.4
	54.4	118 - 42.5
	169.2	342 –1 25

for each group and each interval (see point 3.4.2). Overall achieved concentrations are not presented in the study report.

Text Table inserted by RMS

Accuracy, homogeneity and stability
The accuracy, homogeneity and stability of diet preparations was assessed and found to be acceptable.

3.3.8	Vehicle	None. Test material mixed directly in the diet.	
3.3.9	Concentration in vehicle	See 3.3.7 for concentrations of test material in the diet.	
3.3.10	Total volume	Not applicable.	

Section 6.7(1)
Carcinogenicity -Rat
Annex Point IIA6.7
IUCLID 5.7/1

2 year dietary combined toxicity/ carcinogenicity study in rats

	applied	
3.3.11	Controls	Plain diet.
3.4	**Examinations**	
3.4.1	Body weight	[redacted]
3.4.2	Food consumptio	
3.4.3	Water consumption	
3.4.4	Clinical signs	[redacted]
3.4.5	Macroscopic investigation	See point 3.4.10.
3.4.6	Ophthalmoscopic examination	[redacted]
3.4.7	Haematology	

[redacted]

3.4.8 Clinical Chemistry

[redacted]

3.4.9 Urinalysis

Section 6.7(1)
Carcinogenicity -Rat
Annex Point IIA6.7
IUCLID 5.7/1

2 year dietary combined toxicity/ carcinogenicity study in rats

[redacted]

3.4.10 Pathology

3.4.10.1 Organ Weights

3.4.11 Histopathology

3.4.12 Other examinations

3.5 Statistics

3.6 Further remarks

Section 6.7(1)
Carcinogenicity -Rat

2 year dietary combined toxicity/ carcinogenicity study in rats

Annex Point IIA6.7

IUCLID 5.7/1

4.1 Body weight

4.2 Food consumption

4.3 Water consumption

4.4 Clinical signs

[redacted]

Section 6.7(1)
Carcinogenicity -Rat

2 year dietary combined toxicity/ carcinogenicity study in rats

Annex Point IIA6.7

IUCLID 5.7/1

[redacted]

4.5 Macroscopic investigations

4.6 Ophthalmoscopi examination

4.7 Haematology

4.8 Clinical Chemistry

4.9 Urinalysis

4.10 Pathology

Section 6.7(1)
Carcinogenicity -Rat

2 year dietary combined toxicity/ carcinogenicity study in rats

Annex Point IIA6.7

IUCLID 5.7/1

29.1 Organ Weights

[redacted]

29.2 Histopathology

Section 6.7(1)
Carcinogenicity -Rat

Annex Point IIA6.7

IUCLID 5.7/1

2 year dietary combined toxicity/ carcinogenicity study in rats

[redacted]

Section 6.7(1)
Carcinogenicity -Rat

2 year dietary combined toxicity/ carcinogenicity study in rats

Annex Point IIA6.7

IUCLID 5.7/1

[redacted]

4.11 Other examinations

4.12 Time to tumou

4.13 Other

Section 6.7(1)
Carcinogenicity -Rat

2 year dietary combined toxicity/ carcinogenicity study in rats

Annex Point IIA6.7

IUCLID 5.7/1

5.1 Materials and methods

[redacted]

5.2 Results and discussion

5.3 Conclusion

Section 6.7(1)
Carcinogenicity -Rat

Annex Point IIA6.7

IUCLID 5.7/1

2 year dietary combined toxicity/ carcinogenicity study in rats

[redacted]

The no-effect-level was [redacted] for both sexes, the overall achieved dosages, for rats receiving [redacted] were 47 mg/kg/day for males and 56 mg/kg/day for females (animals assigned to the Lifespan Study).

5.3.1 Reliability [redacted]

5.3.2 Deficiencies

[redacted]

Section 6.7(1) **Carcinogenicity -Rat** **Annex Point IIA6.7** **IUCLID 5.7/1**	**2 year dietary combined toxicity/ carcinogenicity study in rats**
Date	[redacted]
Materials and Methods	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section 6.7(1) **Carcinogenicity -Rat** **Annex Point IIA6.7** **IUCLID 5.7/1**	**2 year dietary combined toxicity/ carcinogenicity study in rats**

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

[redacted]

[redacted]

Section 6.7(2)
Carcinogenicity -Mice

Annex Point IIA6.7 **2 year dietary combined toxicity/ carcinogenicity study in mice**

IUCLID 5.7/2

			Official use only
		30 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**	No claims of guideline compliance are made in the study report. However, this study appears to comply with the requirements of OECD Test Guideline 453 (adopted 12 May 1981).	
2.2	**GLP**	[redacted]	
2.3	**Deviations**		
		3 MATERIALS AND METHODS	
3.1	**Test material**	[redacted]d-Phenothrin).	
3.1.1	Lot/Batch number	[redacted]	[redacted]
3.1.2	Specification		

Section 6.7(2)
Carcinogenicity -Mice

Annex Point IIA6.7 **2 year dietary combined toxicity/ carcinogenicity study in mice**

IUCLID 5.7/2

3.1.2.1	Description	[redacted]
3.1.2.2	Purity	
3.1.2.3	Stability	
3.2	**Test Animals**	
3.2.1	Species	Mouse
3.2.2	Strain	[redacted]
3.2.3	Source	
3.2.4	Sex	
3.2.5	Age/weight at study initiation	
3.2.6	Number of animal per group	[redacted]
3.2.6.1	at interim sacrific	
3.2.6.2	at terminal sacrifice	
3.2.7	Control animals	Yes. See point 3.2.6.
3.3	**Administration/ Exposure**	Oral
3.3.1	Duration of treatment	26, 53 or 78 weeks (Toxicity Study); 104 weeks (Lifetime Study).

Section 6.7(2)
Carcinogenicity -Mice

Annex Point IIA6.7		**2 year dietary combined toxicity/ carcinogenicity study in mice**	
IUCLID 5.7/2			
3.3.2	Interim sacrifice(s)	After 26, 52, 78 weeks (Toxicity Study).	
3.3.3	Final sacrifice	After 104 weeks (Lifespan Study).	
3.3.4	Frequency of exposure	Daily	
3.3.5	Post exposure period	None	
3.3.6	Type	Oral Via the diet.	
3.3.7	Concentration	[redacted] Achieved dosage in mg/kg bw/day are presented in the report (Table 6) for each group and each interval (see point 3.4.2). Overall achieved concentrations are not presented in the study report.	x
3.3.8	Vehicle	[redacted]	
3.3.9	Concentration in vehicle	See 3.3.7 for concentrations of test material in the diet.	
3.3.10	Total volume applied	Not applicable.	
3.3.11	Controls	Plain diet.	

Section 6.7(2)
Carcinogenicity -Mice

Annex Point IIA6.7 **2 year dietary combined toxicity/ carcinogenicity study in mice**

IUCLID 5.7/2

3.4	**Examinations**	[redacted]
3.4.1	Body weight	
3.4.2	Food consumption	
3.4.3	Water consumption	
3.4.4	Clinical signs	
3.4.5	Macroscopic investigation	
3.4.6	Ophthalmoscopic examination	
3.4.7	Haematology	

Section 6.7(2)
Carcinogenicity -Mice

Annex Point IIA6.7 **2 year dietary combined toxicity/ carcinogenicity study in mice**

IUCLID 5.7/2

[redacted]

3.4.8 Clinical Chemistry

3.4.9 Urinalysis

3.4.10 Pathology

3.4.10.1 Organ Weights

3.4.11 Histopathology

Section 6.7(2)
Carcinogenicity -Mice

Annex Point IIA6.7 **2 year dietary combined toxicity/ carcinogenicity study in mice**

IUCLID 5.7/2

[redacted]

3.4.12 Other examinations

3.5 Statistics

3.6 Further remarks

4.1 Body weight

4.2 Food consumption

Section 6.7(2)
Carcinogenicity -Mice

Annex Point IIA6.7 **2 year dietary combined toxicity/ carcinogenicity study in mice**

IUCLID 5.7/2

4.3	**Water consumption**	[redacted]
4.4	**Clinical signs**	
4.5	**Macroscopic investigations**	
4.6	**Ophthalmoscopi examination**	
4.7	**Haematology**	
4.8	**Clinical Chemistry**	
4.9	**Urinalysis**	
4.10	**Pathology**	

Section 6.7(2)
Carcinogenicity -Mice

Annex Point IIA6.7 **2 year dietary combined toxicity/ carcinogenicity study in mice**

IUCLID 5.7/2

30.1 Organ Weights

[redacted]

30.2 Histopathology

Section 6.7(2)
Carcinogenicity -Mice

Annex Point IIA6.7 **2 year dietary combined toxicity/ carcinogenicity study in mice**

IUCLID 5.7/2

[redacted]

Section 6.7(2)
Carcinogenicity -Mice

Annex Point IIA6.7 **2 year dietary combined toxicity/ carcinogenicity study in mice**

IUCLID 5.7/2

[redacted]

4.11 Other examinations

4.12 Time to tumour

4.13 Other

Section 6.7(2)
Carcinogenicity -Mice

Annex Point IIA6.7 **2 year dietary combined toxicity/ carcinogenicity study in mice**

IUCLID 5.7/2

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

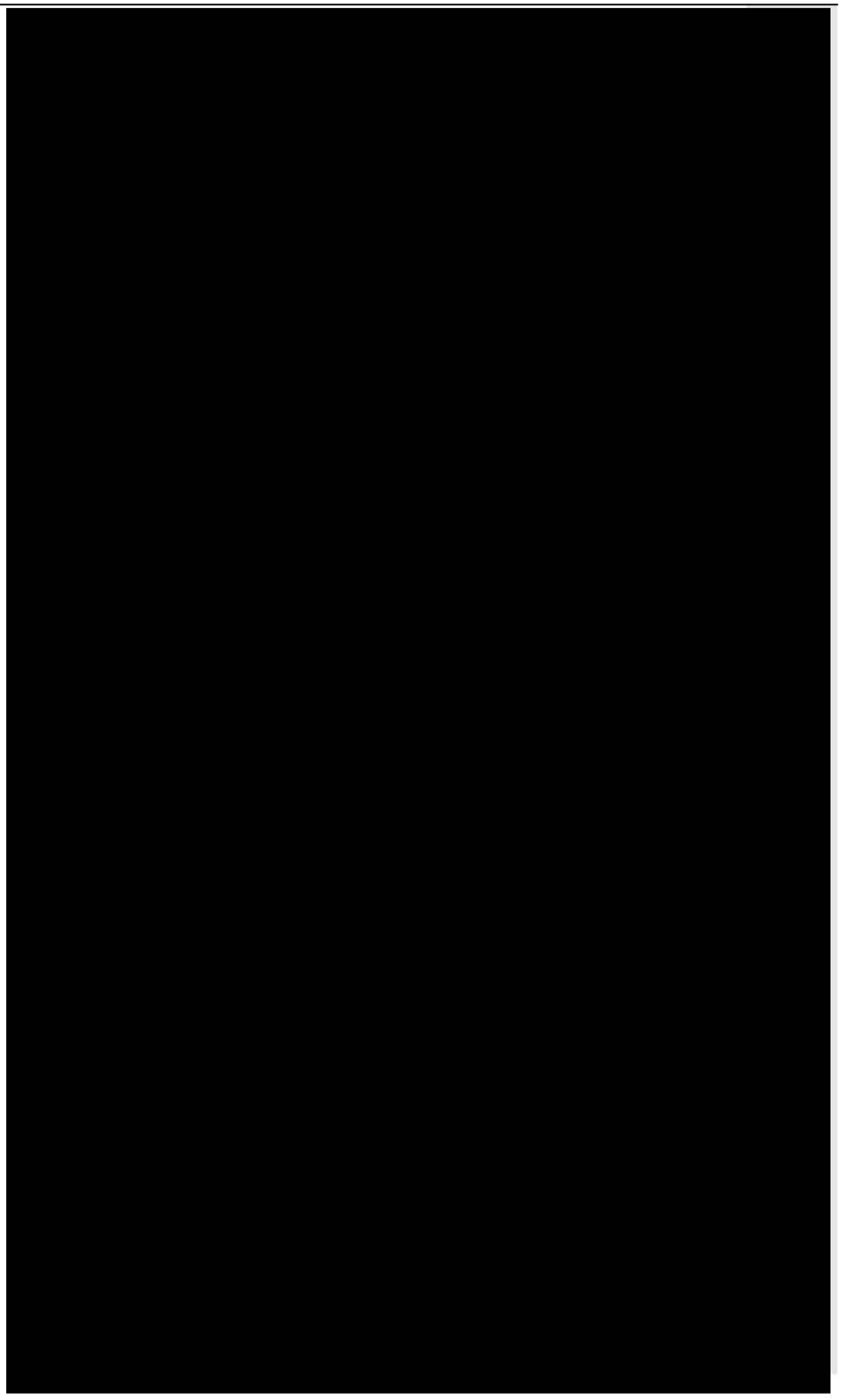
[redacted]

5.2 Results and discussion

Section 6.7(2)
Carcinogenicity -Mice

Annex Point IIA6.7 **2 year dietary combined toxicity/ carcinogenicity study in mice**

IUCLID 5.7/2



Section 6.7(2)
Carcinogenicity -Mice

Annex Point IIA6.7 **2 year dietary combined toxicity/ carcinogenicity study in mice**

IUCLID 5.7/2

5.3 Conclusion

[redacted]

It is concluded that in the study, the no-effect level was at least [redacted] in males (equivalent to ca. 40 mg/kg bw/day) and [redacted] in females (equivalent to 164 mg/kg bw/day).

5.3.1 Reliability [redacted]

5.3.2 Deficiencies

Section 6.7(2)
Carcinogenicity -Mice

Annex Point IIA6.7 **2 year dietary combined toxicity/ carcinogenicity study in mice**

IUCLID 5.7/2

[redacted]

Date

Materials and Methods

Results and discussion

Conclusion

Reliability

Acceptability

Remarks