Section A5.3/03 Annex Point IIA5.3 — Efficacy Data
Fungi in the presence of organic load

			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	[redacted]	
1.2.2	Criteria for data protection		?
1.3	**Guideline study**	Yes, BS EN 1650	
1.4	**Deviations**	yes, see 2.3.4	
		2 METHOD	
2.1	**Test Substance (Biocidal Product)**	Propan-2-ol	
2.1.1	Trade name/ proposed trade name	Not applicable	
2.1.2	Composition of Product tested	70% Propan-2-ol in distilled water	
2.1.3	Physical state and nature	Liquid disinfectant	
2.1.4	Monitoring of active substance concentration	No	
2.1.5	Method of analysis	Not applicable	
2.2	**Reference substance**		
2.2.1	Method of analysis for reference substance	No reference substance tested	
2.3	**Testing procedure**		
2.3.1	Test population / inoculum / test organism	Table 2.3.1.1 Fungal strains employed to test the efficacy of propan-2-ol.	x

Species	Strain/origin	Representative for
Candida albicans	ATCC 10231	Yeast
Aspergillus niger	ATCC 16404	Mould

The test suspension employed contained 2.4-2.7 * 10E7 CFU/ml

2.3.2	Test system	Quantitative suspension test under conditions representative of practical use (e.g. CEN - Phase 2, Step1)	
2.3.3	Application of TS	Aqueous solution, as prescribed by guideline.	
2.3.4	Test conditions	Biocidal efficacy of propan-2-ol tested at 70%; glass distilled water was used instead of sterile hard water and the biocidal substance was tested in one concentration only instead of three as prescribed by the guideline; test was run at 20°C, bovine serum albumin (3g/L) served as organic load, Neutralizer/inactivation medium used as prescribed by guideline	

		EN 1650 (Annex B).
2.3.5	Duration of the test / Exposure time	15 min
2.3.6	Number of replicates performed	As prescribed by guideline
2.3.7	Controls	As prescribed by guideline
2.4	**Examination**	
2.4.1	Effect investigated	Reduction in viability of test organisms using a quantitative suspension test (Phase 2/step 1) as prescribed by the guideline EN1650
2.4.2	Method for recording / scoring of the effect	Determining the number of CFUs for each test organism before and after treatment with the product. CFUs determined only once after termination of exposure.
2.4.3	Intervals of examination	Effect was recorded once after exposure.
2.4.4	Statistics	As prescribed by guideline
2.4.5	Post monitoring of the test organism	Not applicable.
		3 RESULTS
3.1	**Efficacy**	In accordance with the guideline EN1650, the product (70% propan-2-ol) possesses fungicidal activity at 15min exposure at 20°C under dirty conditions (3g/l bovine albumin) for the tested strains.
3.1.1	Dose/Efficacy curve	Not applicable
3.1.2	Begin and duration of effects	Effect was only reported for the given exposure time of 15 min
3.1.3	Observed effects in the post monitoring phase	Not applicable
3.2	**Effects against organisms or objects to be protected**	None reported
3.3	**Other effects**	None reported.
3.4	**Efficay of the reference substance**	Not applicable

3.5 Tabular and/or graphical presentation of the summarised results

Table 3.5.1 Reduction in cfu/ml after 15 min exposure to aqueous propan-2-ol solution (70%).

Species/strain	Reduction of viability (CFU/ml)
Candida albicans ATCC 10231	> 1,0 * 10E4
Aspergillus niger ATCC 16404	> 1,17 * 10E4

3.6 Efficacy limiting factors

3.6.1 Occurrences of resistances: None reported

3.6.2 Other limiting factors: None reported

4 RELEVANCE OF THE RESULTS COMPARED TO FIELD CONDITIONS

4.1 Reasons for laboratory testing: Two different fungal species were tested according to the internationally accepted EN guideline 1650 (as proposed by CEN). Data obtained are relevant for the intended area of use of the product.

4.2 Intended actual scale of biocide application: Not stated

4.3 Relevance compared to field conditions

4.3.1 Application method: The test conditions of the quantitative suspension test (phase 2/step 1) using organic load are representative for the actual conditions during practical use of the product.

4.3.2 Test organism: The 2 tested fungal species are appropriate representatives for the target organisms in the intended area of use.

4.3.3 Observed effect: The obtained efficacy results for the product tested using the test organisms -*Candida albicans* and *Aspergillus niger*- under simulated dirty conditions (3g/l bovine albumin) are relevant for the intended area of use.

4.4 Relevance for read-across

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods: The fungicidal activity of 70% propan-2-ol was tested using a quantitative suspension test (phase 2/ step 1) simulating practical conditions according to the guideline EN 1650. Two fungal species were used as test organisms, *Candida albicans* representative for yeasts and *Aspergillus niger* representative for a mould. 3g/l bovine albumin was used as organic load in the test to simulate dirty conditions. Deviating from the guideline glass distilled water was used instead of sterile hard water. Reduction in viability was determined via CFU counts before and after treatment with the product.

5.2 Reliability: [redacted]

5.3 Assessment of: The result of the study showed that 70% propan-2-ol exhibits sufficient

	efficacy, data analysis and interpretation	fungicidal activity and is effective against the test organisms-*Candida albicans* and *Aspergillus niger* under dirty conditions. These 2 fungal species are representative for moulds and yeasts present in the intended area of use (PT:2, disinfectants used in public and private health areas).
5.4	**Conclusion**	[redacted]
5.5	**Proposed efficacy specification**	

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2008/09/23
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*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*
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	

Appendix 1:CA-Tables:

Section A5.3/04 Efficacy Data
Annex Point IIA5.3 Enveloped virus

			Official use only
		1 REFERENCE	
1.1	**Reference**	Tyler & Ayliffe. 1987. A surface test for virucidal activity of disinfectants: preliminary study with herpes virus. Journal of Hospital Infection 9:22-29.	
1.2	**Data protection**	No	
1.2.1	Data owner		
1.2.2	Criteria for data protection	Not applicable	
1.3	**Guideline study**	No	
1.4	**Deviations**		
		2 METHOD	
2.1	**Test Substance (Biocidal Product)**		
2.1.1	Trade name/ proposed trade name	Not applicable	
2.1.2	Composition of Product tested	Propan-2-ol in distilled water with the following dilutions: 60% and 70%	
2.1.3	Physical state and nature	liquid	
2.1.4	Monitoring of active substance concentration	No	
2.1.5	Method of analysis	Not applicable	
2.2	**Reference substance**		x
2.2.1	Method of analysis for reference substance	No reference substance tested	
2.3	**Testing procedure**		
2.3.1	Test population / inoculum / test organism	Table 2.3.1.1 Viral strain employed to test the efficacy of propan-2-ol.	

Species/strain	Source/origin	Representative for
Herpes simplex virus type 1	not stated	enveloped virus

The test virus was cultivated in Baby hamster kidney cells (BHK). The cells were grown in supplemented Eagle`s media with 10% tryptose phosphate broth and 10% calf serum (ETC), initial density of the applied inoculum in the test system was 3 * 10 E 9 PFU/ml.

2.3.2	Test system	Laboratory test simulating practical conditions - carrier test (e.g. CEN - Phase 2, Step 2)	
2.3.3	Application of TS	Aqueous solution.	

2.3.4	Test conditions	TS tested at two concentrations (60 and 70%), test was run at room temperature, as neutralizer to stop the effect of the biocide the virus was eluted with Eagles media with 10% tryptose phosphate broth and 10% calf serum (ETC) after exposure	x
2.3.5	Duration of the test / Exposure time	1, 5, 10 min	
2.3.6	Number of replicates performed		x
2.3.7	Controls	Virus not exposed to the alcohol	x
2.4	**Examination**		
2.4.1	Effect investigated	The effect of propan-2-ol in 2 concentrations on Herpes simplex virus was investigated and the reduction in Plaque Forming Units/ml after exposure was determined	
2.4.2	Method for recording / scoring of the effect	A Plaque assay based on the method of Russell (1962) was used to record the reduction in viability of the test virus. For the plaque assay, ten-fold dilutions of the recovered virus suspension post exposure were made and added to monolayers of BHK cells which were incubated at 37°C.	
2.4.3	Intervals of examination	Effect was recorded once after exposure to the alcohol	
2.4.4	Statistics		
2.4.5	Post monitoring of the test organism	No	
		3 RESULTS	
3.1	**Efficacy**	Propan-2-ol at the tested concentrations was effective in reducing the PFU of the test virus.	
3.1.1	Dose/Efficacy curve	Not applicable	
3.1.2	Begin and duration of effects	Effect was only reported for the given exposure time	
3.1.3	Observed effects in the post monitoring phase	Not applicable	
3.2	**Effects against organisms or objects to be protected**	None reported	
3.3	**Other effects**	None reported.	
3.4	**Efficay of the reference substance**	Not applicable	

3.5 Tabular and/or graphical presentation of the summarised results

Table 3.5.1 Reduction of plaque forming viruses after exposure to aqueous propan-2-ol solution

Species/strain	Concentration of propan-2-ol	Exposure time (min)	Virus reduction (pfu/ml)
Herpes simplex virus	60%	1	10E4.5 +/- 0.3
	70%	1	10E4.7 +/- 0.2
	60%	5	10E4-7 (no virus recovered)
	70%	5	10E4-7 (no virus recovered)
	60%	10	10E4-7 (no virus recovered)

3.6 Efficacy limiting factors

3.6.1 Occurrences of resistances: None reported

3.6.2 Other limiting factors: None reported

4 RELEVANCE OF THE RESULTS COMPARED TO FIELD CONDITIONS

4.1 Reasons for laboratory testing

The virucidal activity of propan-2-ol in 2 concentrations against a Herpes simplex virus strain was investigated using a carrier test. The surface disinfection activity of propan-2-ol as a biocide against a dried viral preparation was evaluated. The data obtained in this study are relevant for the intended area of use of the alcohol.

4.2 Intended actual scale of biocide application

Not stated

4.3 Relevance compared to field conditions

4.3.1 Application method: The conditions of the carrier test simulate the actual conditions to be considered during the disinfection of general surfaces and equipments contaminated with viruses.

4.3.2 Test organism: The test virus – a strain of Herpes simplex - is an appropriate representative for the target organisms in the intended field of use.

4.3.3 Observed effect: The results obtained in this study are relevant for evaluating the virucidal activity of propan-2-ol against Herpes simplex viruses on contaminated surfaces.

4.4 Relevance for read-across

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

Using a carrier test method the effect of propan-2-ol in various concentrations on Herpes simplex virus was determined. Cover slips x

Section A5.3/04 **Efficacy Data**
Annex Point IIA5.3 Enveloped virus

		(no. 0 or 1.5 chance glass) were contaminated with the test virus and allowed to dry at room temperature for 1h. To act as the input control, one of the cover slips was eluted after drying with ETC medium. The other cover slips were exposed to different concentrations of the alcohol for 1, 5 or 10min. After exposure the virus was recovered by rinsing the cover slips in ETC and finally placed in 1ml of ETC. Ten fold dilutions were then made of the recovery medium. The reduction in viability of the virus was determined via a Plaque assay. The plaque assay was carried out using monolayers of BHK cells. The number of Plaque Forming Units of the treated samples were compared to the untreated samples and the reduction in viability of the test virus was calculated.	
5.2	**Reliability**	[redacted]	
5.3	**Assessment of efficacy, data analysis and interpretation**	The results of the study show that propan-2-ol at a concentration of 60% or 70% was effective against the virus achieving a log10 reduction value of at least 4.	
5.4	**Conclusion**	[redacted]	x
5.5	**Proposed efficacy specification**		x

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2008/09/23
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]

Section A5.3/04 **Efficacy Data**
Annex Point IIA5.3 Enveloped virus

Remarks	[redacted]
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*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*
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 A5.3/05 **Efficacy Data**
Annex Point IIA5.3 Non enveloped virus

Official use only

1 REFERENCE

1.1	**Reference**	Gehrke C, Steinmann J, Goroncy-Bermes P. 2004. Inactivation of Feline Calicivirus, a surrogate of norovirus (formerly Norwalk-like viruses), by different types of alcohol in vitro and in vivo. Journal of Hospital Infection 56:49-55.
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Criteria for data protection	Not applicable
1.3	**Guideline study**	Yes, Guidelines of the German Federal Health Office and the German Association for the Control of Virus Diseases for testing the effectiveness of chemical disinfectants against viruses. Zbl. Hyg. 1990, 189:554-562.
1.4	**Deviations**	Yes, see 2.3.4

2 METHOD

2.1	**Test Substance (Biocidal Product)**	Propan-2-ol
2.1.1	Trade name/ proposed trade name	Not applicable
2.1.2	Composition of Product tested	Propan-2-ol diluted with double-distilled water to 50, 70 and 80%.
2.1.3	Physical state and nature	Liquid disinfectant
2.1.4	Monitoring of active substance concentration	Not applicable.
2.1.5	Method of analysis	Not applicable
2.2	**Reference substance**	Ethanol and propan-1-ol were tested in parallel at similar concentrations.
2.2.1	Method of analysis for reference substance	
2.3	**Testing procedure**	
2.3.1	Test population / inoculum / test organism	Table 2.3.1.1 Virus strain employed to test the virucidal efficacy of propan-2-ol.

Species/strain	Source/origin	Representative for
Feline Calicivirus strain F9	Prof. H. Schirrmeier, Bundesforschungsanstalt für Viruskrankheiten der Tiere, Germany	Naked virus

The virus strain was cultivated in KE-R-cells, a fibroblastoid cell line derived from a whole cat embryo. The KE-R cells were grown with Eagle`s minimum essential medium and 10% fetal calf serum. After a cytopathic effect had developed in the cell culture, the virus was

		harvested by freeze-thawing three times followed by centrifugation to remove cell debris.
2.3.2	Test system	Quantitative suspension test for the basic activity of the product (e.g. CEN - Phase 1)
2.3.3	Application of TS	As prescribed by guideline (concentrations tested: 50, 70 and 80%)
2.3.4	Test conditions	As prescribed by guideline but FCV was used as virus strain in the study and no organic load was used in the test. Test performed at Room temperature, exposure stopped by serial dilution in EMEM Media, KE-R cells to detect cytopathic effect incubated at 37°C
2.3.5	Duration of the test / Exposure time	30 sec; 1, 3 and 5min
2.3.6	Number of replicates performed	aA prescribed by guideline
2.3.7	Controls	As prescribed by guideline
2.4	**Examination**	
2.4.1	Effect investigated	The reduction in virus titre of Feline calicivirus strain F9 after exposure to propan-2-ol at 3 concentrations was investigated.
2.4.2	Method for recording / scoring of the effect	The viral cytopathic effect on KE-R cells was examined using an inverted microscope
2.4.3	Intervals of examination	Reduction in viral infectivity was determined only once after exposure to the test substance
2.4.4	Statistics	As prescribed by guideline
2.4.5	Post monitoring of the test organism	Not applicable.
		3 RESULTS
3.1	**Efficacy**	The efficacy of propan-2-ol increased with increasing exposure times. A concentration of 50% in the suspension test was most effective against the virus.
3.1.1	Dose/Efficacy curve	Not applicable
3.1.2	Begin and duration of effects	Effect was only reported for the given exposure times
3.1.3	Observed effects in the post monitoring phase	Not applicable
3.2	**Effects against organisms or objects to be protected**	None reported
3.3	**Other effects**	None reported.
3.4	**Efficay of the reference substance**	Propan-1-ol was effective (RF>=4) at a concentration of 50 and 70% at an exposure time of >= 0.5 min.

3.5 Tabular and/or graphical presentation of the summarised results

Table 3.5.1 Reduction in virus titre (ID50) after exposure to aqueous propan-2-ol solutions.

Species/strain	Propanol-2-ol (%)	Exposure time (min)	Reduction of virus titre (ID50)
Feline Calicivirus F9	50	0.5	10E2.31
		1	10E3.2
		3	10E>4.9
		5	10E>5.4
	70	0.5	10E2.35
		1	10E2.9
		3	10E>3.92
		5	10E>4.22
	80	0.5	10E1.35
		1	10E1.27
		3	10E1.88
		5	10E2.38

3.6 Efficacy limiting factors

3.6.1 Occurrences of resistances: none reported

3.6.2 Other limiting factors: none reported

4 RELEVANCE OF THE RESULTS COMPARED TO FIELD CONDITIONS

4.1 Reasons for laboratory testing

Using the suspension test method in accordance with the guidelines issued by the German Federal Health Office and the German Association for The Control of Virus Diseases, the efficacy of propan-2-ol in various concentrations against Feline calicivirus, a surrogate for norovirus, was tested. The results obtained in this study are relevant for the intended use of the test substance.

4.2 Intended actual scale of biocide application

Not stated

4.3 Relevance compared to field conditions

4.3.1 Application method: The test conditions of the in-vitro suspension test method are representative for the actual conditions in the main field of use of the test substance.

4.3.2 Test organism: The test organism, Feline calicivirus is a surrogate for norovirus and can be considered an ideal representative for the target organisms in the intended area of use of the biocide. x

4.3.3 Observed effect: The obtained efficacy result of the test substance is relevant for determining the virucidal activity of the product in the intended area of

use.

4.4 Relevance for read-across

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

A suspension test was carried out in accordance with the guidelines of the German Federal Health Office and the German Association for the Control of Virus Diseases for testing the effectiveness of chemical disinfectants against viruses. Propan-2-ol efficacy on feline calicivirus was tested using various aqueous dilutions of the product. The test was carried out in the absence of organic load and thereby deviating from the guideline. The virus was exposed to the alcohol for 0.5, 1, 3 and 5min. At the end of exposure, the action of the alcohol in an aliquot of the test mixture was stopped by serial dilutions (1:10) in EMEM. 0.1 ml of each dilution was transferred into wells of a microtitre plate containing a confluent monolayer of KE-R cells. After incubation the viral cytopathic effect was read using an inverted microscope. The titre reduction is calculated by subtracting the logarithmic titres of the inactivated virus suspension from that of the virus control.

5.2 Reliability

[redacted]

5.3 Assessment of efficacy, data analysis and interpretation

Propan-2-ol was most effective against the tested virus strain at 50% and at an exposure time of >= 3min achieving a log10 reduction of > 4 in virus titre. However, propan-2-ol was less effective against feline calicivirus than Ethanol and Propan-1-ol.

5.4 Conclusion

[redacted]

5.5 Proposed efficacy specification

Evaluation by Competent Authorities

Use separate "evaluation boxes" to provide transparency as to the comments and views submitted

EVALUATION BY RAPPORTEUR MEMBER STATE

Date 2008/09/24

Materials and methods

[redacted]

Conclusion

[redacted]

Reliability

[redacted]

Section A5.3/05 **Efficacy Data**
Annex Point IIA5.3 Non enveloped virus

Acceptability	[redacted]
Remarks	[redacted]
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*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*
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 A6.1.1/01 Acute Toxicity

Annex Point IIA6.1.1 Oral LD_{50} in rats

Official use only

1 REFERENCE

1.1	**Reference**	[redacted] (1971) Acute toxicity and limits of solvent residue for sixteen organic solvents. [redacted]
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Criteria for data protection	No data protection claimed

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	No Study from 1971 (no guidelines available at the time the study was performed)
2.2	**GLP**	[redacted]
2.3	**Deviations**	Not applicable

3 MATERIALS AND METHODS

3.1	**Test material**	Propan-2-ol
3.1.1	Lot/Batch number	No data
3.1.2	Specification	2-propanol
3.1.2.1	Description	No data
3.1.2.2	Purity	Analytical grade
3.1.2.3	Stability	No data
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain	Sprague-Dawley
3.2.3	Source	No data

3.2.4	Sex	both sexes	both sexes	male	male
3.2.5	Age/weight at study initiation	newborn: 0 days (5-8g)	immature: 14 days (16-50g)	young adult: (80-160g)	older adult: (300-470g)
3.2.6	Number of animals per group	6-12	6-12	6	6

3.2.7	Control animals	No data
3.3	**Administration/ Exposure**	Oral
3.3.1	Postexposure period	One week

Section A6.1.1/01 Acute Toxicity

Annex Point IIA6.1.1 Oral LD_{50} in rats

3.3.2		**Oral**	
3.3.3	Type	Gavage	
3.3.4	Concentration	100 % (undiluted)	
3.3.5	Vehicle	None	
3.3.6	Total volume applied	Not further specified	X
3.3.7	Controls	No data	
3.4	**Examinations**	Mortality	X
3.5	**Method of determination of LD_{50}**	Litchfield and Wilcoxon (1949) Probit analysis statistical program via an IBM 1800 calculator	
3.6	**Further remarks**	In newborns the LD_{50} could not be determined due to volume limitations	X
		4 **RESULTS AND DISCUSSION**	
4.1	**Clinical signs**	No data	
4.2	**Pathology**	No data	
4.3	**Other**		
4.4	**LD_{50}**	newborn: < 1.0 ml/kg; immature: 5.6 ml/kg; young adult: 6.0 ml/kg; older adult: 6.8 ml/kg	
		5 **APPLICANT'S SUMMARY AND CONCLUSION**	
5.1	**Materials and methods**	In this study the oral LD_{50} value was determined for immature, young adult and older adult Sprague-Dawley rats.	X
5.2	**Results and discussion**	The determined oral LD_{50} values were in a range of 4400 - 5340 mg/kg bw and 2-propanol was more toxic to immature than to older adult rats.	X
5.3	**Conclusion**	[redacted]	
5.3.1	Reliability	[redacted]	
5.3.2	Deficiencies	[redacted]	

Section A6.1.1/01 Acute Toxicity

Annex Point IIA6.1.1 Oral LD_{50} in rats

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2008/02/21
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	

Section A6.1.1/02 Acute Toxicity

Annex Point IIA6.1.1 Oral LD_{50} in rabbits

Official use only

		1 REFERENCE
1.1	**Reference**	[redacted] (1972) Aliphatic alcohols and alky esters: narcotic and lethal potencies to tadpoles and to rabbits. [redacted]
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Criteria for data protection	No data protection claimed
		2 GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	No Study from 1972 (no guidelines available at the time the study was performed)
2.2	**GLP**	[redacted]
2.3	**Deviations**	Not applicable
		3 MATERIALS AND METHODS
3.1	**Test material**	Propan-2-ol
3.1.1	Lot/Batch number	No data
3.1.2	Specification	Isopropylalcohol
3.1.2.1	Description	No data
3.1.2.2	Purity	No data
3.1.2.3	Stability	No data
3.2	**Test Animals**	
3.2.1	Species	Rabbit
3.2.2	Strain	No data
3.2.3	Source	Regular dealers (no further information available)
3.2.4	Sex	Male / female
3.2.5	Age/weight at study initiation	No data / 1500 - 2500 g
3.2.6	Number of animals per group	10 - 35 (not exactly specified)
3.2.7	Control animals	No data
3.3	**Administration/ Exposure**	Oral
3.3.1	Postexposure period	24 h

Section A6.1.1/02 Acute Toxicity

Annex Point IIA6.1.1 Oral LD_{50} in rabbits

		Oral
3.3.2	Type	Gavage
3.3.3	Concentration	Doses / Concentration not further specified
3.3.4	Vehicle	Not further specified (5 ml of saline solution was used to wash the TS through the catheter)
3.3.5	Concentration in vehicle	No data
3.3.6	Total volume applied	No data
3.3.7	Controls	No data
3.4	**Examinations**	Clinical observation and mortality
3.5	**Method of determination of LD_{50}**	No data
3.6	**Further remarks**	The author also determined a narcotic dose (ND_{50}) of the TS, i.e. the quantity producing stupor and loss of voluntary movements in 50 % of the dosed animals
		4 RESULTS AND DISCUSSION
4.1	**Clinical signs**	No data
4.2	**Pathology**	No data
4.3	**Other**	The ND_{50} was given with 38 mMol/kg bw (2280 mg/kg bw). Higher doses (not further specified) caused disappearance of corneal reflex, nystagmus, dyspnoea and bradycardia.
4.4	**LD_{50}**	133 mMol/kg bw (7980 mg/kg bw)
		5 APPLICANT'S SUMMARY AND CONCLUSION
5.1	**Materials and methods**	The oral LD_{50} value was determined in rabbits dosed with 2-propanol via gavage. Besides the narcotic dose ND_{50} (dose producing stupor and loss of voluntary movements in 50 % of the dosed animals) was determined.
5.2	**Results and discussion**	The LD_{50} value was given with 133 mMol/kg bw corresponding to 7980 mg/kg bw. The narcotic dose ND_{50} was 38 mMol/kg corresponding to 2280 mg/kg bw.
5.3	**Conclusion**	
5.3.1	Reliability	[redacted]
5.3.2	Deficiencies	[redacted]

Section A6.1.1/02 Acute Toxicity

Annex Point IIA6.1.1 Oral LD_{50} in rabbits

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2008/01/15
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	

Section A6.1.1/03 Acute Toxicity

Annex Point IIA6.1.1 Oral LD_{50} in rats

Official use only

		1 REFERENCE
1.1	**Reference**	[redacted] (1948) Further experience with the range finding test in the industrial toxicology laboratory. [redacted]
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Criteria for data protection	No data protection claimed
		2 GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	No Study from 1948 (no guidelines available at the time the study was performed)
2.2	**GLP**	[redacted]
2.3	**Deviations**	Not applicable
		3 MATERIALS AND METHODS
3.1	**Test material**	Propan-2-ol
3.1.1	Lot/Batch number	No data
3.1.2	Specification	2-propanol
3.1.2.1	Description	No data
3.1.2.2	Purity	No data
3.1.2.3	Stability	No data
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain	Sherman
3.2.3	Source	Commercial breeder (not further specified)
3.2.4	Sex	No data
3.2.5	Age/weight at study initiation	No data / no data
3.2.6	Number of animals per group	6
3.2.7	Control animals	No data
3.3	**Administration/ Exposure**	Oral
3.3.1	Postexposure period	No data
		Oral
3.3.2	Type	Not exactly specified (presumably via gavage)

Section A6.1.1/03 Acute Toxicity

Annex Point IIA6.1.1 Oral LD_{50} in rats

3.3.3	Concentration	Not further specified	
3.3.4	Vehicle	No data	
3.3.5	Concentration in vehicle	No data	
3.3.6	Total volume applied	No data	
3.3.7	Controls	No data	
3.4	**Examinations**	Mortality	
3.5	**Method of determination of LD_{50}**	No data	
3.6	**Further remarks**	None	
		4 RESULTS AND DISCUSSION	
4.1	**Clinical signs**	No data	
4.2	**Pathology**	No data	
4.3	**Other**		
4.4	**LD_{50}**	5840 mg/kg bw	
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	The oral LD_{50} value was determined in rats dosed with 2-propanol.	
5.2	**Results and discussion**	The LD_{50} value was given with 5840 mg/kg bw.	
5.3	**Conclusion**		X
5.3.1	Reliability	[redacted]	X
5.3.2	Deficiencies	[redacted]	

Section A6.1.1/03 Acute Toxicity

Annex Point IIA6.1.1 Oral LD_{50} in rats

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2008/01/15
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
	[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	

Section A6.1.2/01 Acute Toxicity

Annex Point IIA6.1.2 Dermal LD_{50} in rabbits

Official use only

		1 REFERENCE
1.1	**Reference**	[redacted] (1948) Further experience with the range finding test in the industrial toxicology laboratory. [redacted]
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Criteria for data protection	No data protection claimed
		2 GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	No Study from 1948 (no guidelines available at the time the study was performed) [redacted]
2.2	**GLP**	[redacted]
2.3	**Deviations**	Not applicable
		3 MATERIALS AND METHODS
3.1	**Test material**	Propan-2-ol
3.1.1	Lot/Batch number	No data
3.1.2	Specification	2-propanol
3.1.2.1	Description	No data
3.1.2.2	Purity	No data
3.1.2.3	Stability	No data
3.2	**Test Animals**	
3.2.1	Species	Rabbit
3.2.2	Strain	No data
3.2.3	Source	No data
3.2.4	Sex	No data
3.2.5	Age/weight at study initiation	No data / no data
3.2.6	Number of animals per group	6 (not exactly specified)
3.2.7	Control animals	No data
3.3	**Administration/ Exposure**	Dermal
3.3.1	Postexposure period	No data

Section A6.1.2/01 Acute Toxicity

Annex Point IIA6.1.2 Dermal LD_{50} in rabbits

		Dermal	
3.3.2	Area covered	No data	
3.3.3	Occlusion	No data	
3.3.4	Vehicle	No data	
3.3.5	Concentration in vehicle	No data	
3.3.6	Total volume applied	No data	
3.3.7	Duration of exposure	24 h	
3.3.8	Removal of test substance	No data	
3.3.9	Controls	No data	
3.4	**Examinations**	Mortality	
3.5	**Method of determination of LD_{50}**	No data	
3.6	**Further remarks**	None	
		4 RESULTS AND DISCUSSION	
4.1	**Clinical signs**	No data	
4.2	**Pathology**	No data	
4.3	**Other**		
4.4	**LD_{50}**	16.4 ml/kg bw (ca. 13100 mg/kg bw assuming a density of 0.8 g/ml)	X
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	The dermal LD_{50} value was determined in rabbits dosed with 2-propanol with an exposure over 24 h.	
5.2	**Results and discussion**	The LD_{50} value was given with 16.4 ml/kg bw corresponding to ca. 13100 mg/kg bw.	X
5.3	**Conclusion**		
5.3.1	Reliability	[redacted]	X
5.3.2	Deficiencies	[redacted]	

Section A6.1.2/01 Acute Toxicity

Annex Point IIA6.1.2 Dermal LD_{50} in rabbits

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2008/02/21
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	

Section A6.1.3/01 Acute Toxicity

Annex Point IIA6.1.3 Acute inhalation toxicity study with rats

Official use only

		1 REFERENCE
1.1	**Reference**	[redacted] (1980) Studies on inhalation toxicity of 2-propanol. [redacted]
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Criteria for data protection	Not applicable
		2 GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	No Study from 1980 (no guidelines available at the time the study was performed)
2.2	**GLP**	[redacted]
2.3	**Deviations**	Not applicable
		3 MATERIALS AND METHODS
3.1	**Test material**	Propan-2-ol
3.1.1	Lot/Batch number	No data
3.1.2	Specification	2-propanol
3.1.3	Description	Physico-chemical properties: boiling point 82.5°C (at 760 mm Hg) spec. gravity: 0.780 (24/4°C)
3.1.4	Purity	No trace of isomer. Purity (not further specified) was checked by gas chromatography, infrared spectroscopy and mass spectrometry
3.1.5	Stability	No data
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain	Sprague-Dawley
3.2.3	Source	Canadian Breeding Farms, La Prairie, Quebec
3.2.4	Sex	Male / female
3.2.5	Age/weight at study initiation	No data / 200 – 280 g
3.2.6	Number of animals per group	10 males / 10 females
3.2.7	Control animals	No data
3.3	**Administration/ Exposure**	Inhalation
3.3.1	Postexposure period	15 days

Section A6.1.3/01 Acute Toxicity

Annex Point IIA6.1.3 Acute inhalation toxicity study with rats

		Inhalation	
3.3.2	Concentrations	Nominal concentration range: 4000 – 26100 ppm	X
3.3.3	Type of exposure	Whole body	
3.3.4	Vehicle	None	
3.3.5	Concentration in vehicle	Not applicable	
3.3.6	Duration of exposure	8 hrs	
3.3.7	Controls	No data	
3.4	**Examinations**	Signs of toxicity, mortality, and body weight; gross morphology at necropsy on all surviving animals; main organs sampled for histopathological evaluation	
3.5	**Method of determination of LD_{50}**	Litchfield & Wilcoxon (1949)	
3.6	**Further remarks**	None	
		4 **RESULTS AND DISCUSSION**	
4.1	**Clinical signs**	≥ 8000 ppm: concentration-dependent irritation of mucous membranes, ataxia, prostration, narcosis 18000 – 20000 ppm: few deaths within 48 hrs 20000 – 22000 ppm: paralysis of hind legs in males and females during the first 5 days after exposure	X
4.2	**Pathology**	26100 ppm: 20/20 animals died; narcosis within 60 min 4000 – 8000 ppm: congestion of liver, lung and spleen 18000 – 20000 ppm: survivors / died animals: slight congestion of brain; foamy vacuolisation of liver cells, acute pneumonia and oedema of spleen in all animals 21000 ppm: extensive pneumonia, oedema of brain and lungs, foamy vacuolisation of liver cells accompanied by severe focal cytoplasmic degradation	
4.3	**Other**	No	
4.4	**LD_{50}**	19000 ppm (17380 – 20760 ppm) for females 22500 ppm (19200 – 26400 ppm) for males	

Section A6.1.3/01 Acute Toxicity

Annex Point IIA6.1.3 Acute inhalation toxicity study with rats

		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	In this study rats were exposed via inhalation to nominal concentrations of 4000 – 26100 ppm 2-propanol over 8 hrs	X
5.2	**Results and discussion**	The LC_{50} was in a range of 19000 – 22500 ppm (47500 – 56250 mg/m^3). Exposure to high levels of 2-propanol caused typical lesions of chemical pneumonia and pulmonary oedema accompanied by foamy vacuolization of liver cells and severe focal cytoplasmic degradation.	X
5.3	**Conclusion**	[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
Date	2008/02/27
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	

Section A6.1.3/02 Acute Toxicity

Annex Point IIA6.1.3 Inhalative LC_{50} in rats

Official use only

1 REFERENCE

1.1	**Reference**	[redacted] (1948) Further experience with the range finding test in the industrial toxicology laboratory. [redacted]
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Criteria for data protection	No data protection claimed

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	No Study from 1948 (no guidelines available at the time the study was performed)
2.2	**GLP**	[redacted]
2.3	**Deviations**	Not applicable

3 MATERIALS AND METHODS

3.1	**Test material**	Propan-2-ol
3.1.1	Lot/Batch number	No data
3.1.2	Specification	2-propanol
3.1.2.1	Description	No data
3.1.2.2	Purity	No data
3.1.2.3	Stability	No data
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain	Sherman
3.2.3	Source	No data
3.2.4	Sex	No data
3.2.5	Age/weight at study initiation	No data / no data
3.2.6	Number of animals per group	6
3.2.7	Control animals	No data
3.3	**Administration/ Exposure**	Inhalation
3.3.1	Postexposure period	14 days

Section A6.1.3/02 Acute Toxicity

Annex Point IIA6.1.3 Inhalative LC_{50} in rats

		Inhalation		
3.3.2	Concentrations	Nominal concentration	16000 ppm	
		Analytical concentration	no data	
3.3.3	Particle size	Not applicable		
3.3.4	Type or preparation of particles	Not applicable		
3.3.5	Type of exposure	Probably whole body (not exactly specified)		
3.3.6	Vehicle	Air		
3.3.7	Concentration in vehicle	No data		
3.3.8	Duration of exposure	8 h		
3.3.9	Controls	No data		
3.4	**Examinations**	Mortality		
3.5	**Method of determination of LD_{50}**	No data		
3.6	**Further remarks**	Exposure to vapours		
		4 RESULTS AND DISCUSSION		
4.1	**Clinical signs**	No data		
4.2	**Pathology**	No data		
4.3	**Other**	No		
4.4	**LD_{50}**	4/6 animals died within 14 days after single 8 h exposure to 16000 ppm corresponding to ca. 40000 mg/m³		
		5 APPLICANT'S SUMMARY AND CONCLUSION		
5.1	**Materials and methods**	In this study rats were exposed over 8 h to 16000 ppm corresponding to ca. 40000 mg/m³ 2-propanol.		
5.2	**Results and discussion**	From this study a LC_{50} value (8 h) of < 40000 mg/m³ can be derived.		
5.3	**Conclusion**			
5.3.1	Reliability	[redacted]		X
5.3.2	Deficiencies	[redacted]		

Section A6.1.3/02 Acute Toxicity

Annex Point IIA6.1.3 Inhalative LC_{50} in rats

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2008/01/17
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
	[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	

Section 6.1.4/01 Acute Eye Irritation

Annex Point IIA6.1.4 Study with rabbits

Official use only

		REFERENCE
1.1	**Reference**	[redacted] (1999) Eye irritation: Updated reference chemicals data bank. [redacted]
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Criteria for data protection	No data protection claimed
		GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	Yes [redacted]
2.2	**GLP**	[redacted]
2.3	**Deviations**	No
		MATERIALS AND METHODS
3.1	**Test material**	Propan-2-ol
3.1.1	Lot/Batch number	No data
3.1.2	Specification	Isopropanol
3.1.2.1	Description	No data
3.1.2.2	Purity	99.9 %
3.1.2.3	Stability	No data

Section 6.1.4/01 Acute Eye Irritation

Annex Point IIA6.1.4 Study with rabbits

3.2	**Test Animals**		
3.2.1	Species	Rabbit	
3.2.2	Strain	NZW	
3.2.3	Source	No data	
3.2.4	Sex	No data	
3.2.5	Age/weight at study initiation	No data / no data	
3.2.6	Number of animals per group	4	
3.2.7	Control animals	No data	
3.3	**Administration/ Exposure**		
3.3.1	Preparation of test substance	Not further specified (undiluted application)	
3.3.2	Amount of active substance instilled	0.1 mL	
3.3.3	Exposure period	24 h	
3.3.4	Postexposure period	3 days	X
3.4	**Examinations**		
3.4.1	Ophthalmoscopic examination	Not further specified	
3.4.1.1	Scoring system	A modified MAS (maximum average score) representing maxima calculated at ≥ 24 h following installation was calculated according to the weighed scoring scheme of Draize et al. (1944).	
3.4.1.2	Examination time points	24, 48 and 72 h after installation	
3.4.2	Other investigations		
3.5	**Further remarks**		
		4 **RESULTS AND DISCUSSION**	
4.1	**Clinical signs**	No data	
4.2	**Average score**		X
4.2.1	Cornea	Not further specified	X
4.2.2	Iris	Not further specified	X
4.2.3	Conjunctiva	Not further specified	X
4.2.3.1	Redness	Not further specified	X
4.2.3.2	Chemosis	Not further specified	X
4.3	**Reversibility**	Not further specified	X

Section 6.1.4/01 Acute Eye Irritation

Annex Point IIA6.1.4 Study with rabbits

4.4	**Other**	No
4.5	**Overall result**	Modified MAS: 30.5 (maximum of 110) MAS (maximum average score) = maximum of averaged scores of individual animals at 24 h or longer
		APPLICANT'S SUMMARY AND CONCLUSION
5.1	**Materials and methods**	In this compilation the results of tests with different chemicals according to OECD Guideline 405 have been published.
5.2	**Results and discussion**	2-propanol was moderately eye irritating in a valid test according to OECD Guideline 405.
5.3	**Conclusion**	
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

Date	2008/02/27
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

Section 6.1.4/01 Acute Eye Irritation

Annex Point IIA6.1.4 Study with rabbits

	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	

CA-Table 1. [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 6.1.4/02 Acute Dermal Irritation

Annex Point IIA6.1.4 Study with rabbits

Official use only

		1 **REFERENCE**
1.1	**Reference**	[redacted] (1996) Skin irritation: Reference chemicals data bank. [redacted]
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Criteria for data protection	No data protection claimed
		2 **GUIDELINES AND QUALITY ASSURANCE**
2.1	**Guideline study**	Yes [redacted]
2.2	**GLP**	[redacted]
2.3	**Deviations**	No
		3 **MATERIALS AND METHODS**
3.1	**Test material**	Propan-2-ol
3.1.1	Lot/Batch number	No data
3.1.2	Specification	Isopropanol
3.1.2.1	Description	No data
3.1.2.2	Purity	100 %
3.1.2.3	Stability	No data
3.2	**Test Animals**	
3.2.1	Species	Rabbit
3.2.2	Strain	Albino
3.2.3	Source	No data
3.2.4	Sex	No data
3.2.5	Age/weight at study initiation	No data / no data
3.2.6	Number of animals per group	3
3.2.7	Control animals	No data
3.3	**Administration/ Exposure**	Dermal
3.3.1	Application	
3.3.1.1	Preparation of test substance	Not further specified (undiluted application)

Section 6.1.4/02 Acute Dermal Irritation

Annex Point IIA6.1.4 Study with rabbits

3.3.1.2	Test site and Preparation of Test Site	Application to intact skin (flank) Not further specified
3.3.2	Occlusion	Semi-occlusive
3.3.3	Vehicle	None
3.3.4	Concentration in vehicle	Not applicable
3.3.5	Total volume applied	0.5 ml
3.3.6	Removal of test substance	Not further specified
3.3.7	Duration of exposure	4 h
3.3.8	Postexposure period	3 days
3.3.9	Controls	No data
3.4	**Examinations**	
3.4.1	Clinical signs	No data
3.4.2	Dermal examination	Yes
3.4.2.1	scoring system	According to the scale originally proposed by Draize et al. (1944) and adopted by OECD Guideline 404
3.4.2.2	Examination time points	At least 24, 48 and 72 h after patch removal
3.4.3	Other examinations	No
3.5	**Further remarks**	None

4 **RESULTS AND DISCUSSION**

4.1 Clinical signs	No data
4.2 Average score	Not further specified
4.3 Reversibility	Not further specified
4.4 Other	No
4.5 Overall result	The primary irritation index (PII) was given with 0.78 (maximum of PII being 8). PII (primary irritation index) is defined as: $\frac{\sum(\text{erythema grades at 24/48/72 hr}) + \sum(\text{oedema grades at 24/48/72 hr})}{3 * \text{number of animals}}$

Section 6.1.4/02 Acute Dermal Irritation

Annex Point IIA6.1.4 Study with rabbits

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

In this compilation the results of tests with different chemicals according to OECD Guideline 404 have been published.

5.2 Results and discussion

2-propanol was not skin irritating in rabbits in a valid test according to OECD Guideline 404.

5.3 Conclusion

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
Date	2008/01/21
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	

Section A6.1.4/03 Acute Dermal Irritation

Annex Point IIA6.1.4 Human Data

Official use only

	REFERENCE	
1.1	**Reference**	Basketter DA, Chamberlain M, Griffiths HA, Rowson M, Whittle E & York M (1997) The classification of skin irritants by human patch test. Food Chem Toxicol 35, 845 – 852
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Criteria for data protection	No data protection claimed
	GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	No
2.2	**GLP**	[redacted]
2.3	**Deviations**	Not applicable
	MATERIALS AND METHODS	
3.1	**Test material**	Propan-2-ol
3.1.1	Lot/Batch number	No data
3.1.2	Specification	2-propanol
3.1.2.1	Description	No data
3.1.2.2	Purity	No data
3.1.2.3	Stability	No data
3.2	**Test Animals**	
3.2.1	Species	Human
3.2.2	Strain	
3.2.3	Source	
3.2.4	Sex	No data
3.2.5	Age/weight at study initiation	No data
3.2.6	Number of animals per group	31 human volunteers
3.2.7	Control animals	32 human volunteers
3.3	**Administration/ Exposure**	Dermal
3.3.1	Application	
3.3.1.1	Preparation of test substance	Not further specified (undiluted application)
3.3.1.2	Test site and Preparation of Test Site	Outer skin area of upper arm Not further specified

Section A6.1.4/03 Acute Dermal Irritation

Annex Point IIA6.1.4 Human Data

3.3.2	Occlusion	Semi-occlusive (25 mm Plain Hill Top Chamber)
3.3.3	Vehicle	None
3.3.4	Concentration in vehicle	100 %
3.3.5	Total volume applied	0.2 mL
3.3.6	Removal of test substance	Not further specified
3.3.7	Duration of exposure	4 h
3.3.8	Postexposure period	72 h after patch removal
3.3.9	Controls	20 % sodium dodecyl sulfate (SDS)
3.4	**Examinations**	
3.4.1	Clinical signs	Not further specified
3.4.2	Dermal examination	Yes
3.4.2.1	scoring system	Clinical observations graded from no reaction (grade 0) to strongly positive reaction (grade +++ with strong, often spreading erythema with oedema)
3.4.2.2	Examination time points	24, 48 and 72 h after patch removal
3.4.3	Other examinations	No
3.5	**Further remarks**	None
		4 **RESULTS AND DISCUSSION**
4.1	**Clinical signs**	No data
4.2	**Average score**	Not further specified
4.3	**Reversibility**	Not further specified
4.4	**Other**	No
4.5	**Overall result**	None of the 31 treated subjects reacted positive, while 17/32 subjects treated with 20 % sodium dodecyl sulphate reacted positive.
		APPLICANT'S SUMMARY AND CONCLUSION
5.1	**Materials and methods**	In this study 31 human volunteers were tested in a patch test.
5.2	**Results and discussion**	2-propanol was not skin irritating.
5.3	**Conclusion**	
5.3.1	Reliability	[redacted]
5.3.2	Deficiencies	[redacted]

Section A6.1.4/03 Acute Dermal Irritation

Annex Point IIA6.1.4 Human Data

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2008/01/21
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	

Section 6.1.4/04 Acute Eye Irritation

Annex Point IIA6.1.4 Study with rabbits

Official use only

		1 REFERENCE
1.1	**Reference**	[redacted] (1980) Dose-response studies with chemical irritants in the albino rabbit eye as a basis for selecting optimum testing conditions for predicting hazard to the human eye. [redacted]
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Criteria for data protection	No data protection claimed
		2 GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	No [redacted]
2.2	**GLP**	[redacted]
2.3	**Deviations**	Not applicable
		3 MATERIALS AND METHODS
3.1	**Test material**	Propan-2-ol
3.1.1	Lot/Batch number	No data
3.1.2	Specification	2-propanol
3.1.2.1	Description	No data
3.1.2.2	Purity	70 %
3.1.2.3	Stability	No data
3.2	**Test Animals**	
3.2.1	Species	Rabbit
3.2.2	Strain	New Zealand albino
3.2.3	Source	No data
3.2.4	Sex	Male / female
3.2.5	Age/weight at study initiation	Young adult / no data
3.2.6	Number of animals per group	3 - in preliminary study 6 - follow up study: mid and high dose group 9 - follow up study: low dose group
3.2.7	Control animals	No untreated eye was used as control

Section 6.1.4/04 Acute Eye Irritation

Annex Point IIA6.1.4 Study with rabbits

3.3 Administration/ Exposure		
3.3.1 Preparation of test substance	Not further specified (undiluted application)	X
3.3.2 Amount of active substance instilled	0.01, 0.03 and 0.1 mL in preliminary and follow up study.	
3.3.3 Exposure period	No data (no rinsing)	
3.3.4 Postexposure period	21 days	
3.4 Examinations		
3.4.1 Ophthalmoscopic examination	Yes	
3.4.1.1 Scoring system	According to Draize et al. (1944)	
3.4.1.2 Examination time points (days after dosing)	Days 1, 2, 3, 4, 7 and 14 (preliminary study) Days 1, 3, 7, 14 and 21 (follow up study)	
3.4.2 Other investigations	No	
3.5 Further remarks	None	
	4 **RESULTS AND DISCUSSION**	
4.1 Clinical signs	No data	
4.2 Average score	(see table A6.1.4/04_01)	
4.2.1 Cornea	Not further specified	
4.2.2 Iris	Not further specified	
4.2.3 Conjunctiva	Not further specified	
4.2.3.1 Redness	Not further specified	
4.2.3.2 Chemosis	Not further specified	

Section 6.1.4/04 Acute Eye Irritation

Annex Point IIA6.1.4 Study with rabbits

4.3	**Reversibility**	Yes (see table A6.1.4/04_01)
4.4	**Other**	No
4.5	**Overall result**	2-propanol caused moderate eye irritating effects in rabbits.
		5 **APPLICANT'S SUMMARY AND CONCLUSION**
5.1	**Materials and methods**	2-propanol (70 %) was tested in a modified Draize test with rabbits at applied volumes of 0.01, 0.03 and 0.1 mL.
5.2	**Results and discussion**	2-propanol caused moderate eye irritating effects in a modified Draize test with rabbits. The effects were concentration dependent but also were reversible within 14 days p.a.
5.3	**Conclusion**	
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
Date	2008/02/21
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	

Table A6.1.4/04_01 Results of eye irritation study

I. Preliminary study

Dose	0.01 mL	0.03 mL	0.1 mL
Maximum Draize score (x ± SE)	9 ± 1	31 ± 5	56 ± 16
Number of days to return to normal	3 – 3 – 3	7 – 7 – 7	7 – 7 – 14

Draize score (x ± SE)	II. Follow up study (scores at various times after instillation)						
day	1	3	7	14	21	Maximum	Median day to clear
0.01 mL	21±3	4±1	0±0	0±0	0±0	21±3	7
0.03 mL	36±4	19±4	4±1	2±2	2±2	36±4	14
0.10 mL	37±1	18±3	4±2	1±1	1±1	37±1	14

Section A6.1.4/05 Acute Dermal Irritation

Annex Point IIA6.1.4 Study with rabbits, guinea pigs and humans

					Official use only
		1 **REFERENCE**			
1.1	**Reference**	[redacted] (1975) Interspecies comparison of skin irritancy. [redacted]			
1.2	**Data protection**	No			
1.2.1	Data owner	Not applicable			
1.2.2	Criteria for data protection	No data protection claimed			
		2 **GUIDELINES AND QUALITY ASSURANCE**			
2.1	**Guideline study**	Yes [redacted]			X
2.2	**GLP**	[redacted]			
2.3	**Deviations**	Guinea pigs: 2 instead of 4 application sites per animal due to size of animal			
		3 **MATERIALS AND METHODS**			
3.1	**Test material**	Propan-2-ol			
3.1.1	Lot/Batch number	No data			
3.1.2	Specification	2-propanol			
3.1.2.1	Description	No data			
3.1.2.2	Purity	No data			
3.1.2.3	Stability	No data			
3.2	**Test Animals**				
3.2.1	Species	Rabbit	guinea pig	Humans	
3.2.2	Strain	No data	Hartley		
3.2.3	Source	No data	No data		
3.2.4	Sex	No data	No data	No data	
3.2.5	Age/weight at study initiation	No data / no data	young adults / no data	No data / no data	
3.2.6	Number of animals per group	6 (4 test sites/animal)	No data on number of animals (2 test sites/animal)	6 (8 test sites/volunteer)	X
3.2.7	Control animals	Control site on the same animal	Control site on the same animal	Control site on the same subject	X

Section A6.1.4/05 Acute Dermal Irritation

Annex Point IIA6.1.4 Study with rabbits, guinea pigs and humans

3.3 Administration/ Exposure	Dermal	
3.3.1 Application		
3.3.1.1 Preparation of test substance	Not further specified (undiluted application)	X
3.3.1.2 Test site and Preparation of Test Site	Testing on abraded and intact skin: rabbit: abrasion in a tic-tac-toe pattern guinea pig: not further specified human: single criss-cross design	
3.3.2 Occlusion	Patch test (not further specified)	
3.3.3 Vehicle	None	
3.3.4 Concentration in vehicle	Not applicable	
3.3.5 Total volume applied	No data	
3.3.6 Removal of test substance	No data	
3.3.7 Duration of exposure	4 hrs	
3.3.8 Postexposure period	48 hrs Most subjects were re-examined after one month for delayed reactions	X
3.3.9 Controls	Control site on the same animal or volunteer, respectively	X
3.4 Examinations		
3.4.1 Clinical signs	No data	
3.4.2 Dermal examination	Yes	
3.4.2.1 scoring system	<u>For human subjects:</u> 0 - 0.4 .....negligible 0.5 - 1.4 .....slight 1.5 – 2.4 .....moderate > 2.4 .....severe tissue destruction or irreversible change .....corrosive (for intact skin sites only) <u>For animals:</u> 0 - 0.4 .....negligible 0.5 - 1.9 .....slight 2.0 – 4.9 .....moderate 5.0 – 8.0 .....severe tissue destruction or irreversible change .....corrosive	
3.4.2.2 Examination time points	4, 24 and 48 hrs after exposure	
3.4.3 Other examinations	No	
3.5 Further remarks	None	

Section A6.1.4/05 Acute Dermal Irritation

Annex Point IIA6.1.4 Study with rabbits, guinea pigs and humans

4 **RESULTS AND DISCUSSION**

4.1 Average score

	Rabbit	Guinea Pig	Humans
mean scores on intact skin	0.0	0.0	0.0
mean scores / abraded skin	0.0	0.0	0.8
PII (abraded and intact skin)	0.0	0.0	0.4

4.2 Reversibility Yes

4.3 Other examinations No

4.4 Overall result 2-propanol was not irritating in rabbits, guinea pigs and humans.

5 **APPLICANT'S SUMMARY AND CONCLUSION**

5.1 Materials and methods 2-propanol was tested in a patch test (revised FHSA procedure proposed by FDA) with humans, rabbits and guinea pigs.

5.2 Results and discussion 2-propanol had negligible effects on skin of rabbits, guinea pigs and humans.

5.3 Conclusion [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

Date 2008/02/21

Materials and Methods [redacted]

Results and discussion [redacted]

Conclusion [redacted]

Reliability [redacted]

Section A6.1.4/05 Acute Dermal Irritation

Annex Point IIA6.1.4 Study with rabbits, guinea pigs and humans

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	

Section A6.1.5/01 Skin sensitisation

Annex Point IIA6.1.5 Local Lymph Node Assay (LLNA)

			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted] (1998) Strategies for identifying false positive responses in predictive skin sensitization tests. [redacted]	
1.2	**Data protection**	No	
1.2.1	Data owner	Not applicable	
1.2.2	Criteria for data protection	No data protection claimed	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	No [redacted]	X
2.2	**GLP**	[redacted]	
2.3	**Deviations**	Not applicable	X
		3 MATERIALS AND METHODS	
3.1	**Test material**	Propan-2-ol	
3.1.1	Lot/Batch number	No data	
3.1.2	Specification	2-propanol	
3.1.2.1	Description	No data	
3.1.2.2	Purity	No data	
3.1.2.3	Stability	No data	
3.1.2.4	Preparation of test substance for application	Used as delivered (no solvent)	
3.1.2.5	Pretest performed on irritant effects	No data	
3.2	**Test Animals**		
3.2.1	Species	Mouse	
3.2.2	Strain	CBA	
3.2.3	Source	No data	
3.2.4	Sex	No data	
3.2.5	Age/weight at study initiation	No data / no data	
3.2.6	Number of animals per group	4	
3.2.7	Control animals	Yes	

Section A6.1.5/01 Skin sensitisation

Annex Point IIA6.1.5 Local Lymph Node Assay (LLNA)

3.3	**Administration/ Exposure**	Non-Adjuvant	
3.3.1	Induction schedule	Groups of 4 mice are treated with 25 µl of 2-propanol on the dorsum of both ears. Treatment is performed once daily for 3 consecutive days. 5 days following initiation all mice are injected via the tail vein with 250 µl PBS containing 20 µCi tritiated thymidine. 5 hrs later the mice are killed and the amount of incorporated tritiated thymidine in draining lymph nodes is analysed to determine induction of sensitization.	
3.3.2	Way of Induction	Topical	
3.3.3	Concentrations used for induction	10, 25 or 50 %	
3.3.4	Concentration Freunds Complete Adjuvant (FCA)	Not applicable	
3.3.5	Challenge schedule	Not applicable	
3.3.6	Concentrations used for challenge	Not applicable	
3.3.7	Rechallenge	No	
3.3.8	Scoring schedule	5 days and 5 hours after initiation	
3.3.9	Removal of the test substance	No	
3.3.10	Positive control substance	No data	
3.4	**Examinations**		
3.4.1	Pilot study	No	
3.5	**Further remarks**		
		4 RESULTS AND DISCUSSION	
4.1	**Results of pilot studies**	Not applicable	
4.2	**Results of test**		
4.2.1	24h after challenge	Not applicable	
4.2.2	48h after challenge	Not applicable	
4.2.3	Other findings	Stimulation indices: 1.7 / 1.1 / 1.0 compared with sham treated controls.	X
4.3	**Overall result**	None of the tested animals reacted positive.	X

Section A6.1.5/01 Skin sensitisation

Annex Point IIA6.1.5 Local Lymph Node Assay (LLNA)

		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	The authors studied possible skin sensitising effects of 2-propanol in a Local Lymph Node Assay (LLNA) with CBA mice.	
5.2	**Results and discussion**	None of the tested animals reacted positive.	X
5.3	**Conclusion**		X
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
Date	2008/02/21
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	

Section A6.2/01 Percutaneous absorption (in vivo test)

Annex Point IIA6.2 Dermal absorption and pharmacokinetic study in male and female F-344 rats

Official use only

	1 REFERENCE	
1.1	**Reference**	[redacted] (1998) Dermal absorption and pharmacokinetics of isopropanol in the male and female F-344 rat. [redacted]
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Criteria for data protection	No data protection claimed
	2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	No
2.2	**GLP**	[redacted]
2.3	**Deviations**	Not applicable
	3 MATERIALS AND METHODS	
3.1	**Test material**	2-propanol and 2-propanol-2-^{14}C
3.1.1	Lot/Batch number	No data
3.1.2	Specification	No data
3.1.2.1	Description	No data
3.1.2.2	Purity	> 99 %
3.1.2.3	Stability	No data
3.1.2.4	Radiolabelling	^{14}C
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain	F-344
3.2.3	Source	Charles River Kingston
3.2.4	Sex	Male / female
3.2.5	Age/weight at study initiation	10 – 12 weeks / 140 – 246 g
3.2.6	Number of animals per group	3 – 4
3.2.7	Control animals	No data
3.3	**Administration/ Exposure**	Dermal
3.3.1	Preparation of test site	The hair from all animals was clipped from the thoracic region immediately posterior to the interscapular area of each animal ca. 24 hrs prior to application.
3.3.2	Concentration of test substance	70 % aqueous solution

Section A6.2/01	Percutaneous absorption (in vivo test)	
Annex Point IIA6.2	Dermal absorption and pharmacokinetic study in male and female F-344 rats	
3.3.3 Specific activity of test substance		
3.3.4 Volume applied	0.3 ml/animal	
3.3.5 Size of test site	4.3 cm^2	
3.3.6 Exposure period	4 hours	
3.3.7 Sampling time	Dermal blood kinetic studies: blood was sampled at 30 min and at 1, 2 and 4 hrs during exposure and at 4.5, 5, 6, 8, and 24 hrs. Disposition studies: urine, cage wash samples, expired volatile organics and expired CO_2 were collected at 8, 24 and 48 hrs following dosing; faeces were collected at 24 and 48 hrs Washing efficiency studies: urine and cage wash samples, expired volatile organics, expired CO_2 and faeces were collected and analysed for a period of 24 hrs following TS administration	
3.3.8 Samples	Urine, faeces, exhaled air, skin with substance not removable, liquid used for washing the skin	
	4 RESULTS AND DISCUSSION	
4.1 Toxic effects, clinical signs	No data	
4.2 Dermal irritation	No data	
4.3 Recovery of labelled compound	84 – 86 %	X
4.4 Percutaneous absorption	Dermal absorption rates: 0.78 - 0.85 $mg/cm^2/hr$ (m) and 0.77 - 0.78 $mg/cm^2/hr$ (f)	
	5 APPLICANT'S SUMMARY AND CONCLUSION	

Section A6.2/01 Percutaneous absorption (in vivo test)

Annex Point IIA6.2 Dermal absorption and pharmacokinetic study in male and female F-344 rats

5.1	**Materials and methods**	Dosing solutions were 70 % (by weight). The hair from all animals was clipped from the thoracic region immediately posterior to the interscapular area of each animal ca. 24 hrs prior to application. On the morning of each study chambers fabricated from 3.18-cm-diameter (external) borosilicate glass tubing were attached to the animals. The surface area of skin enclosed by the cells was 4.3 cm^2 and the aqueous test solution was observed to completely wet the surface of the skin. Aqueous TS solutions (0.3 ml) were delivered by syringe to the chambers through a small hole, which was covered immediately after application. Male rats received a mean dose of 0.18 g and female rats a dose of 0.1762 g. Dermal blood kinetic studies: aqueous TS was administered to a total of 8 rats (4 of each sex) and excess material was removed at 4 hrs. Dermal exposure sites were washed repeatedly with distilled water and dried. Blood was sampled at 30 min and at 1, 2 and 4 hrs during exposure and at 4.5, 5, 6, 8, and 24 hrs. Disposition studies: Groups of 3 male or female rats were dosed with 0.3 ml ^{14}C-IPA/rat and were placed immediately into individual metabolism chambers. After 4 hrs, rats were removed briefly from the chambers, unabsorbed material was removed, the sites were washed with distilled water and dried (all washings and swabs were saved for subsequent radioactivity analysis by LSS). The animals were returned to the chambers and urine, cage wash samples, expired volatile organics and expired CO_2 were collected at 8, 24 and 48 hrs following dosing and analysed by LSS. Faeces were collected at 24 and 48 hrs, homogenised with distilled water and analysed by LSS. Washing efficiency studies with ^{14}C-IPA: Groups of 3 male or female rats were treated as for disposition studies. After ca. 5 min the dose was removed from the chambers and unabsorbed liquid at the exposure site was recovered. Animals were placed in metabolism chambers and urine and cage wash samples, expired volatile organics, expired CO_2 and faeces were collected and analysed for a period of 24 hrs following TS administration.	
5.2	**Results and discussion**	Dermal blood kinetic studies: Quantifiable levels were reached by 1 hr and increased steadily through 4 hrs, reaching maximum concentrations of 0.19 µmol/g (m) and 0.24 µmol/g (f) at 4 hrs. IPA concentrations were below quantifiable levels at the 6-hr sampling in males and at the 8-hr sampling in females. 84 – 86 % of the dose was recovered from the application site. The dermal absorption rates (calculated by two independent methods, i.e. based on CO_2 recovery or based on total recovery of radioactivity) were 0.78 - 0.85 mg/cm^2/hr (m) or 0.77 - 0.78 mg/cm^2/hr (f) with calculated permeability coefficients of 1.37 - 1.5 * 10^{-3} cm/hr (m) or 1.35 - 1.37 * 10^{-3} cm/hr (f).	X
5.3	**Conclusion**	[redacted]	
5.3.1	Reliability	[redacted]	
5.3.2	Deficiencies	[redacted]	X

Section A6.2/01 Percutaneous absorption (in vivo test)

Annex Point IIA6.2 Dermal absorption and pharmacokinetic study in male and female F-344 rats

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2010/01/19
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	

Table 6.2/01: Total recovery of radioactivity from male and female F-344 rats

	[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 A6.2/02
Annex Point IIA6.2

Absorption after exposure via inhalation (*in vivo* test with rats)

			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted] (1988) Teratogenicity of n-propanol and isopropanol administered at high inhalation concentrations to rats. [redacted]	X
1.2	**Data protection**	No	
1.2.1	Data owner	Not applicable	
1.2.2	Criteria for data protection	No data protection claimed	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	No	
2.2	**GLP**	[redacted]	
2.3	**Deviations**	Not applicable	
		3 MATERIALS AND METHODS	
3.1	**Test material (unlabelled test item)**	Propan-2-ol	
3.1.1	Lot/Batch number	No data	
3.1.2	Specification	Isopropanol	
3.1.2.1	Description	No data	
3.1.2.2	Purity	97.6 % (reagent grade)	
3.1.2.3	Stability	No data	
3.1.2.4	Molecular formula	C_3-H_8-O	
3.2	**Test material (labelled test item)**	Not applicable	
3.2.1	Lot/Batch number		
3.2.2	Specification		
3.2.2.1	Description		
3.2.2.2	Radiochemical purity		
3.2.2.3	Stability		
3.2.2.4	Molecular formula		
3.2.2.5	Radiolabelling		
3.3	**Test Animals**		
3.3.1	Species	Rat	
3.3.2	Strain	Sprague-Dawley	
3.3.3	Source	Charles River Breeding Laboratories, Wilmington, MA	
3.3.4	Sex	Female	