6.2.3 Tissue distribution in rats (high dose)

Section 6.2.3/01 **Tissue distribution in rats (high dose)**

Annex point IIA 6.2

Official use only

1 REFERENCE

1.1 Reference [redacted]

1.2 Data protection Yes

1.2.1 Data owner Sumitomo Chemical Co., Ltd.

1.2.3 Criteria for data protection Data submitted to the MS after 13 May 2000 on existing a.s for the purpose of entry into Annex I

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study In-house method equivalent to Directive 88/302/EEC, Part B Toxicokinetics, (1988)

2.2 GLP [redacted]

2.3 Deviations [redacted]

3 MATERIALS AND METHODS

3.1 Test material [redacted]

3.1.1 Lot/Batch No [redacted]

3.1.2 Specification [redacted]

3.1.3 Description [redacted]

3.1.4 Purity [redacted]

3.1.5 Stability [redacted]

3.1.6 Specific activity [redacted]

3.2 Test animals

3.2.1 Species Rats

3.2.2 Strain	[redacted]
3.2.3 Source	[redacted]
3.2.4 Sex	Male and female
3.2.5 Number of animals/group	[redacted]
3.3 Administration	Oral
3.3.1 Duration of treatment	Single dose
3.3.2 Dose levels	1000 mg/kg
3.3.3 Sample collection	[redacted]
3.3.4 Analysis	[redacted]

4 RESULTS

4.1 Tissue residues

[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSIONS

5.1 Materials and methods

[redacted]

5.2 Results and discussion

The highest concentrations of radioactivity were detected in the blood, liver, kidney and fat of male rats and in the liver, kidney and fat of females. [redacted] A total of less than 1.3% of the dose was retained in all tissues at any time point. Biological half-lives of ^{14}C concentrations were generally shorter for males

than for females. [redacted]

5.3 Conclusion

When compared to the previous study at a low dose (see 6.2.2) there were no significant dose-dependent differences in time courses (peak time points and half lives) of ^{14}C concentrations, which means that there was no tendency to accumulation of ^{14}C in any particular tissues at higher doses

5.3.1 Reliability [redacted]

5.3.2 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
[redacted]

[redacted]

Comments from...

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

6.2.4 Absorption, distribution, metabolism and excretion in rats (pyridyl-2,6-^{14}C)

Section 6.2.4/01
Annex point IIA 6.2

Absorption, distribution, metabolism and excretion in rats (pyridyl-2,6-^{14}C)

Official use only

1 REFERENCE

1.1 Reference

[redacted]

1.2 Data protection

Yes

1.2.1 Data owner

Sumitomo Chemical Co., Ltd.

1.2.3 Criteria for data protection

Data submitted to the MS after 13 May 2000 on existing a.s for the purpose of entry into Annex I

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study

In-house method equivalent, in part, to US-EPA Guidelines: Subdivision F. Rat Metabolism Series 85-1, Directive 88/302/EEC, Part B Toxicokinetics

2.2 GLP

[redacted]

2.3 Deviations

[redacted]

3 MATERIALS AND METHODS

3.1 Test material

[redacted]

3.1.1 Lot/Batch No

[redacted]

3.1.2 Specification

[redacted]

3.1.3 Description

[redacted]

3.1.4 Purity

[redacted]

3.1.5 Stability

[redacted]

3.1.6 Specific activity	[redacted]
3.2 Test animals	
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 Number of animals/group	[redacted]
3.3 Administration	Oral
3.3.1 Duration of treatment	Single dose
3.3.2 Dose levels	[redacted]
3.3.3 Sample collection	[redacted]
3.3.4 Analysis	[redacted]

4 RESULTS

4.1 Excretion	[redacted]
4.2 Tissue residues	[redacted]

[redacted]

4.3 Identity of metabolites

[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSIONS

5.1 Materials and methods

[redacted]

5.2 Results and discussion

[redacted] Pyriproxyfen was extensively metabolised [redacted] Unchanged pyriproxyfen was present in both excreta. [redacted]

5.3 Conclusion

Pyriproxyfen was rapidly excreted in rats, mainly in the faeces. Tissue residues 7 days after dosing were low in all dose groups.

[redacted]

5.3.1 Reliability

[redacted]

5.3.2 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

[redacted]

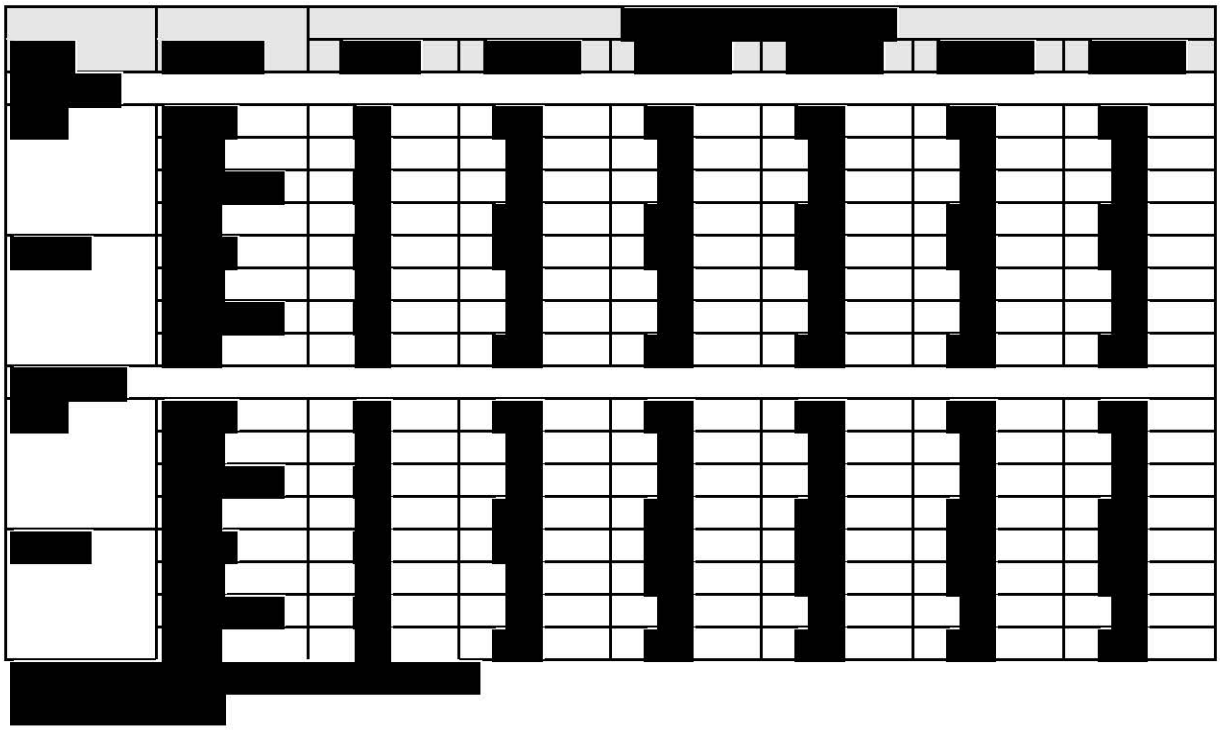
[redacted]

The conclusion as presented in the DAR is included above.

Comments from...

[redacted]

[redacted]



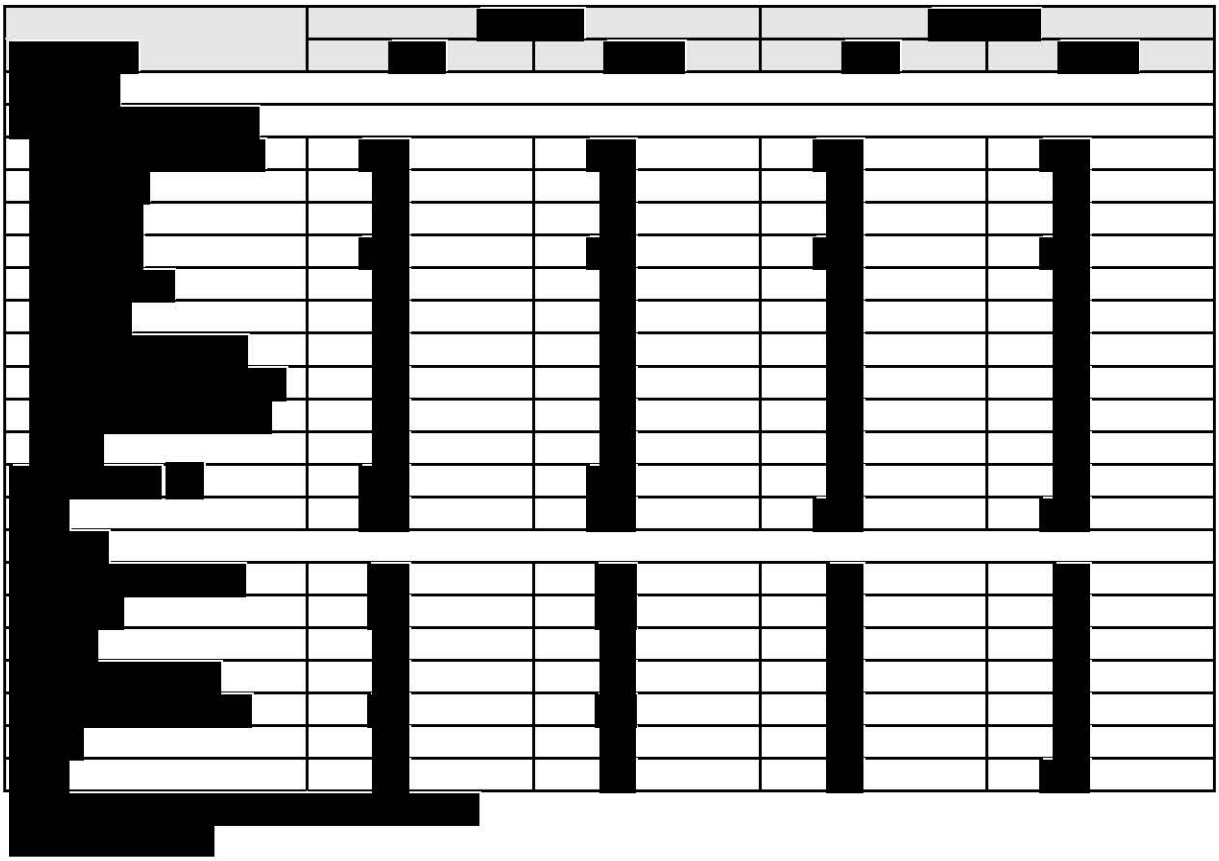
[redacted]

[redacted]

[redacted]

[redacted]

[redacted]



[redacted]

6.2.5 Comparative metabolism study of pyriproxyfen in rats and mice

Section 6.2.5/01 **Comparative metabolism study of pyriproxyfen in rats and mice**

Annex point IIA 6.2

Official use only

1 REFERENCE

1.1 Reference [redacted]

1.2 Data protection No

1.2.1 Data owner Sumitomo Chemical Co., Ltd.

1.2.3 Criteria for data protection -

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study [redacted]

2.2 GLP [redacted]

2.3 Deviations [redacted]

[redacted] AND METHODS

3.1 Test material [redacted]

3.1.1 Lot/Batch No [redacted]

3.1.2 Specification [redacted]

3.1.3 Description

3.1.4 Purity [redacted]

3.1.5 Stability [redacted]

3.1.6 Specific activity [redacted]

3.2 Test animals

3.2.1 Species Rat and mouse

3.2.2 Strain [redacted]

[redacted]

3.2.3 Source [redacted]

3.2.4 Sex Males and females

3.2.5 Number of animals/group [redacted]

[redacted]

3.3 Administration

3.3.1 Duration of treatment Single oral dose

3.3.2 Dose levels 2 and 1000 mg/kg

3.3.3 Sample collection [redacted]

3.3.4 Analysis [redacted]

4 RESULTS

4.1 Excretion [redacted]

[redacted]

4.2 Tissue residues [redacted]

4.3 Identity of metabolites [redacted]

[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSIONS

5.1 Materials and methods

[redacted]

5.2 Results and discussion

Radioactivity was rapidly eliminated by both rats and mice and very little radioactivity was retained in tissues.

[redacted]

5.3 Conclusion

The previous and present studies have shown that there are significant sex-related differences in metabolic reactions of pyriproxyfen (4'-hydroxylation, 5''-hydroxylation, ether cleavage) in the rat, but not in the mouse.

5.3.1 Reliability

[redacted]

5.3.2 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
Comments from

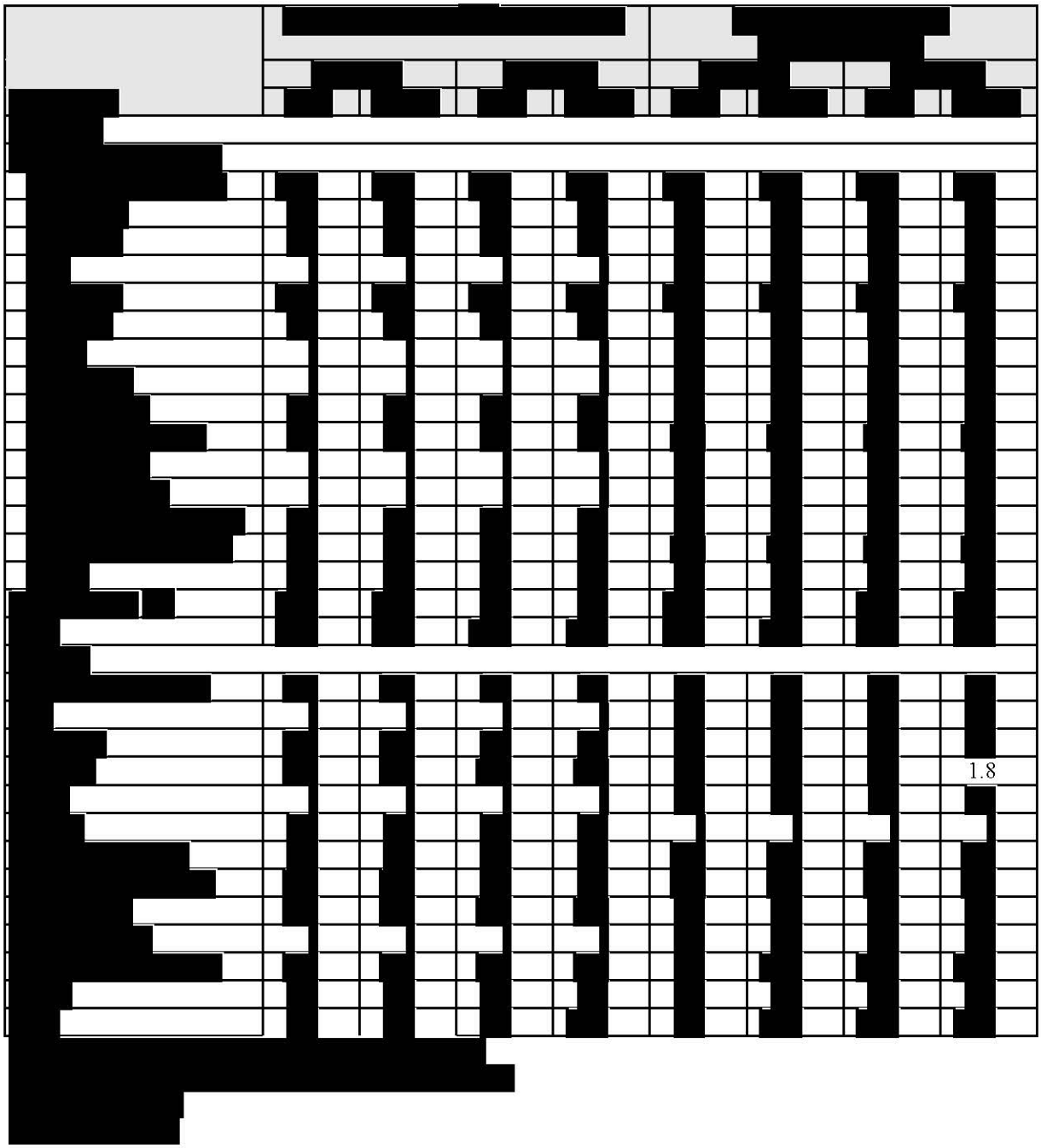
[redacted]

[redacted]

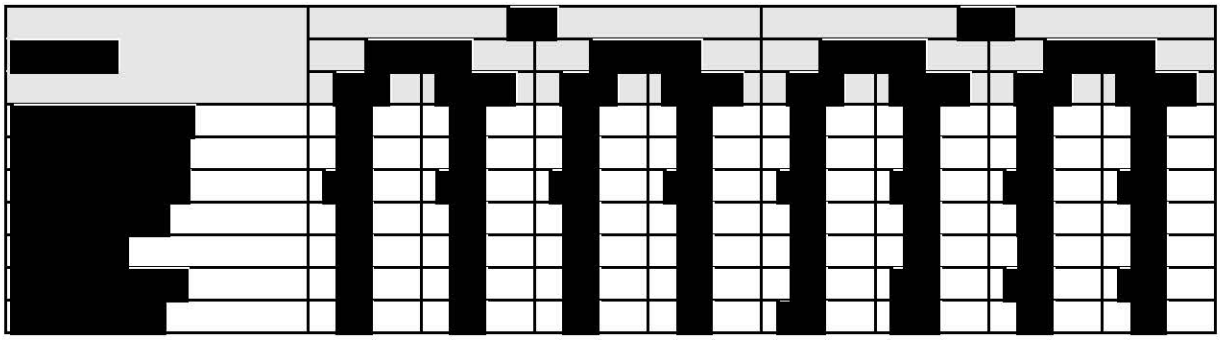
[redacted]

[redacted]

[redacted]



[redacted]



6.2.6 Percutaneous absorption

Section 6.2.6 Annex Point IIA 6.2	Percutaneous absorption	
	Justification for non-submission of data As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier. If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable	Official use only
Other existing data [Yes] **Limited exposure [Yes]**	**Technically not feasible [ ]** **Scientifically unjustified [ ]** **Other justification [ ]**	
Detailed justification:	There is no exposure to the active substance as pyriproxyfen is not synthesised and the product is not produced within the EU. A study on the active ingredient is therefore not considered necessary and has not been conducted. A dermal absorption study of a formulation is shown in Document IIIB, Section 6.	
Undertaking of intended data submission [ ]	Not applicable	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	Evaluation by Rapporteur Member State	
[redacted]	[redacted]	
[redacted]	[redacted]	
[redacted]	[redacted]	
[redacted]	[redacted]	
	[redacted]	
[redacted]		
[redacted]		

[redacted]

[redacted]

6.3 Short term repeated dose toxicity (28 days)

6.3.1 Repeated dose toxicity (oral)

Section A6.3.1/01 Repeated dose oral toxicity study in rats

Annex Point IIA6.3

Official use only

1 REFERENCE

1.1 Reference	[redacted]
1.2 Data protection	Yes
1.2.1 Data owner	Sumitomo Chemical Co., Ltd.
1.2.3 Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s for the purpose of entry into Annex I

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study	No, in house method which was broadly similar to OECD 407
2.2 GLP	[redacted]
2.3 Deviations	[redacted]

3 MATERIALS AND METHODS

3.1 Test material	[redacted]
3.1.1 Lot/Batch No	[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	
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 per group	[redacted]
3.2.7 Control animals	Yes
3.3 Administration / Exposure	
3.3.1 Duration of treatment	28 days
3.3.2 Frequency of exposure	Daily
3.3.3 Post exposure period	None
3.3.4 Oral	
3.3.4.1 Type	In food
3.3.4.2 Concentration	[redacted] 0, 29.3, 97.6, 286 and 913 mg/kg bw/day for male rats and 0, 28.8, 95.8, 286 and 869 mg/kg bw/day for female rats)[redacted] Food consumption was *ad libitum*
3.3.4.3 Vehicle	[redacted]
3.3.4.4 Concentration in vehicle	[redacted]
3.3.4.5 Total volume applied	[redacted]
3.3.4.6 Controls	[redacted]
3.4 Examinations	
3.4.1 Observations	
3.4.1.1 Clinical signs	[redacted]
3.4.1.2 Mortality	[redacted]
3.4.2 Body weight	[redacted]
3.4.3 Food consumption	[redacted]
3.4.4 Water consumption	[redacted]
3.4.5 Ophthalmoscopic examination	[redacted]
3.4.6 Haematology	[redacted]

3.4.7 Clinical chemistry

[redacted]

3.4.8 Urinalysis

[redacted]

3.5 Sacrifice and pathology

3.5.1 Organ weights

[redacted]

3.5.2 Gross and histopathology

[redacted]

3.5.3 Other examinations

[redacted]

3.5.4 Statistics

[redacted]

3.6 Further remarks

None

4 RESULTS

4.1 Observations

4.1.1 Clinical signs

[redacted]

[redacted]

4.1.2 Mortality

[redacted]

4.2 Body weight gain

[redacted]

4.3 Food consumption and compound intake

[redacted]

4.4 Ophthalmoscopic examination

[redacted]

4.5 Blood analysis

4.5.1 Haematology

[redacted]

4.5.2 Clinical chemistry

[redacted]

4.5.3 Urinalysis

[redacted]

[redacted]

4.6 Sacrifice and pathology

4.6.1 Organ weights

[redacted]

4.6.2 Gross and histopathology

[redacted]

4.7 Other examinations

None

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted]

5.2 Results and discussion

[redacted]

	[redacted]
5.3 Conclusion	No-observed-adverse effect-level (NOAEL) was [redacted] 29.3 mg/kg bw/day for males and 28.8 mg/kg bw/day for females) - based on clinical chemistry changes [redacted]
5.3.1 LO(A)EL	[redacted] (97.6 mg/kg bw/day for males and 95.8 mg/kg bw/day for females)
5.3.2 NO(A)EL	[redacted] (equivalent to 29.3 mg/kg bw/day for males and 28.8 mg/kg bw/day for females)
5.3.3 Other	None
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	
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
Comments From	
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[redacted]		[redacted]		[redacted]		[redacted]		[redacted]		[redacted]	
[redacted]		[redacted]		[redacted]		[redacted]		[redacted]		[redacted]	
[redacted]		[redacted]		[redacted]		[redacted]		[redacted]		[redacted]	
[redacted]		[redacted]		[redacted]		[redacted]		[redacted]		[redacted]	
[redacted]		[redacted]		[redacted]		[redacted]		[redacted]		[redacted]	
[redacted]		[redacted]		[redacted]		[redacted]		[redacted]		[redacted]	
[redacted]											
[redacted]		[redacted]		[redacted]		[redacted]		[redacted]		[redacted]	
[redacted]		[redacted]		[redacted]		[redacted]		[redacted]		[redacted]	
[redacted]		[redacted]		[redacted]		[redacted]		[redacted]		[redacted]	
[redacted]		[redacted]		[redacted]		[redacted]		[redacted]		[redacted]	
[redacted]		[redacted]		[redacted]		[redacted]		[redacted]		[redacted]	
[redacted]		[redacted]		[redacted]		[redacted]		[redacted]		[redacted]	

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Section A6.3.1/02 **Repeated dose oral toxicity study in dogs**

Annex Point IIA6.3.1

Official use only

1 REFERENCE

1.1 Reference [redacted]

1.2 Data protection Yes

1.2.1 Data owner Sumitomo Chemical Co., Ltd.

1.2.3 Criteria for data protection Data submitted to the MS after 13 May 2000 on existing a.s for the purpose of entry into Annex I

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study Yes

In-house method equivalent to guidelines of toxicity studies of drugs on repeated administration, Notification No.118 of the Pharmaceutical Affairs Bureau, Ministry of Health and Welfare, February 15 1984

2.2 GLP [redacted]

2.3 Deviations [redacted]

3 MATERIALS AND METHODS

3.1 Test material	[redacted]
3.1.1 Lot/Batch No	[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	
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]
3.2.7 Control animals	Yes
3.3 Administration / Exposure	
3.3.1 Duration of treatment	28 Days
3.3.2 Frequency of exposure	Daily
3.3.3 Post exposure period	None
3.3.4 Oral	
3.3.4.1 Type	[redacted]
3.3.4.2 Concentration	0, [redacted] 1000 mg/kg bw/day
3.3.4.3 Vehicle	[redacted]
3.3.4.4 Concentration in vehicle	[redacted]
3.3.4.5 Total volume applied	[redacted]
3.3.4.6 Controls	[redacted]
3.4 Examinations	
3.4.1 Observations	

3.4.1.1 Clinical signs

3.4.1.2 Mortality

3.4.2 Body weight

3.4.3 Food consumption

3.4.4 Water consumption

3.4.5 Ophthalmoscopic examination

3.4.6 Haematology

3.4.7 Clinical chemistry

3.4.8 Urinalysis

3.4.9 Faeces

3.5 Sacrifice and pathology

3.5.1 Organ weights

3.5.2 Gross and histopathology

3.5.4 Statistics [redacted]

3.6 Further remarks

4 RESULTS

4.1 Observations

4.1.1 Clinical signs [redacted]

4.1.2 Mortality [redacted]

4.2 Body weight gain [redacted]

4.3 Food consumption and compound intake [redacted]

4.4 Ophthalmoscopic examination [redacted]

4.5 Blood analysis

4.5.1 Haematology [redacted]

4.5.2 Clinical chemistry [redacted]

4.5.3 Urinalysis and faecal examination [redacted]

4.6 Sacrifice and pathology

4.6.1 Organ weights [redacted]

4.6.2 Gross and histopathology [redacted]

4.7 Other examinations None

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods [redacted]

5.2 Results and Discussion

[redacted]

5.3 Conclusion The only treatment related change noted was on the liver.

5.3.1 LO(A)EL 1000 mg/kg bw/day

5.3.2 NO(A)EL 300 mg/kg bw/day

5.3.3 Other None

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
[redacted]

Comments from..

[redacted]

[redacted]

[redacted]	[redacted]		[redacted]	
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

6.3.2 Repeated dose toxicity (dermal)

Section A6.3.2/01 Repeated dose toxicity (dermal)

Annex Point
IIA 6.3.2

Official use only

1 REFERENCE

1.1 Reference [redacted]

1.2 Data protection Yes

1.2.1 Data owner Sumitomo Chemical Co., Ltd.

1.2.3 Criteria for data protection Data submitted to the MS after 13 May 2000 on existing a.s for the purpose of entry into Annex I

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study Yes

US EPA FIFRA § 82-2, OECD 410

2.2 GLP [redacted]

2.3 Deviations [redacted]

3 MATERIALS AND METHODS

3.1 Test material [redacted]

3.1.1 Lot/Batch No [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

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 per group	[redacted]
3.2.7 Control animals	Yes
3.3 Administration / Exposure	
3.3.1 Duration of treatment	21 days
3.3.2 Frequency of exposure	Daily
3.3.3 Post exposure period	None
3.3.4 Dermal	
3.3.4.1 Area covered	25 cm^2
3.3.4.2 Occlusion	Occlusive
3.3.4.3 Vehicle	[redacted]
3.3.4.4 Concentration in vehicle	[redacted]
3.3.4.5 Total volume applied	[redacted]
3.3.4.6 Dose	0, 100, 300 and 1000 mg./kg
3.3.4.7 Duration of exposure	6 hours
3.3.4.8 Removal of substance	[redacted]
3.3.4.9 Controls	[redacted]
3.4 Examinations	
3.4.1 Observations	
3.4.1.1 Clinical signs	[redacted]
3.4.1.2 Mortality	[redacted]
3.4.2 Body weight	[redacted]
3.4.3 Food consumption	[redacted]
3.4.4 Water consumption	[redacted]
3.4.5 Ophthalmoscopic examination	[redacted]
3.4.6 Haematology	[redacted]

[redacted]

3.4.7 Clinical chemistry

[redacted]

3.4.8 Urinalysis

[redacted]

3.5 Sacrifice and pathology

3.5.1 Organ weights

[redacted]

3.5.2 Gross and histopathology

[redacted]

3.5.3 Other examinations

[redacted]

3.5.4 Statistics

[redacted]

3.6 Further remarks

4 RESULTS

4.1 Observations

4.1.1 Clinical signs

[redacted]

4.1.2 Mortality

4.2 Body weight gain

4.3 Food consumption

4.4 Ophthalmoscopic examination

4.5 Blood 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

4.7 Other examinations Not applicable

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods [redacted]

5.2 Results and discussion [redacted]

5.3 Conclusion No treatment related effects were observed at any dose level

5.3.1 LO(A)EL No effects were observed at any dose level

5.3.2 NO(A)EL 1000 mg/kg bw/day, the highest dose tested

5.3.3 Other None

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
[redacted]

Comments from...

[redacted]

[redacted]

[redacted]

[redacted]

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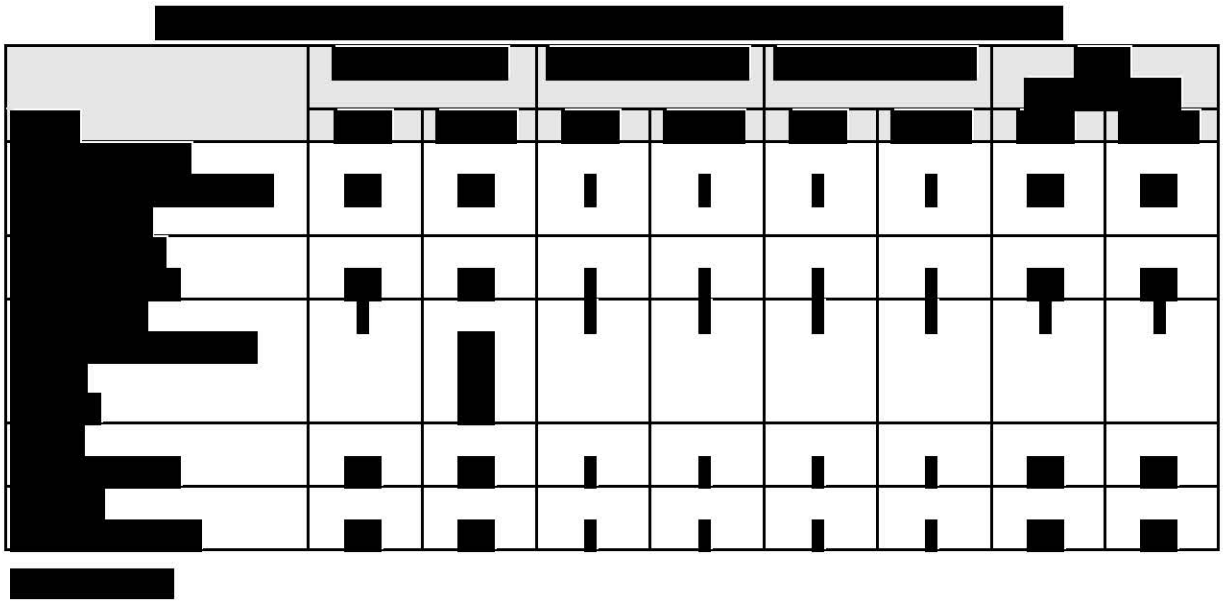


[redacted]

6.3.3 Repeated dose toxicity (inhalation)

Section A6.3.3/01 **Repeated dose toxicity (inhalation)**

Annex Point IIA6.3.3

Official use only

1 REFERENCE

1.1 Reference [redacted]

1.2 Data protection Yes

1.2.1 Data owner Sumitomo Chemical Co., Ltd.

1.2.3 Criteria for data protection Data submitted to the MS after 13 May 2000 on existing a.s for the purpose of entry into Annex I

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study Yes

In-house method equivalent to OECD 412, EEC B.8

2.2 GLP [redacted]

2.3 Deviations [redacted]

3 MATERIALS AND METHODS

3.1 Test material	[redacted]	
3.1.1 Lot/Batch No	[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		
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 per group	[redacted]	
3.2.7 Control animals	Yes, both vehicle only and untreated controls	
3.3 Administration / Exposure		
3.3.1 Duration of treatment	28 Days	
3.3.2 Frequency of exposure	Daily	
3.3.3 Post exposure period	None	
3.3.4 Inhalation		
3.3.4.1 Concentrations	Nominal concentration	Not included in the report
	Analytical concentration	269, 482 and 1000[mg/m³]
3.3.4.2 Particle size	[redacted]	
3.3.4.3 Type or preparation of particles	[redacted]	
3.3.4.4 Type of exposure	Whole body	

3.3.4.5 Vehicle	[redacted]
3.3.4.6 Concentration in vehicle	[redacted]
3.3.4.7 Duration of exposure	4 h or other
3.3.4.8 Controls	Vehicle and untreated controls

3.4 Examinations

3.4.1 Observations	
3.4.1.1 Clinical signs	[redacted]
3.4.1.2 Mortality	[redacted]
3.4.2 Body weight	[redacted]
3.4.3 Food consumption	[redacted]
3.4.4 Water consumption	[redacted]
3.4.5 Ophthalmoscopic examination	[redacted]
3.4.6 Haematology	[redacted]
3.4.7 Clinical chemistry	[redacted]
3.4.8 Urinalysis	[redacted]

3.5 Sacrifice and pathology

3.5.1 Organ weights	[redacted]
3.5.2 Gross and	[redacted]

histopathology [redacted]

3.5.3 Other examinations [redacted]

3.5.4 Statistics [redacted]

3.6 Further remarks None

4 RESULTS

4.1 Observations

4.1.1 Clinical signs [redacted]

4.1.2 Mortality [redacted]

4.2 Body weight gain [redacted]

4.3 Food consumption [redacted]

4.4 Water consumption [redacted]

[redacted]

4.5 Ophthalmoscopic examination

[redacted]

4.6 Blood analysis

4.6.1 Haematology

[redacted]

4.6.2 Clinical chemistry

[redacted]

4.6.3 Urinalysis

[redacted]

4.7 Sacrifice and pathology

4.7.1 Organ weights

[redacted]

4.7.2 Gross and histopathology

[redacted]

[redacted]

[redacted]

4.8 Other examinations None

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods [redacted]

5.2 Results and discussion [redacted]

5.3 Conclusion No-observed-adverse-effect-level was 482 mg/m^3/day (0.482 mg/l/day)

5.3.1 LO(A)EL 1000 mg/m^3/day

5.3.2 NO(A)EL 482 mg/m^3/day

5.3.3 Other None

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
[redacted]

[redacted]

Comments from...

[redacted]

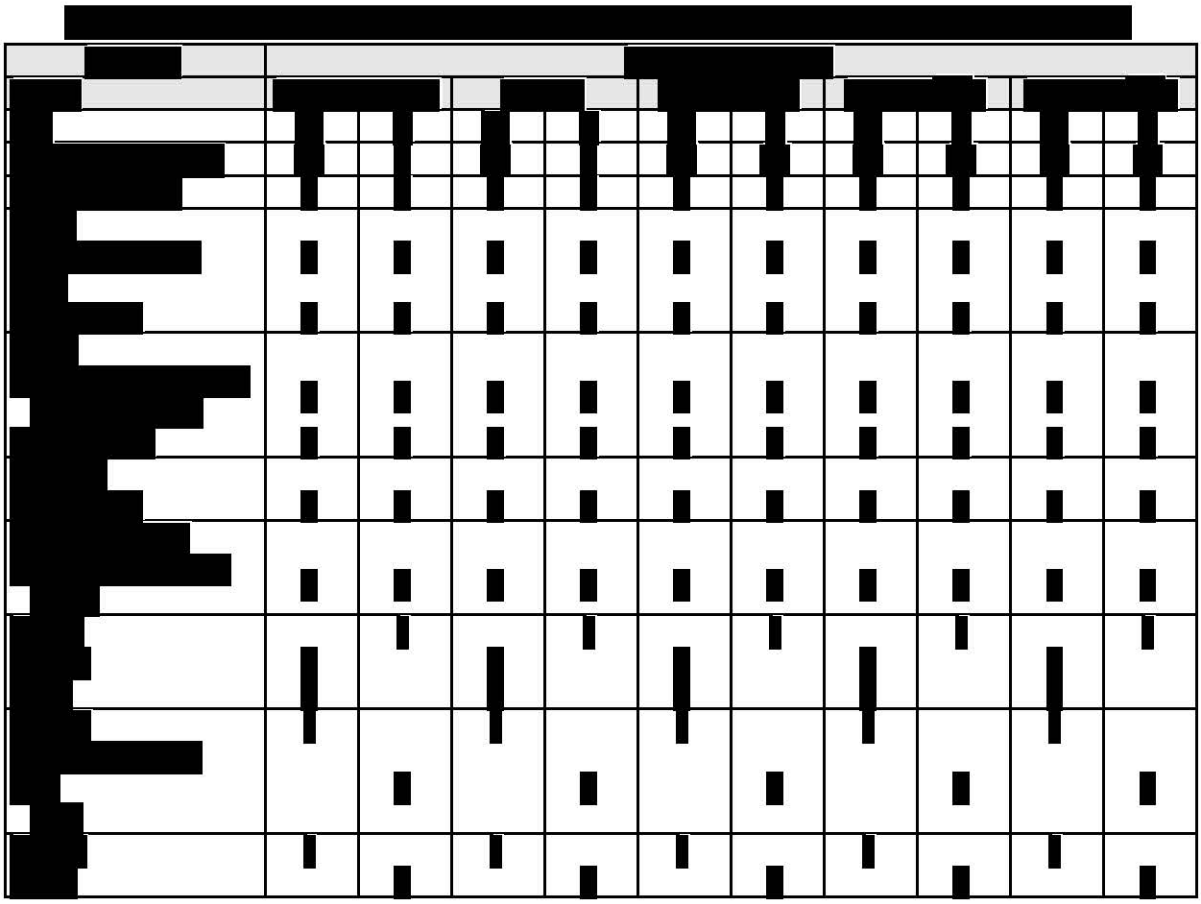
[redacted]

[redacted]

[redacted]

[redacted]

[redacted]



6.4 Subchronic toxicity

6.4.1 Subchronic oral toxicity

Section A 6.4.1/01 90 Day toxicity study in rats

Annex Point
IIA 6.4.1

Official use only

1 REFERENCE

1.1 Reference	[redacted]
1.2 Data protection	Yes
1.2.1 Data owner	Sumitomo Chemical Co., Ltd.
1.2.3 Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s for the purpose of entry into Annex I

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study	Yes US EPA FIFRA § 82-1, Japanese MAFF 59 Nohsan No.4200, and OECD 408
2.2 GLP	[redacted]
2.3 Deviations	[redacted]

3 MATERIALS AND METHODS

3.1 Test material	[redacted]
3.1.1 Lot/Batch No	[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	
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 per group	[redacted]
3.2.7 Control animals	Yes
3.3 Administration / Exposure	
3.3.1 Duration of treatment	93 Days
3.3.2 Frequency of exposure	Daily
3.3.3 Post exposure period	None
3.3.4 Oral	
3.3.4.1 Type	In food
3.3.4.2 Concentration	[redacted] 0, 23, 118, 309 and 642 mg/kg bw/day for male rats and 0, 28, 141, 356 and 784 mg/kg bw/day for female rats. Food consumption per day was ad libitum
3.3.4.3 Vehicle	[redacted]
3.3.4.4 Concentration in vehicle	[redacted]
3.3.4.5 Total volume applied	[redacted]
3.3.4.6 Controls	[redacted]
3.4 Examinations	
3.4.1 Observations	
3.4.1.1 Clinical signs	[redacted]
3.4.1.2 Mortality	[redacted]
3.4.2 Body weight	[redacted]
3.4.3 Food consumption	[redacted]
3.4.4 Water consumption	[redacted]
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

3.5.2 Gross and histopathology

3.5.3 Other examinations

3.5.4 Statistics

3.6 Further remarks

4 RESULTS

4.1 Observations

4.1.1 Clinical signs

4.1.2 Mortality

4.2 Body weight gain

4.3 Food consumption and compound intake

4.4 Water consumption

4.5 Ophthalmoscopic examination

4.6 Blood analysis

4.6.1 Haematology

4.6.2 Clinical chemistry

4.6.3 Urinalysis

[redacted]

4.7 Sacrifice and pathology

4.7.1 Organ weights

[redacted]

4.7.2 Gross and histopathology

[redacted]

4.8 Other examinations

[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted]

5.2 Results and discussion

[redacted]

[redacted]

5.3 Conclusion The liver and red blood cells are the target organs for pyriproxyfen toxicity

5.3.1 LO(A)EL The LOAEL was [redacted] 118 mg/kg bw/day in male rats and 141 mg/kg bw/day in female rats)

5.3.2 NO(A)EL The NOAEL was [redacted] 23 mg/kg bw/day in male rats and 28 mg/kg bw/day in female rats)

5.3.3 Other None

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
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

Draft Assessment Report of pyriproxyfen (91/414/EEC).

Comments from...

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

	[redacted]		[redacted]		[redacted]		[redacted]		[redacted]	
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]										
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]										
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Section A 6.4.1/02 **6 Month toxicity study in rats**

Annex Point IIA 6.4.1

Official use only

1 REFERENCE

1.1 Reference	[redacted]
1.2 Data protection	Yes
1.2.1 Data owner	Sumitomo Chemical Co., Ltd.
1.2.3 Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s for the purpose of entry into Annex I

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study	No, but the study generally complied with OECD 452
	[redacted]
2.2 GLP	[redacted]
2.3 Deviations	[redacted]

3 MATERIALS AND METHODS

3.1 Test material	[redacted]
3.1.1 Lot/Batch No	[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	
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 per group	[redacted]
3.2.7 Control animals	Yes
3.3 Administration / Exposure	
3.3.1 Duration of treatment	26 Weeks
3.3.2 Frequency of exposure	Daily
3.3.3 Post exposure period	None
3.3.4 Oral	
3.3.4.1 Type	In food
3.3.4.2 Concentration	[redacted] 0, 4.80, 24.0, 121 and 682 mg/kg bw/day in males and 0, 5.36, 27.5, 136 and 688 mg/kg bw/day[redacted] Food consumption was *ad libitum*
3.3.4.3 Vehicle	[redacted]
3.3.4.4 Concentration in vehicle	[redacted]
3.3.4.5 Total volume applied	[redacted]
3.3.4.6 Controls	[redacted]
3.4 Examinations	
3.4.1 Observations	
3.4.1.1 Clinical signs	[redacted]
3.4.1.2 Mortality	[redacted]
3.4.2 Body weight	[redacted]
3.4.3 Food consumption	[redacted]
3.4.4 Water consumption	[redacted]
3.4.5 Ophthalmoscopic	[redacted]

examination

3.4.6 Haematology

3.4.7 Clinical chemistry

3.4.8 Urinalysis

ty

3.5 Sacrifice and pathology

3.5.1 Organ weights

3.5.2 Gross and histopathology

3.5.3 Other examinations

3.5.4 Statistics

3.6 Further remarks None

4 RESULTS

4.1 Observations

4.1.1 Clinical signs

4.1.2 Mortality

4.2 Body weight gain

4.3 Food consumption and compound intake

4.4 Ophthalmoscopic examination

4.5 Blood analysis

4.5.1 Haematology

4.5.2 Clinical chemistry

4.5.3 Urinalysis

4.6 Sacrifice and pathology

4.6.1 Organ weights

[redacted]

4.6.2 Gross and histopathology

[redacted]

4.7 Other examinations

[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted]

5.2 Results and discussion

[redacted]

[redacted]

5.3 Conclusion

The No-observed-adverse effect-level was [redacted] 24.0 mg/kg/day (males) and 27.5 mg/kg/day (female) based on changes in haematology and clinical chemistry in males and females [redacted]

5.3.1 LO(A)EL

[redacted] 121 mg/kg bw/day for male rats and 136 mg/kg bw/day for female rats

5.3.2 NO(A)EL

[redacted] 24.0 mg/kg bw/day for male rats and 27.5 mg/kg bw/day for female rats

5.3.3 Other

None

5.3.4 Reliability

[redacted]

5.3.5 Deficiencies

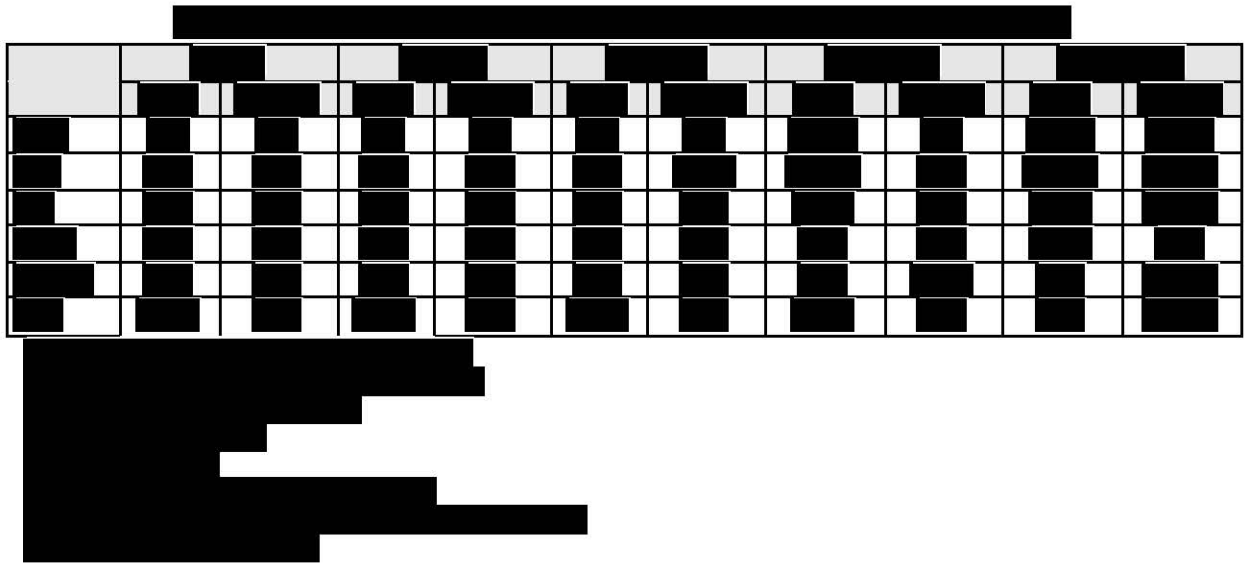
[redacted]

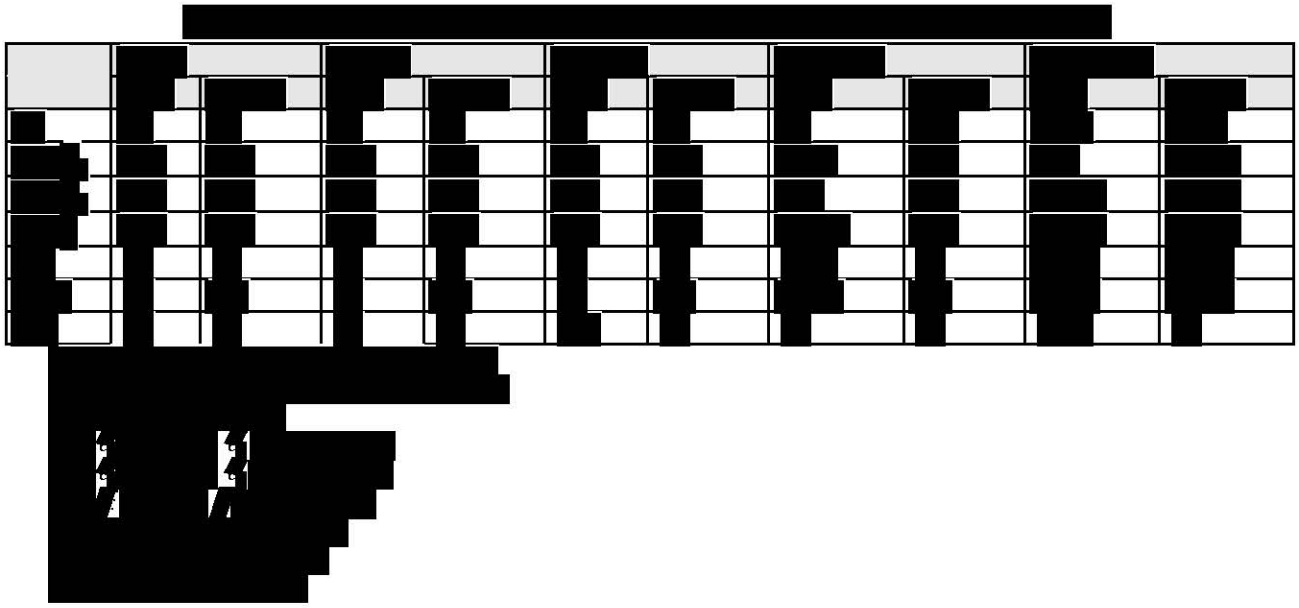
Evaluation by Competent Authorities
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
Evaluation by Rapporteur Member State
[redacted]
Comments from...
[redacted]

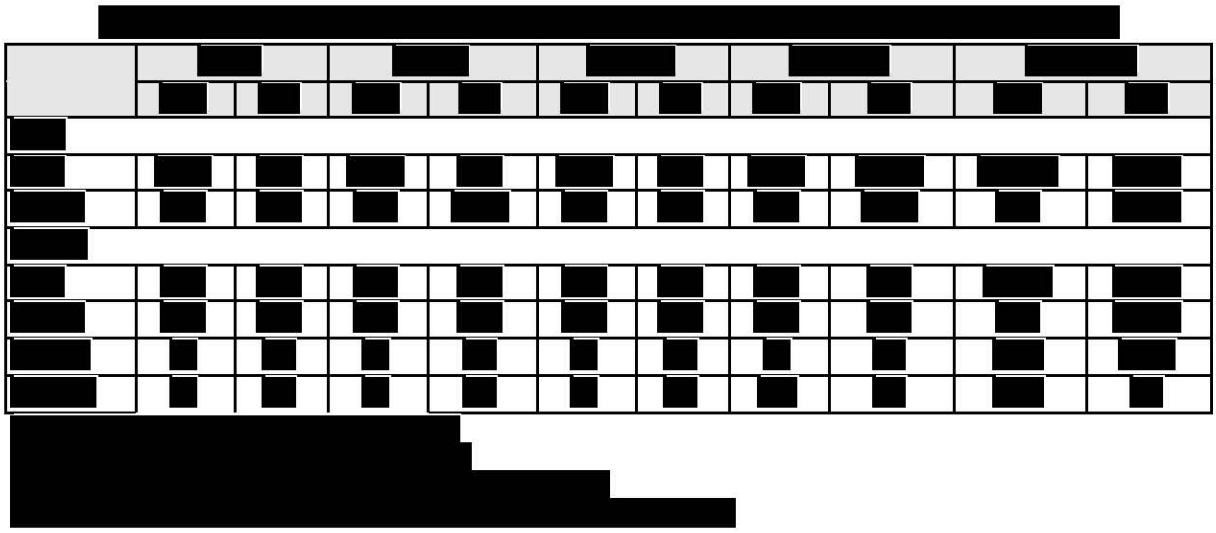
[redacted]

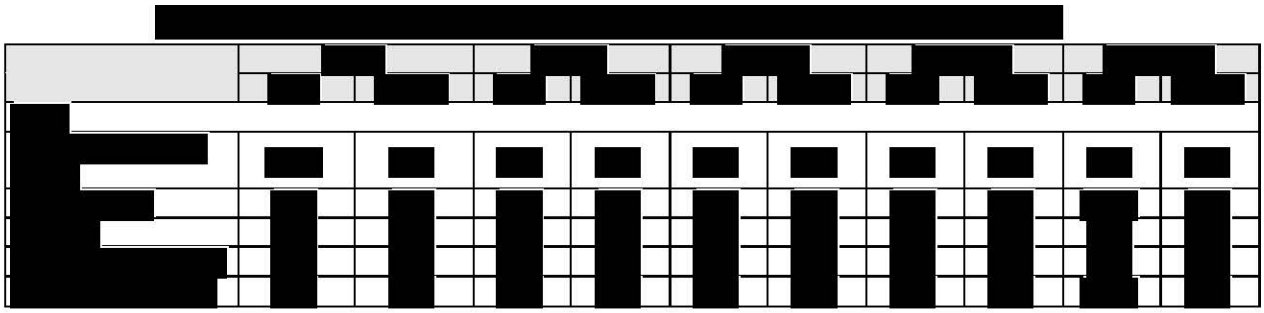
[redacted]

[redacted]









Section A 6.4.1/03 **90 Day toxicity study in dogs**

Annex Point IIA 6.4.1

Official use only

1 REFERENCE

1.1 Reference [redacted]

1.2 Data protection Yes

1.2.1 Data owner Sumitomo Chemical Co., Ltd.

1.2.3 Criteria for data protection Data submitted to the MS after 13 May 2000 on existing a.s for the purpose of entry into Annex I

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study Yes

In-house method equivalent to guidelines of toxicity studies of drugs on repeated administration, Directive 88/302/EEC Part B, Sub-chronic oral toxicity test: 90-day repeated oral dose study using non-rodent species and OECD 409

2.2 GLP [redacted]

2.3 Deviations [redacted]

3 MATERIALS AND METHODS

3.1 Test material [redacted]

3.1.1 Lot/Batch No [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

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]
3.2.7 Control animals	Yes
3.3 Administration / Exposure	
3.3.1 Duration of treatment	91 days
3.3.2 Frequency of exposure	Daily
3.3.3 Post exposure period	None
3.3.4 Oral	
3.3.4.1 Type	[redacted]
3.3.4.2 Concentration	0, 100, 300 and 1000mg/kg bw/day
3.3.4.3 Vehicle	[redacted]
3.3.4.4 Concentration in vehicle	[redacted]
3.3.4.5 Total volume applied	[redacted]
3.3.4.6 Controls	[redacted]
3.4 Examinations	
3.4.1 Observations	
3.4.1.1 Clinical signs	[redacted]
3.4.1.2 Mortality	[redacted]
3.4.2 Body weight	[redacted]
3.4.3 Food consumption	[redacted]
3.4.4 Water consumption	[redacted]
3.4.5 Ophthalmoscopic examination	[redacted]
3.4.6 Haematology	[redacted]

[redacted]

3.4.7 Clinical chemistry

[redacted]

3.4.8 Urinalysis

[redacted]

3.4.9 Electrocardiogram

[redacted]

3.5 Sacrifice and pathology

3.5.1 Organ weights

[redacted]

3.5.2 Gross and histopathology

[redacted]

3.5.3 Other examinations

3.5.3.1 Faecal examination

[redacted]

3.5.3.2 Liver function test

[redacted]

3.5.3.3 Renal function test

[redacted]

3.5.3.4 Electron microscopy

[redacted]

3.5.4 Statistics [redacted]

3.6 Further remarks None

4 RESULTS

4.1 Observations

4.1.1 Clinical signs [redacted]

4.1.2 Mortality [redacted]

4.2 Body weight gain [redacted]

4.3 Food consumption [redacted]

4.4 Ophthalmoscopic examination [redacted]

4.5 Blood analysis

4.5.1 Haematology [redacted]

4.5.2 Clinical chemistry [redacted]

4.5.3 Urinalysis [redacted]

4.6 Sacrifice and pathology

4.6.1 Organ weights [redacted]

4.6.2 Gross and histopathology

4.7 Other examinations

4.7.1 Faecal examination

4.7.2 Liver function test

4.7.3 Renal function test

4.7.4 Electron microscopy

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods