98/8 Doc IIIA section No.	**6.1.1/02**	**Acute toxicity – Oral**
91/414 Annex Point addressed	**II 5.2.1 / 02**	Acute toxicity - oral

1.2	**Title**	Acute oral LD_{50} in the mouse of technical CGA 64'250
1.3 project N° Syngenta File N° (SAM)	**Report and/or**	78 52 43 64250 / 1529
1.4	**Lab. Report N°**	78 52 43
1.5 Reference to original study / report	**91/414 Cross**	5.2.1 / 02
1.6	**Authors**	Report: [redacted] (1979) Summary:
1.7	**Date of report**	May 7, 1979
1.8 owner	**Published /**	Unpublished / Syngenta
2.1	**Testing facility**	[redacted]
2.2 experimental work	**Dates of**	Experimental start February 27, 1979
3.	**Objectives**	Investigation of acute oral toxicity in mice
4.1	**Test substance**	CGA 64'250, technical grade active ingredient
x4.2	**Specification**	[redacted]
4.3 stability	**Storage**	not applicable (single treatment only)
4.4 vehicle	**Stability in**	not applicable
4.5 vehicle	**Homogeneity in**	not applicable
4.6	**Validity**	not applicable
5 solvent	**Vehicle /**	2% aqueous carboxymethylcellullose (CMC)
6	**Physical form**	viscous liquid
7.1	**Test method**	not specified
7.2	**Justification**	The procedures followed are in-line with current Guideline requirements.
7.3	**Copy of method**	A description of the method is part of the original study report as submitted under Reference 5.2.1 / 02.
8 method	**Choice of**	Standard procedure for the intended purpose
9	**Deviations**	Only formal deviations (see details below) from EC Directive 92/69 B1.
10.1 laboratory	**Certified**	not applicable
10.2 authority	**Certifying**	not applicable

10.3	**GLP**	no
10.4	**Justification**	When the study was performed, GLP was not compulsory
11.1	**GEP**	not applicable
11.2	**Type of facility (official or officially recognised)**	[redacted]
11.3	**Justification**	not applicable

x12.1	**Test system**	Strain: Source Age:	Mouse, Tif: MAG (SPF) Syngenta Ltd. Animal Production, 4332 Stein, Switzerland young adult (4 to 5 weeks)
12.2	**Procedure**	Dose levels: Group size: Dose regimen: Observation period:	800, 1'500, 2'500 and 3'000 mg/kg b.w. 5 males and 5 females single oral gavage of 10 or 20 ml/kg. The animals were fasted overnight before the treatment. 14 days. Body weights were measured weekly.

13 Findings

Dose	Mortality	Onset of death	Clinical signs, Autopsy
Males			
800 mg/kg 1'500 mg/kg 2'500 mg/kg 3'000 mg/kg	0 / 5 4 / 5 4 / 5 5 / 5	 Day 1 - 2 Day 3 - 4 Day 1 - 2	Sedation, Dyspnea, Abnormal Body Position, Ruffled Fur were observed in all groups with increasing severity. No effects on body weight gain.
Females			
800 mg/kg 1'500 mg/kg 2'500 mg/kg 3'000 mg/kg	1 / 5 0 / 5 5 / 5 5 / 5	Day 1 Day 1 - 3 Day 1 - 3	Sedation, Dyspnea, Abnormal Body Position, Ruffled Fur were observed in all groups with increasing severity. No effects on body weight gain.
LD_{50}: 1'490 mg/kg (1'138 - 1'875 mg/kg) calculated according to the logit model including 95% confidence limits			All symptoms were reversible within 10 - 11 days. No substance related gross organ changes were seen.

14 Statistics	see above
15 References (published)	none
16 Unpublished data	none
x17 Reliability Indicator	1

Data Protection Claim	Yes

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	12.11.2004
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
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	

PP 2.504/WM/ 24.10.1994

98/8 Doc IIIA section No.	**6.1.2/01**	**Acute toxicity – Dermal**
91/414 Annex Point addressed	**II 5.2.2 / 01**	Acute toxicity - percutaneous

1.2	**Title**	Acute dermal LD_{50} in the rat of technical CGA 64'250
1.3	**Report and/or project N° Syngenta File N° (SAM)**	78 52 45 64250 / 1531
1.4	**Lab. Report N°**	78 52 45
1.5	**91/414 Cross Reference to original study / report**	5.2.2 / 01
1.6	**Authors**	Report: [redacted] (1978b) Summary:
1.7	**Date of report**	January 22, 1979
1.8	**Published / owner**	Unpublished / Syngenta
2.1	**Testing facility**	[redacted]
2.2	**Dates of experimental work**	November 8 to 29, 1978
3.	**Objectives**	Investigation of acute dermal toxicity in rats
4.1	**Test substance**	CGA 64'250, technical grade active ingredient
4.2	**Specification**	[redacted]
4.3	**Storage stability**	not applicable (single treatment only)
4.4	**Stability in vehicle**	not applicable
4.5	**Homogeneity in vehicle**	not applicable
4.6	**Validity**	not applicable
5	**Vehicle / solvent**	None, the test article was applied in undiluted form.
6	**Physical form**	viscous liquid
7.1	**Test method**	According to Noakes, D.N. and Sanderson, D.M., Brit. J. Ind. Med. 26, 59-64, 1969
7.2	**Justification**	The procedures followed are mainly in-line with current Guideline requirements.
7.3	**Copy of method**	A description of the method is included in Report 5.2.2 / 01.
8	**Choice of method**	Standard procedure for the intended purpose
9	**Deviations**	Only formal deviations (see details below) from EC Directive 92/69 B3.
10.1	**Certified laboratory**	not applicable
10.2	**Certifying authority**	not applicable
10.3	**GLP**	no

10.4	**Justification**	When the study was performed, GLP was not compulsory
11.1	**GEP**	not applicable
11.2 (official or officially recognised)	**Type of facility**	[redacted]
11.3	**Justification**	not applicable

x12.1	**Test system**	Strain:	Rat, Sprague-Dawley derived. Tif: RAIf (SPF)
		Source	[redacted]
		Age:	young adult (8 to 9 weeks)
x12.2	**Procedure**	Dose levels:	3'000 and 4'000 mg/kg b.w.
		Group size:	5 males and 5 females
		Dose regimen:	single dermal application under occlusive dressing for 24 hours. The skin was clipped 24 hours before the treatment.
		Observation period:	14 days. Body weights were measured weekly.

13 Findings

Dose	Mortality	Onset of death	Clinical signs, Autopsy
Males			
3'000 mg/kg 4'000 mg/kg	0 / 5 0 / 5		Dyspnea, Abnormal Body Position and, Ruffled Fur were observed in both groups. No effects on body weight gain.
Females			
3'000 mg/kg 4'000 mg/kg	0 / 5 0 / 5		Dyspnea, Abnormal Body Position and, Ruffled Fur were observed in both groups. No effects on body weight gain.
LD_{50}: greater than 4'000 mg/kg			All symptoms were reversible within 9 days. No substance related gross organ changes were seen.

14	**Statistics**	see above
15 (published)	**References**	none
16 data	**Unpublished**	none
x17	**Reliability Indicator**	1

Data Protection Claim	Yes

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	12.11.2004
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
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	

PP 2.504/WM/ 24.10.1994

98/8 Doc IIIA section No.	**6.1.2/02**	**Acute toxicity – Dermal**
91/414 Annex Point addressed	**II 5.2.2 / 02**	Acute toxicity - percutaneous

1.2	**Title**	Acute dermal LD_{50} in the rabbit of technical CGA 64'250
1.3	**Report and/or project N° Syngenta File N° (SAM)**	79 03 75 64250 / 1532
1.4	**Lab. Report N°**	79 03 75
1.5	**91/414 Cross Reference to original study / report**	5.2.2 / 02
1.6	**Authors**	Report: [redacted] (1979a) Summary:
1.7	**Date of report**	July 2, 1979
1.8	**Published / owner**	Unpublished / Syngenta
2.1	**Testing facility**	[redacted]
2.2	**Dates of experimental work**	Start of the experiment May 31, 1979
3.	**Objectives**	Investigation of acute dermal toxicity in rabbitts
4.1	**Test substance**	CGA 64'250, technical grade active ingredient
x4.2	**Specification**	[redacted]
4.3	**Storage stability**	not applicable (single treatment only)
4.4	**Stability in vehicle**	not applicable
4.5	**Homogeneity in vehicle**	not applicable
4.6	**Validity**	not applicable
5	**Vehicle / solvent**	The test article was applied in undiluted form.
6	**Physical form**	viscous liquid
7.1	**Test method**	According to Noakes, D.N. and Sanderson, D.M., Brit. J. Ind. Med. 26, 59-64, 1969
7.2	**Justification**	The procedures followed are mainly in-line with current Guideline requirements.
7.3	**Copy of method**	A description of the method is included in Report 5.2.2 / 02.
8	**Choice of method**	Standard procedure for the intended purpose
9	**Deviations**	Only formal deviations (see details below) from EC Directive 92/69 B3.
10.1	**Certified laboratory**	not applicable
10.2	**Certifying authority**	not applicable
10.3	**GLP**	no

10.4	**Justification**	When the study was performed, GLP was not compulsory
11.1	**GEP**	not applicable
11.2	**Type of facility (official or officially recognised)**	[redacted]
11.3	**Justification**	not applicable

x12.1	**Test system**	Strain:	Rabbit, New Zealand White
		Source	[redacted]
		Age:	not specified
x12.2	**Procedure**	Dose levels:	0 (controls), 2'000 and 6'000 mg/kg b.w.
		Group size:	3 males and 3 females
		Dose regimen:	single dermal application under occlusive dressing for 24 hours. The skin was clipped 24 hours before the treatment.
		Observation period:	14 days. Body weights were measured weekly.

13 Findings

Dose	Mortality	Onset of death	Clinical signs, Autopsy
Males			
0 mg/kg 2'000 mg/kg 6'000 mg/kg	0 / 3 0 / 3 0 / 3		In the treated groups, the skin showed irritation during the first day. No effects on body weight gain.
Females			
0 mg/kg 2'000 mg/kg 6'000 mg/kg	0 / 3 0 / 3 0 / 3		In the treated groups, the skin showed irritation during the first day. No effects on body weight gain.
LD_{50}: greater than 6'000 mg/kg			The symptoms were reversible within 2 days. No substance related gross organ changes were seen.

14	**Statistics**	not applicable
15	**References (published)**	none
16	**Unpublished data**	none
x17	**Reliability Indicator**	1

Data Protection Claim	Yes

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	12.11.2004
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
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	

PP 2.504/WM/ 24.10.1994

98/8 Doc IIIA section No.	**6.1.3**	**Acute toxicity – Inhalation**
91/414 Annex Point addressed	**II 5.2.3 / 01**	Acute toxicity - inhalation

1.2	**Title**	CGA 64'250 tech.: Acute aerosol inhalation toxicity in the rat
1.3	**Report and/or project N° Syngenta File N° (SAM)**	87 14 71 64250 / 1533
1.4	**Lab. Report N°**	87 14 71
1.5	**91/414 Cross Reference to original study / report**	5.2.3 / 01
1.6	**Authors**	Report: [redacted] (1988) Summary:
1.7	**Date of report**	January 14, 1988
1.8	**Published / owner**	Unpublished / Syngenta
2.1	**Testing facility**	[redacted]
2.2	**Dates of experimental work**	November 18 to December 9, 1987
3.	**Objectives**	Investigation of acute inhalation toxicity in rats
4.1	**Test substance**	CGA 64'250, technical grade active ingredient
4.2	**Specification**	[redacted]
4.3	**Storage stability**	not applicable (single treatment only)
4.4	**Stability in vehicle**	not applicable
4.5	**Homogeneity in vehicle**	not applicable
4.6	**Validity**	not applicable
5	**Vehicle / solvent**	In order to generate an inhalable aerosol, the test material was dissolved (30% (w/w)) in absolute ethanol
6	**Physical form**	viscous liquid
7.1	**Test method**	According to the OECD Guideline 403 from May 12, 1981
7.2	**Justification**	The procedures followed are in-line with current requirements.
7.3	**Copy of method**	OECD Guidelines for Testing of Chemicals, Section 4, Health Effects
8	**Choice of method**	Standard procedure for the intended purpose
9	**Deviations**	Method is in-line with EC Directive 92/69 B2.
10.1	**Certified laboratory**	yes
10.2	**Certifying authority**	Swiss Federal Department of the Interior and Intercantonal Office for the Control of Medicaments.
10.3	**GLP**	yes

10.4	**Justification**	not applicable
11.1	**GEP**	not applicable
11.2 (official or officially recognised)	**Type of facility**	[redacted]
11.3	**Justification**	not applicable

12.1	**Test system**	Strain:	Rat, Sprague-Dawley derived. Tif: RAIf (SPF)
		Source	[redacted]
		Age:	young adult (7 to 8 weeks), weight range 194 to 232g
12.2	**Procedure**	Dose levels:	0 (solvent controls) and 5'800 mg/m^3
		Group size:	5 males and 5 females
		Dose regimen:	4 hours nose-only exposure to the inhalation atmosphere.
		Observation period:	14 days. Body weights were measured weekly.

13.1 Inhalation atmosphere

Exposure Group	controls	test article
Nominal concentration	32.2 g/m^3 ethanol	10'983 mg/m^3
Actual conc. in breathing zone	-	5'836 $\pm$ 186 mg/m^3 *
Mass Median Aerodyn. Diameter	-	2.3 - 2.6 µm
Air flow	32 l/min	32 l/min
Chamber Temperature	23.0 °C	22.6 °C
Relative humidity	59%	60%
* mean $\pm$ standard deviation		

X13.2 Findings in animals

Dose	Mortality	Onset of death	Clinical signs, Autopsy
Males			
0 mg/m^3 5'800 mg/m^3	0 / 5 0 / 5		Sedation, Dyspnea, Abnormal Body Position, Ruffled Fur were observed. No effects on body weight gain.
Females			
0 mg/m^3 5'800 mg/m^3	0 / 5 0 / 5		Sedation, Dyspnea, Abnormal Body Position, Ruffled Fur were observed. No effects on body weight gain.
LC_{50}: greater than 5'000 mg/m^3			All symptoms were reversible within 9 days. No substance related gross organ changes were seen.

14	**Statistics**	In the absence of mortality, statistical methods were not applicable to mortality data. Body weights were analysed by an analysis of variance.
15 (published)	**References**	none
16 data	**Unpublished**	none
17	**Reliability Indicator**	1

Data Protection Claim	Yes

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	14.1.2005
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
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	

98/8 Doc IIIA section No.	**6.1.4/01**	**Acute toxicity – Skin and eye irritation**
91/414 Annex Point addressed	**II 5.2.4 / 01**	Acute toxicity - skin irritation

1.2	**Title**	Skin irritation in the rabbit after single application of technical CGA 64'250
1.3	**Report and/or project N° Syngenta File N° (SAM)**	78 52 49 64250 / 1535
1.4	**Lab. Report N°**	78 52 49
1.5	**91/414 Cross Reference to original study / report**	5.2.4 / 01
1.6	**Authors**	Report: [redacted] (1978a) Summary: [redacted]
1.7	**Date of report**	October 26, 1978
1.8	**Published / owner**	Unpublished / Syngenta
2.1	**Testing facility**	[redacted]
2.2	**Dates of experimental work**	not specified
3.	**Objectives**	Investigation of skin irritating potency in rabbits
4.1	**Test substance**	CGA 64'250, technical grade active ingredient
4.2	**Specification**	[redacted]
4.3	**Storage stability**	not applicable (single treatment only)
4.4	**Stability in vehicle**	not applicable
4.5	**Homogeneity in vehicle**	not applicable
4.6	**Validity**	not applicable
5	**Vehicle / solvent**	The test article was applied in undiluted form
6	**Physical form**	viscous liquid
7.1	**Test method**	According to a standard method of the US Association of Food and Drug Officials "Appraisal of the Safety of Chemicals in Foods, Drugs and cosmetics" (1959).
7.2	**Justification**	The procedures followed are mainly in-line with current Guideline requirements
7.3	**Copy of method**	A description of the method is included in Report 5.2.4 / 01.
8	**Choice of method**	Standard procedure for the intended purpose
9	**Deviations**	The test substance was applied to both flanks. On one side, the skin was abraded. The exposure period was 24 hours instead of the 4 hours recommended today. Body weights were not measured. Other deviations are mainly formal (see details below) from EC Directive 92/69 B4.
10.1	**Certified laboratory**	not applicable

10.2	**Certifying authority**	not applicable
10.3	**GLP**	No
10.4	**Justification**	When the study was performed, GLP was not compulsory
11.1	**GEP**	not applicable
11.2	**Type of facility (official or officially recognised)**	[redacted]
11.3	**Justification**	not applicable

12.1	**Test system**	Strain:	Rabbit, Himalayan
		Source	[redacted]
		Age:	not specified, weight range 1.5 to 2.0 kg
12.2	**Procedure**	Dose levels:	0.5 ml
		Group size:	3 males and 3 females
		Dose regimen:	single dermal application under occlusive dressing for 24 hours to an area of 2.5 x 2.5 cm..
		Observation period:	7 days.

13 Findings (Draize scores)

Individual	24 hours	48 hours	3 days	7 days
1 (male)	0 / 0	0 / 0	0 / 0	0 / 0
2 (male)	1 / 1	1 / 0	0 / 0	0 / 0
3 (male)	1 / 1	1 / 1	1 / 1	0 / 0
4 (female)	2 / 1	0 / 0	0 / 0	0 / 0
5 (female)	2 / 1	2 / 2	1 / 1	0 / 0
6 (female)	2 / 1	1 / 1	1 / 1	0 / 0
mean score	**1.33 / 0.83**	**0.83 / 0.66**	**0.5 / 0.5**	**0 / 0**

first number = score of erythema, second number = score for edema.
All values are given for the intact treated skin.

Proposed Classification according to EC-Directive 93/21: Non irritating

14	**Statistics**	None
15	**References (published)**	None
16	**Unpublished data**	None
x17	**Reliability Indicator**	1

Data Protection Claim	Yes

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	12.11.2004
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
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	

PP 2.504/WM/ 24.10.1994

98/8 Doc IIIA section No.	**6.1.4/02**	**Acute toxicity – Skin and eye irritation**
91/414 Annex Point addressed	**II 5.2.5 / 01**	Acute toxicity - eye irritation

1.2	**Title**	Eye irritation in the rabbit after single application of technical CGA 64'250
1.3	**Report and/or project N° Syngenta File N° (SAM)**	78 52 48 64250 / 1536
1.4	**Lab. Report N°**	78 52 48
1.5	**91/414 Cross Reference to original study / report**	5.2.5 / 01
1.6	**Authors**	Report: [redacted] Summary:
1.7	**Date of report**	October 26, 1978
1.8	**Published / owner**	Unpublished / Syngenta
2.1	**Testing facility**	[redacted]
2.2	**Dates of experimental work**	not specified
3.	**Objectives**	Investigation of eye irritating potency in rabbits
4.1	**Test substance**	CGA 64'250, technical grade active ingredient
4.2	**Specification**	[redacted]
4.3	**Storage stability**	not applicable (single treatment only)
4.4	**Stability in vehicle**	not applicable
4.5	**Homogeneity in vehicle**	not applicable
4.6	**Validity**	not applicable
5	**Vehicle / solvent**	The test article was applied in undiluted form.
6	**Physical form**	viscous liquid
7.1	**Test method**	According to a standard method of the US Association of Food and Drug Officials "Appraisal of the Safety of Chemicals in Foods, Drugs and cosmetics" (1959).
7.2	**Justification**	The procedures followed are mainly in-line with current Guideline requirements
7.3	**Copy of method**	A description of the method is included in Report 5.2.5 / 01.
8	**Choice of method**	Standard procedure for the intended purpose
9	**Deviations**	The test substance was applied to the conjunctival sac. In three individuals, the eye was rinsed with physiological saline 30 seconds after the treatment. Grading of occular lesions after 1 hour was not performed. Application of multiplication factors for scoring Body weights were not measured. Other deviations are mainly formal (see details below) from EC Directive 92/69 B5.

10.1 laboratory	**Certified**	not applicable
10.2 authority	**Certifying**	not applicable
10.3	**GLP**	no
10.4	**Justification**	When the study was performed, GLP was not compulsory
11.1	**GEP**	not applicable
11.2 (official or officially recognised)	**Type of facility**	[redacted]
11.3	**Justification**	not applicable

12.1	**Test system**	Strain:	Rabbit, Himalayan
		Source	[redacted]
		Age:	not specified, weight range 1.5 to 2.0 kg
12.2	**Procedure**	Dose levels:	0.1 g
		Group size:	3 males and 3 females
		Dose regimen:	the test substance was instilled once in the conjunctival sac.
		Observation period:	7 days.

13 Findings (Draize scores)

Individual	**24 hours**		**48 hours**		**3 days**		**7 days**	
	A	B	A	B	A	B	A	B
Cornea Opacity	0/1/1	0/0/0	0/0/1	0/0/0	0/0/0	0/0/0	0/0/0	0/0/0
Iris Lesions	0/0/0	0/0/0	0/0/0	0/0/0	0/0/0	0/0/0	0/0/0	0/0/0
Conjunctiva - redness - chemosis	 0/0/1 0/0/1	 0/1/0 0/1/0	 0/0/0 0/0/0	 0/0/0 0/0/0	 0/0/0 0/0/0	 0/0/0 0/0/0	 0/0/0 0/0/0	 0/0/0 0/0/0
The numbers are the individual scores in the three animals tested. Group A: Eyes not rinsed. Group B: Eyes rinsed 30 seconds after the application.								

Proposed Classification according to EC-Directive 93/21: Non irritating

14	**Statistics**	none
15 (published)	**References**	none
16 data	**Unpublished**	none
x17	**Reliability Indicator**	1

Data Protection Claim	Yes

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	12.11.2004
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
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	

PP 2.504/WM/ 24.10.1994

98/8 Doc IIIA section No.	6.1.5/01	Acute toxicity – Skin sensitisation
91/414 Annex Point addressed	II 5.2.6 / 01	Acute toxicity - skin sensitisation

1.2	Title	Skin sensitizing (contact allergenic) effect in Guinea pigs of technical CGA 64'250
1.3	Report and/or project N° Syngenta File N° (SAM)	78 52 50 64250 / 1537
1.4	Lab. Report N°	78 52 50
1.5	91/414 Cross Reference to original study / report	5.2.6 / 01
1.6	Authors	Report: [redacted] Summary:
1.7	Date of report	February 8, 1979
1.8	Published / owner	Unpublished / Syngenta
2.1	Testing facility	[redacted]
2.2	Dates of experimental work	November 6, 1978 to January 4, 1979
3.	Objectives	Investigation of skin sensitizing potential
4.1	Test substance	CGA 64'250, technical grade active ingredient
4.2	Specification	[redacted]
4.3	Storage stability	not applicable. The testing dilution was freshly prepared for each treatment.
4.4	Stability in vehicle	not applicable
4.5	Homogeneity in vehicle	not applicable
4.6	Validity	not applicable
5	Vehicle / solvent	First week of induction phase: 0.1% CGA 64'250 in propylene glycol Second and third week of induction: 0.1% CGA 64'250 in propylene glycol / complete Freund's adjuvans (1:1) Challenge injection: 0.1% CGA 64'250 in propylene glycol
6	Physical form	viscous liquid
7.1	Test method	According to Th. Maurer et al.: The optimization test in the Guinea pig. A method for the predictive evaluation of the contact allergenicity of chemicals. Agents and Actions 5(2), 174-179, 1975.
7.2	Justification	The procedures followed are in-line with the OECD Guideline 406. Although it is not among the recommended methods cited in the EC-Directive 92/69, B6, the test is scientifically sound and of proven sensitivity.
7.3	Copy of method	A short description of the method is included in Report 5.2.6 / 01 It is described in full detail in the reference cited above.
8	Choice of method	Standard procedure for the intended purpose
9	Deviations	Deviations are mainly formal (see details below). The methodological deviations are discussed above (point 7.2).

10.1 laboratory	**Certified**	not applicable
10.2 authority	**Certifying**	not applicable
10.3	**GLP**	no
10.4	**Justification**	When the study was performed, GLP was not compulsory
11.1	**GEP**	not applicable
11.2 (official or officially recognised)	**Type of facility**	[redacted]
11.3	**Justification**	not applicable

12.1	**Test system**	Strain:	Guinea pig, Pirbright White
		Source	[redacted]
		Age:	not specified, weight range 350 to 490 g
12.2	**Procedure**	Group size:	10 males and 10 females (test group and vehicle controls).
		Induction phase Dose regimen:	0.1 ml intracutaneous injections as described in Point 5. 10 injections were made.
		Challenge phase First challenge:	After a two weeks treatment-free reaction period one intracutaneous injection of the test dilution.
		Second challenge:	One epicutaneous administration of CGA 64'250 in 10% vaseline at a subirritant concentration under occlusive dressing (24 hours).

13 Findings

Incidence of positive reactions		
	First challenge	**Second challenge**
propiconazole	2 / 20	3 / 19
vehicle controls	4 / 19	0 / 18

Proposed Classification according to EC-Directive 93/21: Non sensitizing

14	**Statistics**	Exact Fisher test for comparison of the probability of two binominal distributions
15 (published)	**References**	none
16 data	**Unpublished**	none
x17	**Reliability Indicator**	1

Data Protection Claim	Yes

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	12.11.2004
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
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	

PP 2.504/WM/ 24.10.1994

98/8 Doc IIIA section No.	6.1.5/02	Acute toxicity – Skin sensitisation
91/414 Annex Point addressed	II 5.2.6 / 02	Acute toxicity - skin sensitisation

1.2	Title	CGA 64250 tech. - Skin sensitization in the Guinea Pig (Maximization test)
1.3	Report and/or project N° Syngenta File N° (SAM)	993101 64250 / 4197
1.4	Lab. Report N°	993101
1.5	91/414 Cross Reference to original study / report	5.2.6 / 02
1.6	Authors	Report: [redacted]
1.7	Date of report	September 7, 1999
1.8	Published / owner	Unpublished / Syngenta
2.1	Testing facility	[redacted]
2.2	Dates of experimental work	July 29, 1999 to August 26, 1999
3.	Objectives	Investigation of skin sensitizing potential
4.1	Test substance	CGA 64'250, technical grade active ingredient
x4.2	Specification	[redacted]
4.3	Storage stability	not applicable. The testing dilution was freshly prepared for each treatment.
4.4	Stability in vehicle	not applicable
4.5	Homogeneity in vehicle	not applicable
4.6	Validity	not applicable
5	Vehicle / solvent	Day 0, animals received intradermal injections of CGA64250 in peanut oil On Day 8, test animals received epidermal induction applications of undiluted CGA 64250 On day 21, animals were challenged with an epidermal application of vehicle alone (Vaseline) and 30% CGA 64250 in Vaseline.
6	Physical form	CGA 54250 ia a viscous liquid
7.1	Test method	According to Magnussin B and Kligman AM (1969). The identification of contact allergens by animal assays. The guinea pig maximization test. J Invest Dermatol., 52, 268-276
7.2	Justification	The procedures followed are in-line with the OECD Guideline 406.
7.3	Copy of method	A short description of the method is included in Report 5.2.6 / 01 It is described in full detail in the reference cited above.
8	Choice of method	Standard procedure for the intended purpose
9	Deviations	None
10.1	Certified laboratory	Yes
10.2	Certifying authority	Swiss Federal Department of the Interior and Intercantonal Office for the Control of Medicaments.

10.3	**GLP**	Yes
10.4	**Justification**	Not applicable
11.1	**GEP**	not applicable
11.2	**Type of facility (official or officially recognised)**	[redacted]
11.3	**Justification**	not applicable
12.1	**Test system**	Strain: Guinea pig, Himalayan Spotted Source [redacted] Age: Young Adult, 1-2 months
X12.2	**Procedure**	Group size: 10 males and 10 females test group; 5 males and 5 females vehicle controls). <u>Induction phase</u> Dose regimen: 0.1 ml intracutaneous injections as described in Point 5. 3 pairs of injections were made; adjuvant/physiological saline; CGA 64250 in peanut oil; CGA64250 in 1:1 adjuvant/physiological saline. Control animals received adjuvant/physiological saline; 50% peanut oil with 1:1 adjuvant/physiological saline; peanut oil. For the epidermal application induction, neat CGA 64250 was applied. <u>Challenge phase</u> First challenge: After a two weeks treatment-free reaction period one chamber containing the vehicle alone, or a 30% CGA 64250 soln in peanut oil was placed on the flank, and left for 24 hours.

13. Findings	Positive Skin Reactions after Challenge			
	Vehicle Flank		Test Flank	
	24 Hours	48 Hours	24 Hours	48 Hours
Control Group	0/10	0/10	0/10	0/10
Test Item Group	0/20	0/20	6/20	10/20

Based on these results, CGA 64250 tech is required to be classified as "May cause sensitisation by skin contact" according to the Commission Directive 93/21/EEC

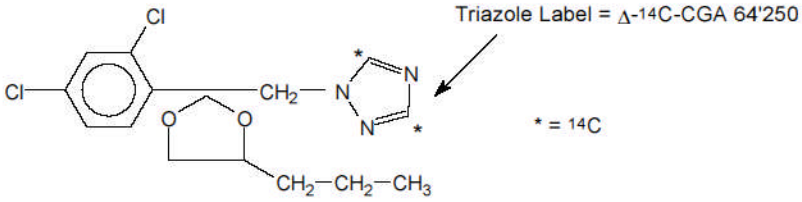
14	**Statistics**	Not applicable
15	**References (published)**	none
16	**Unpublished data**	none
17	**Reliability Indicator**	1

Data Protection Claim	Yes

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	12.11.2004
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
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	

98/8 Doc IIIA section No.	6.2/01	Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study
91/414 Annex Point addressed	II 5.1.1 / 01	Absorption, distribution and excretion in rats

1.2	Title	Distribution, degradation and excretion of CGA 64'250 in the rat
1.3 project N° Syngenta File N° (SAM)	Report and/or	24 / 79 64250/1545
1.4	Lab. Report N°	24 / 790
1.5 Reference to original study / report	91/414 Cross	5.1.1 / 01
1.6	Authors	Report: [redacted] Summary:
1.7	Date of report	July 18, 19798
1.8 owner	Published /	no / SYNGENTA Ltd.
2.1	Testing facility	[redacted]
2.2 experimental work	Dates of	not specified
3.	Objectives	To determine the fate of the test compound given by the oral route based on urinary and fecal excretion and the amount of radioactivity expired and that remaining in the animals. Establish an overall balance of radioactivity. To characterise the metabolite pattern in urine.
4.1	Test substance	Common name: Propiconazole Label: Triazole-^{14}C-Propiconazole
4.2	Specification	[redacted]
4.3 stability	Storage	not applicable
4.4 vehicle	Stability in	not applicable
4.5 vehicle	Homogeneity in	not applicable
4.6	Validity	not applicable
5 solvent	Vehicle /	ethanol / polyethyleneglycol 200 / water (30 / 20 / 50)
6	Physical form	viscous liquid



7.1	**Test method**	The method is outlined in the original report. Testing guidelines were not available at the time when the study was conducted. Measurement of radioactivity was done using standard scintillation mixtures. Feces and tissues were combusted before scintillation. Characterization of urinary radioactivity was done by two-dimentional TLC on silica gel using two solvent systems (water / formic acid / methanol / chloroform 2:4:20:75 and water / butanol / acetic acid 17:66:17).
7.2	**Justification**	The procedures followed are in-line with sound scientific principles.
7.3	**Copy of method**	The original report contains all relevant information.
8	**Choice of method**	not applicable
9	**Deviations**	Deviations from 87/302/EEC: Six days excretion period instead of 7 days. In view of the low residues found in tissues, this shorter observation period can be justified. Further deviations are mainly formal (see below).
10.1	**Certified laboratory**	no
10.2	**Certifying authority**	not applicable
10.3	**GLP**	no
10.4	**Justification**	When the study was conducted, GLP regulations were not enacted.
11.1	**GEP**	not applicable
11.2	**Type of facility (official or officially recognised)**	[redacted]
11.3	**Justification**	not applicable

12 Test system

Animals:
Strain: Rat, Sprague Dawley derived, Tif RAIf (SPF)
Source: [redacted]
Weight: 188-238 g

Doses and administration
Test substance was suspended in the vehicle.
Doses of 0.5 mg/kg bw and 25 mg/kg bw were used.

Each animal received a single administration of about 1 ml of appropriate dose suspension orally by gavage.

Group*	animals	µCi	Sample collection
B1	2 males	29.8	Urine, feces and expired CO2 were collected in 24 hour intervals over six days. Determination of residual radioactivity in tissues
B2	2 females	29.8	
D1	2 males	295	
D2	2 females	295	

* The group designation is made according to international standards

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13 Findings

Animal observations: No treatment-realated findings were noted on appearance and behaviour.

Absorption: Estimated on the basis of urinary excretion and on the amount remaining in the carcass, the absorption was higher than 60% of the administered dose in all groups.

Excretion: The mean excretion data in the different groups were as follows:

Group	B1		B2		D1		D2	
	Urine	Feces	Urine	Feces	Urine	Feces	Urine	Feces
24 hrs	46.00	30.51	57.40	18.81	51.39	29.77	58.59	18.75
48 hrs	7.85	10.77	3.63	12.61	7.74	7.76	4.02	11.29
72 hrs	1.12	0.80	0.69	0.94	0.92	0.58	0.39	1.02
144 hrs	0.46	0.27	0.25	0.23	0.34	0.17	0.16	0.24
Total	**55.46**	**42.10**	**61.98**	**32.59**	**60.39**	**38.27**	**63.16**	**31.29**
Expired air (0-144 hrs)	0.13%		0.1%		0.08%		0.05%	
Tissue Residues	0.38 %		0.31 %		0.19 %		0.12 %	
Total Recovery	98.63 %		95.67 %		99.25 %		95.05 %	

Urine was the major route of excretion. Excretion was rapid at both dose levels with around 78% of the administered radioactivity excreted after 24 hours and around 95% within 48 hours.

Tissue residues: The following table outlines the mean residues found in selected tissues 144 hours after the administration. The values were given in ppm propiconazole equivalents.

Group	B1	B2	D1	D2
Spleen	LQ	LQ	0.018	0.019
Liver	0.015	0.011	0.498	0.326
Fat	LD	LD	LQ	LQ
Kidney	0.003	0.004	0.114	0.123
Muscle	LQ	LD	0.021	0.011
Blood	0.01	0.011	0.019	0.017
Brain	LD	LD	LD	LD
Heart	LQ	LQ	0.012	0.012
Lungs	0.003	0.004	0.035	0.037
Gonads	LQ	LQ	0.022	0.092
Carcass	LQ	LQ	0.025	0.018

LD = Limit of detection = 0.33 x LQ
LQ = Limit of quantification 0.001 - 0.01 ppm (low) 0.003 - 0.07 ppm (high dose)

In all groups the highest residues were found in the liver. Reflecting the 50 fold higher dose administered, liver residues were approximately 40 times higher in the high than in the low dose group.

Metabolite pattern: The metabolite pattern in the urine was very similar in males and females, irrespective of the dose administered. Several rather polar fractions were found, none of which corresponded to the unchanged parent.

Conclusion: Propiconazole was at least partially absorbed from the intestinal tract. Irrespective of the dose administered or the sex of the animals, about two thirds of the administered dose were excreted with the urine. Six days after a single dose residues in tissues were generally low, being highest in the liver.

The metabolite pattern in the urine was similar in both sexes and in both dose groups with only slight, quantitative differences. No unchanges parent was found.

14 Statistics not applicable

15 References (published) none

16 Unpublished data none

17 Reliability Indicator 1

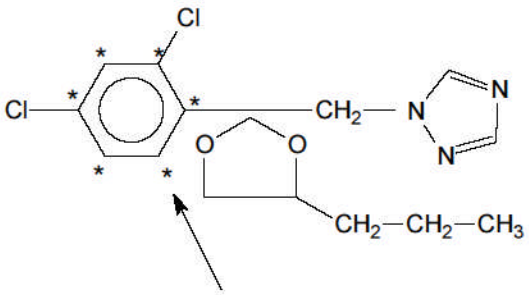
Data Protection Claim	Yes

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	15.11.2004
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
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	

PP 2.504 / WM / 27. 10. 1994

98/8 Doc IIIA section No.	6.2/02	Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study
91/414 Annex Point addressed	II 5.1.1 / 02	Absorption, distribution and excretion in rats

1.2	Title	[U-^{14}C]-Phenyl CGA 64'250: Absorption, distribution, metabolism and excretion in the rat
1.3	Report and/or project N° Syngenta File N° (SAM)	380 / 105 64250/1553
1.4	Lab. Report N°	HUK 5871-380 / 105
1.5	91/414 Cross Reference to original study / report	5.1.1 / 02
1.6	Authors	Report: [redacted] Summary:
1.7	Date of report	June 8, 1989
1.8	Published / owner	no / SYNGENTA Ltd.
2.1	Testing facility	[redacted]
2.2	Dates of experimental work	April 1987 to February 1988
3.	Objectives	To determine the fate of the test compound given by the oral or intravenous route based on urinary, biliary and fecal excretion, the amount of radioactivity expired and that remaining in the animals. Establish an overall balance of radioactivity. To characterise the metabolite pattern in urine and feces.
4.1	Test substance	Common name: Propiconazole Label: Phenyl-^{14}C-Propiconazole



Phenyl Label = Φ-^{14}C-CGA 64'250

4.2	Specification	[redacted]
4.3	Storage stability	not applicable
4.4	Stability in vehicle	Dose formulations were investigated over 20 hrs (i.v. formulation) or 44 days (oral formulations). Both were found to be stable over the intended time periods.
4.5	Homogeneity in vehicle	not applicable
4.6	Validity	not applicable

5 solvent	**Vehicle /**	oral route: ethanol / polyethyleneglycol 200 / water (1 / 2 / 2) intravenous: physiological saline
6	**Physical form**	viscous liquid
7.1	**Test method**	According to the U.S. FIFRA Subdiv. F § 85-1 Measurement of radioactivity was done using standard scintillation mixtures. Feces and tissues were homogenized and combusted before scintillation. Characterization of urinary radioactivity was done by two-dimentional TLC on silica gel using two solvent systems for dimension 1 (urine: ethyl acetate / propanol / water / formic acid 65 / 25 / 10 / 2, feces ethyl acetate / propanol 75 / 25). Dimension 2 was run with chloroform / methanol / water / formic acid 75 / 20 / 2 / 4. Eight analytical standards were used to identify the major metabolites in urine and feces.
7.2	**Justification**	not applicable
7.3	**Copy of method**	The original report contains all relevant information.
8 method	**Choice of**	not applicable
9	**Deviations**	Deviations from 87/302/EEC: none
10.1 laboratory	**Certified**	yes
10.2 authority	**Certifying**	UK MAFF
10.3	**GLP**	yes
10.4	**Justification**	not applicable
11.1	**GEP**	not applicable
11.2 (official or officially recognised)	**Type of facility**	[redacted]
11.3	**Justification**	not applicable

12 Test system

Animals:

Strain: Rat, Sprague Dawley Crl:CD (SD) BR

Source: Charles River (UK) Ltd., Margate, England

Age: 6 to 10 weeks

Weight: 142-198 g

Doses and administration

Test substance was suspended in the vehicle and administered by oral gavage or intravenous injection. Doses of 0.5 mg/kg bw and 50 mg/kg bw were used.

Each animal received administrations of about 1 ml

Group	animals	Dose	Sample collection
A	5 m, 5 f	0.5 mg/kg i.v.	In all groups, urine and feces were collected after 6, 12, 24 hrs and thereafter in daily intervals for 7 days. Group C was terminated after 5 days. Air was collected after 6, 12 and 24 hrs.
B	5 m, 5 f	0.5 mg/kg oral	
C	5 m, 5 f	0.5 mg/kg oral after 14 days of pretreatment	
D	5 m, 5 f	50 mg/kg oral	