Section A6.6.3/01-04 *In-vitro* gene mutation in mammalian cells

Annex Point IIA VI.6.6.3 Mouse lymphoma assay

3.1.1	Lot/Batch number	[redacted]
3.1.2	Specification	[redacted]
3.1.3	Description	[redacted]
3.1.4	Purity	[redacted] X2
3.1.5	Stability	[redacted] X3
3.2	**Study Type**	[redacted]
3.2.1	Organism/cell type	[redacted]
3.2.2	Deficiencies / Proficiencies	[redacted]
3.2.3	Metabolic activation system	[redacted]
3.2.4	Positive control	[redacted]
3.3	**Administration / Exposure; Application of test substance**	
3.3.1	Concentrations	[redacted]
3.3.2	Way of application	[redacted]
3.3.3	Incubation time	[redacted]
3.3.4	Number of cells incubated	[redacted]
3.3.5	Other modifications	[redacted]
3.4	**Examinations**	[redacted]
3.4.1	Number of cells evaluated	[redacted]

4 RESULTS AND DISCUSSION

Section A6.6.3/01-04 *In-vitro* gene mutation in mammalian cells

Annex Point IIA VI.6.6.3 Mouse lymphoma assay

4.1 Genotoxicity / Carcinogenicity

4.1.1 without metabolic activation

[redacted]

4.1.2 with metabolic activation

[redacted]

4.2 Cytotoxicity

[redacted]

Section A6.6.3/01-04 *In-vitro* gene mutation in mammalian cells

Annex Point IIA VI.6.6.3 Mouse lymphoma assay

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted] X4

5.2 Results and discussion

[redacted] X5

5.3 Conclusion

Negative or questionable test results were observed when the Mouse lymphoma Assay was carried out on Iodine, Potassium Iodine and Polyvinylpyrrolidone iodine. X6

The study results presented in the publication were summarized by independent experts panels as follows:

"Potassium iodide, I_2, and povidone-iodine (0.1–10 mg/mL) did not show mutagenic effects in L5178Y mouse lymphoma cells ... [redacted]

"Povidone iodine, iodine and potassium iodide were negative in the L5178 Y mouse lymphoma assay in the absence of activation, however, iodine and povidone iodine showed marginal activity in the presence of [redacted]

Both panels came to the conclusion "that stable iodine has been tested for genotoxicity in a variety of eukaryotic cell systems and has been found to be without mutagenic activity" [redacted]

5.3.1 Reliability [redacted]

5.3.2 Deficiencies [redacted]

Section A6.6.3/01-04 *In-vitro* gene mutation in mammalian cells

Annex Point IIA VI.6.6.3 Mouse lymphoma assay

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

Section A6.6.3/01 *In-vitro* gene mutation in mammalian cells

Annex Point IIA VI.6.6 Mouse lymphoma assay

Table A6.6.3/01-1: Table for Mouse Lymphoma Assay

Section A6.6.4/01-03 *In-vivo* mutagenicity study

Annex Point IIA VI.6.6.4 Bone marrow chromosome aberration test

[redacted]

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1 REFERENCE

1.1 Reference

[1] Merkle, J. and Zeller, H.J. (1979): Absence of Povidone-Iodine-Induced Mutagenicity in Mice and Hamsters. J. Pharmaceut. Sci. 68(1): 100-102
Doc. No. 592-017 (published); Section A6.6.4/01

[2] Expert Group on Vitamins and Minerals (2002): Revised Review of Iodine, p. 43
Doc. No. 681-001 (published); Section A6.6.4/02

[3] Expert Group on Vitamins and Minerals (2003): Revised Review of Iodine, p. 206
Doc. No. 592-033 (published); Section A6.6.4/03

1.2 Data protection [redacted]

1.2.1 Data owner [redacted]

1.2.2 Companies with letter of access [redacted]

1.2.3 Criteria for data protection [redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study [redacted] X1

The respective OECD Guideline 475 was adopted in 1997.

2.2 GLP [redacted]

2.3 Deviations Compared with OECD 475: No tests with positive control substances were performed.

Section A6.6.4/01-03 ***In-vivo* mutagenicity study**

Annex Point IIA VI.6.6.4 Bone marrow chromosome aberration test

3 MATERIALS AND METHODS

3.1	**Test material**	Polyvinylpyrrolidone iodine [redacted]
3.1.1	Lot/Batch number	[redacted]
3.1.2	Specification	[redacted]
3.1.2.1	Description	[redacted]
3.1.2.2	Purity	[redacted] X2
3.1.2.3	Stability	[redacted] X3
3.1.2.4	Maximum tolerable dose	[redacted] LD_{50} (i.p., Chinese hamster) = 165 mg/kg [redacted]
3.2	**Test Animals**	
3.2.1	Species	Chinese hamster
3.2.2	Strain	Not indicated.
3.2.3	Source	[redacted]
3.2.4	Sex	Male and Female
3.2.5	Age/weight at study initiation	[redacted]
3.2.6	Number of animals per group	[redacted]
3.2.7	Control animals	[redacted]
3.3	**Administration/ Exposure**	Intraperitoneal
3.3.1	Number of applications	[redacted]
3.3.2	Interval between applications	[redacted]
3.3.3	Sacrificing of animals	[redacted]

Section A6.6.4/01-03 ***In-vivo* mutagenicity study**

Annex Point IIA VI.6.6.4 Bone marrow chromosome aberration test

3.3.4	Dose applied	[redacted]
3.3.5	Vehicle	[redacted]
3.3.6	Concentration in vehicle	[redacted]
3.3.7	Total volume applied	[redacted]
3.3.8	Controls	[redacted]
3.3.9	Substance used as Positive Control	[redacted]
3.4	**Examinations**	
3.4.1	Clinical signs	[redacted]
3.4.2	Tissue	[redacted]
3.5	**Further remarks**	[redacted]

4. RESULTS AND DISCUSSION

4.1	**Clinical signs**	[redacted]
4.2	**Bone marrow cells**	[redacted]
4.3	**Genotoxicity**	[redacted]
4.4	**Other**	[redacted]

Section A6.6.4/01-03 *In-vivo* mutagenicity study

Annex Point IIA VI.6.6.4 Bone marrow chromosome aberration test

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted] X4

5.2 Results and discussion

[redacted]

5.3 Conclusion

Polyvinylpyrrolidone iodine USP did not show any indication of mutagenic potential *in vivo*. [redacted] Thus, Iodine has no mutagenic activity *in vivo* under test conditions.

[redacted]

5.3.1 Reliability

[redacted]

5.3.2 Deficiencies

[redacted]

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]

Section A6.6.4/01-03 *In-vivo* mutagenicity study

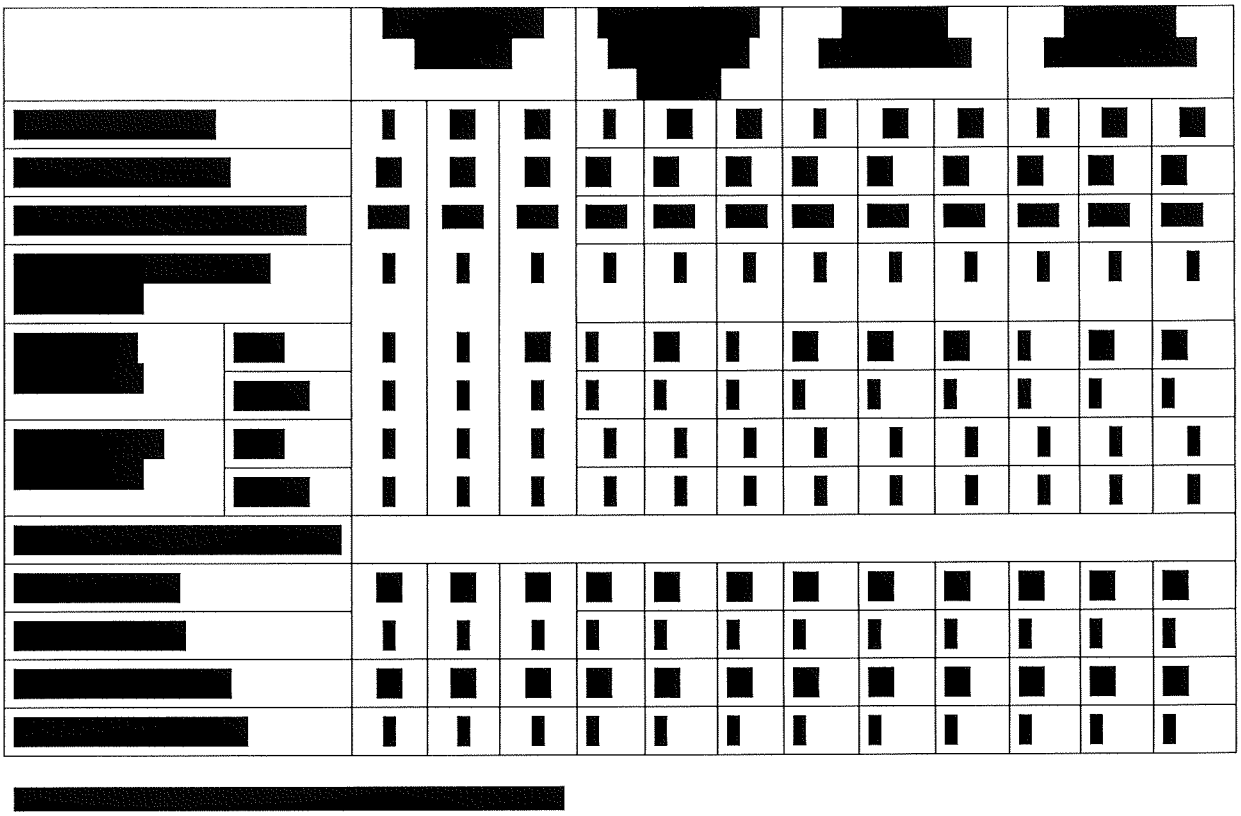
Annex Point IIA VI.6.6.4 Bone marrow chromosome aberration test

Remarks	[redacted]

Section A6.6.4/01-03 Genotoxicity *in vivo*

Annex Point IIA VI.6.6.4 Bone marrow chromosome aberration test

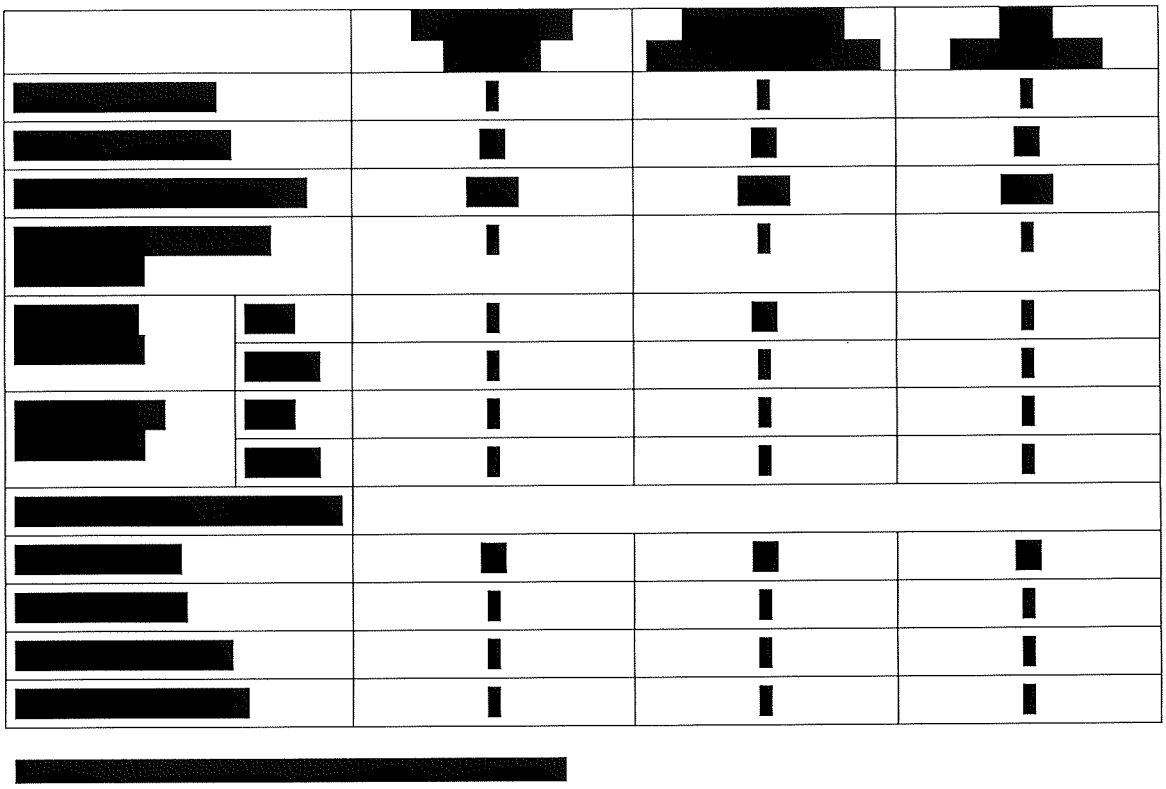
Table A6.6.4-1. Table for Cytogenetic *In-Vivo*-Test: Chromosomal Analysis after single application



Section A6.6.4/01-03 Genotoxicity *in vivo*

Annex Point IIA VI.6.6.4 Bone marrow chromosome aberration test

Table A6.6.4-2. Table for Cytogenetic *In-Vivo*-Test: Chromosomal Analysis after 5 applications



Section A6.6.5.1/01-03 *In-vivo* mutagenicity study

Annex Point IIA VI.6.6.5 Mouse micronucleus assay

[redacted]

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1 REFERENCE

1.1 Reference

[1] Merkle, J. and Zeller, H.J. (1979): Absence of Povidone-Iodine-Induced Mutagenicity in Mice and Hamsters. J. Pharmaceut. Sci. 68(1): 100-102
Doc. No. 592-017 (published); Section A6.6.5.1/01

[2] Expert Group on Vitamins and Minerals (2002): Revised Review of Iodine, p. 43
Doc. No. 681-001 (published); Section A6.6.5.1/02

[3] Expert Group on Vitamins and Minerals (2003): Revised Review of Iodine, p. 206
Doc. No. 592-033 (published); Section A6.6.5.1/03

1.2 Data protection [redacted]

1.2.1 Data owner [redacted]

1.2.2 Companies with letter of access [redacted]

1.2.3 Criteria for data protection [redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study [redacted] X1

The respective OECD Guideline 474 was adopted in 1997.

[redacted]

One of the references of OECD Guideline 474 is the publications [redacted]

2.2 GLP [redacted]

2.3 Deviations

Compared with OECD 474: Tests with positive control substances are not reported.

Section A6.6.5.1/01-03 *In-vivo* mutagenicity study

Annex Point IIA VI.6.6.5 Mouse micronucleus assay

3 MATERIALS AND METHODS

3.1	**Test material**	Polyvinylpyrrolidone iodine [redacted]	
3.1.1	Lot/Batch number	[redacted]	
3.1.2	Specification	[redacted]	
3.1.2.1	Description	[redacted]	
3.1.2.2	Purity	[redacted]	X2
3.1.2.3	Stability	[redacted]	X3
3.1.2.4	Maximum tolerable dose	[redacted] LD_{50} (i.p., NMRI mouse) = 360 mg/kg [redacted]	
3.2	**Test Animals**		
3.2.1	Species	Mouse	
3.2.2	Strain	NMRI	
3.2.3	Source	[redacted]	
3.2.4	Sex	Male and Female	
3.2.5	Age/weight at study initiation	[redacted]	
3.2.6	Number of animals per group	[redacted]	
3.2.7	Control animals	[redacted]	
3.3	**Administration/ Exposure**	Intraperitoneal	
3.3.1	Number of applications	[redacted]	
3.3.2	Interval between applications	[redacted]	
3.3.3	Postexposure period	[redacted]	X4
3.3.4	Dose applied	[redacted]	
3.3.5	Vehicle	[redacted]	
3.3.6	Concentration in vehicle	[redacted]	
3.3.7	Total volume applied	[redacted]	
3.3.8	Controls	[redacted]	
3.3.9	Substance used as Positive Control	[redacted]	

Section A6.6.5.1/01-03 *In-vivo* mutagenicity study

Annex Point IIA VI.6.6.5 Mouse micronucleus assay

3.4 Examinations

3.4.1 Clinical signs [redacted]

3.4.2 Tissue [redacted]

3.5 Further remarks [redacted]

4. RESULTS AND DISCUSSION

4.1 Clinical signs [redacted]

4.2 Normochromatic and polychromatic erythrocytes [redacted]

4.3 Genotoxicity [redacted]

4.4 Other [redacted]

Section A6.6.5.1/01-03 *In-vivo* mutagenicity study

Annex Point IIA VI.6.6.5 Mouse micronucleus assay

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted] X5

5.2 Results and discussion

[redacted]

5.3 Conclusion

Polyvinylpyrrolidone iodine USP did not show any indication of mutagenic potential in an *in vivo* muatgenicity assay in mice [redacted] it is concluded that two i.p. doses of [redacted] Iodine [redacted] do not produce an increase of micronuclei in normochromatic and polychromatic erythrocytes of the bone marrow of NMRI mice. Thus, Iodine revealed no mutagenic activity *in vivo* under test conditions.

[redacted]

5.3.1 Reliability [redacted]

5.3.2 Deficiencies [redacted]

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date [redacted]

Materials and Methods [redacted]

Results and discussion [redacted]

Conclusion [redacted]

Reliability [redacted]

Acceptability [redacted]

Remarks [redacted]

Section A6.6.5.1/01-03 *In-vivo* mutagenicity study

Annex Point IIA VI.6.6.4 Mouse micronucleus assay

Table A6.6.5.1 Table for Micronucleus Test *In Vivo*

Section A6.6.6/01-03 Germ cell effects

Annex Point IIA VI.6.6.6 Dominant lethal assay

[redacted]

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1 REFERENCE

1.1 Reference

[1] Merkle, J. and Zeller, H.J. (1979): Absence of Povidone-Iodine-Induced Mutagenicity in Mice and Hamsters. J. Pharmaceut. Sci. 68(1): 100-102
Doc. No. 592-017 (published); Section A6.6.6/01

[2] Expert Group on Vitamins and Minerals (2002): Revised Review of Iodine, p. 43
Doc. No. 681-001 (published); Section A6.6.6/02

[3] Expert Group on Vitamins and Minerals (2003): Revised Review of Iodine, p. 206
Doc. No. 592-033 (published); Section A6.6.6/03

1.2 Data protection [redacted]

1.2.1 Data owner [redacted]

1.2.2 Companies with letter of access [redacted]

1.2.3 Criteria for data protection [redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study [redacted] X1

The respective OECD Guideline 478 was adopted in 1984.

[redacted]

2.2 GLP [redacted]

[redacted]

2.3 Deviations

Compared with OECD 478: Tests results with positive control substances are not reported.

Section A6.6.6/01-03 Germ cell effects

Annex Point IIA VI.6.6.6 Dominant lethal assay

3 MATERIALS AND METHODS

3.1	**Test material**	Polyvinylpyrrolidone iodine [redacted]
3.1.1	Lot/Batch number	[redacted]
3.1.2	Specification	[redacted]
3.1.2.1	Description	[redacted]
3.1.2.2	Purity	[redacted] X2
3.1.2.3	Stability	[redacted] X3
3.1.2.4	Maximum tolerable dose	[redacted] LD_{50} (i.p., NMRI mouse) = 360 mg/kg bw [redacted]
3.2	**Test Animals**	
3.2.1	Species	Mouse
3.2.2	Strain	NMRI
3.2.3	Source	[redacted]
3.2.4	Sex	Male (treated) and female (mated to treated males)
3.2.5	Age/weight at study initiation	[redacted]
3.2.6	Number of animals per group	[redacted]
3.2.7	Control animals	[redacted]
3.3	**Administration/ Exposure**	Intraperitoneal
3.3.1	Number of applications	[redacted]
3.3.2	Interval between applications	[redacted]
3.3.3	Sacrificing of animals	[redacted]
3.3.4	Dose applied	[redacted]
3.3.5	Vehicle	[redacted]
3.3.6	Concentration in vehicle	[redacted]
3.3.7	Total volume applied	[redacted]
3.3.8	Controls	[redacted]

Section A6.6.6/01-03 Germ cell effects

Annex Point IIA VI.6.6.6 Dominant lethal assay

3.3.9	Substance used as Positive Control	[redacted]
3.4	**Examinations**	
3.4.1	Clinical signs	[redacted]
3.4.2	Reproductive parameters	[redacted]
3.5	**Further remarks**	[redacted]

4. RESULTS AND DISCUSSION

4.1	**Clinical signs**	[redacted]
4.2	**Conception rate and Mutagenicity Index**	[redacted]
4.3	**Genotoxicity**	[redacted]
4.4	**Other**	[redacted]

Section A6.6.6/01-03 Germ cell effects

Annex Point IIA VI.6.6.6 Dominant lethal assay

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted] X4

5.2 Results and discussion

[redacted]

5.3 Conclusion

Polyvinylpyrrolidone iodine USP showed no effect on average number of implantation or mutagenicity index. During all other mating periods there was not any indication of mutagenic potential *in vivo*. [redacted] is concluded that a single i.p. dose of [redacted] Iodine [redacted] also do not affect NMRI mice when a Dominant Lethal Assay is carried out. Thus, Iodine has no mutagenic activity *in vivo* under test conditions.

[redacted] "Doses of 72 mg/kg bw povidone iodine (given by i.p. injection) were not mutagenic in the mouse dominant lethal assay [redacted] "The mutagenicity data for iodine are generally negative". [redacted]

5.3.1 Reliability [redacted]

5.3.2 Deficiencies [redacted]

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date [redacted]

Materials and Methods [redacted]

Results and discussion [redacted]

Section A6.6.6/01-03 Germ cell effects

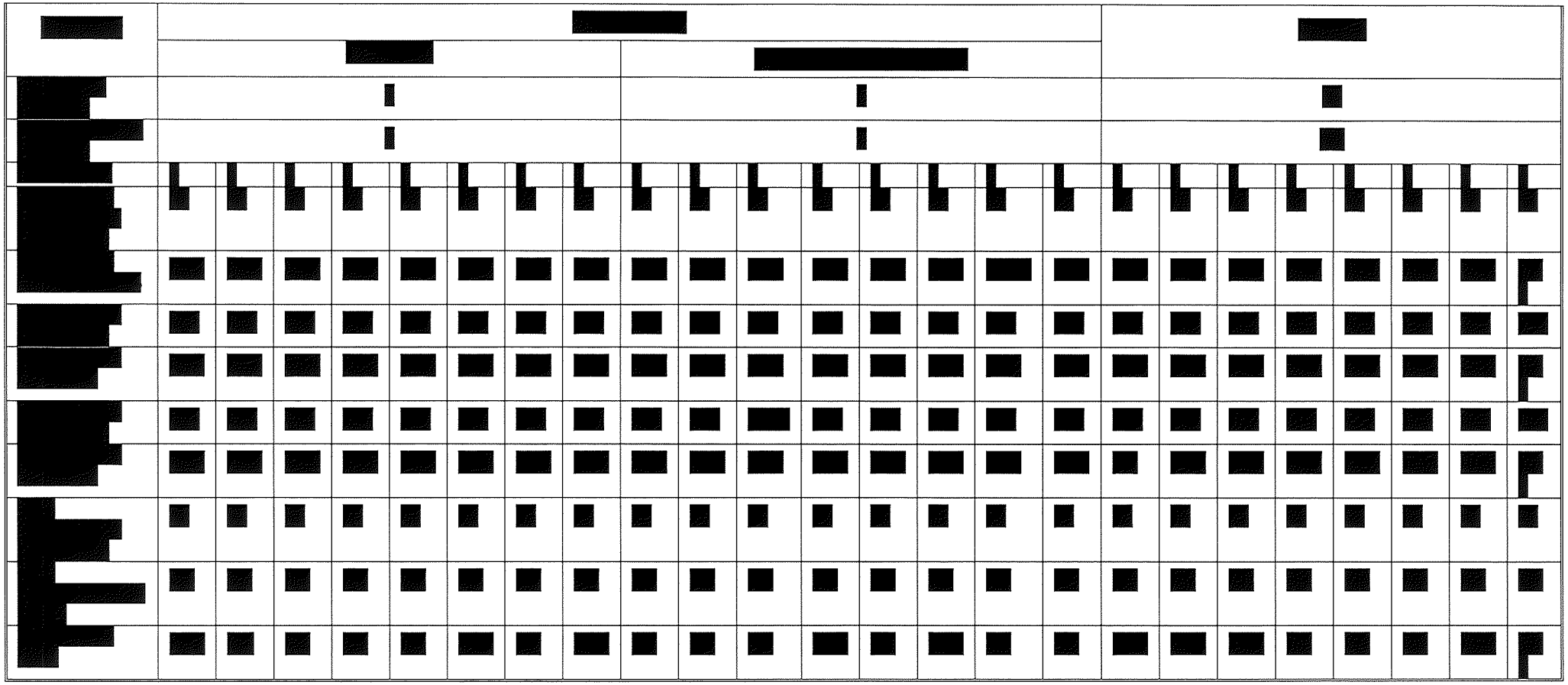
Annex Point IIA VI.6.6.6 Dominant lethal assay

Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

Section A6.6.6/01-03 ***In-vivo* mutagenicity study**

Annex Point IIA VI.6.6.4 Dominant lethal assay

Table A6.6.6-1 **Table for Genotoxicity *In-Vivo*-Test: Dominant Lethal Assay**



Section A6.6.7/01-04 Further testing if metabolites of concern are formed in mammals

Annex Point IIA VI.6.6.7

Transformation assay

[redacted]

				Official use only
		1	**REFERENCE**	
1.1	Reference	[1]	Kessler, F.K., Laskin, D. L., Borzelleca, J.F., Carchman, R.A. (1980): Assessment of povidone-iodine using two in vitro assays; J. Environ. Pathol. & Toxicol. 4-2,3, pp. 327-335 Doc. No. 592-019 (published); Section A6.6.7/01	
		[2]	California Environmental Protection Agency, Department of Pesticide Regulation, Medical Toxicology Branch (2005), Summary of Toxicology Data, Iodine and related Iodine Complexes, p. 127; 213 http://www.cdpr.ca.gov/docs/toxsums/pdfs/718c.pdf Doc. No. 581-013 (published); Section A6.6.7/02	
		[3]	Expert Group on Vitamins and Minerals (2002): Revised Review of Iodine, p. 42 Doc. No. 681-001 (published); Section A6.6.7/03	
		[4]	Expert Group on Vitamins and Minerals (2003): Revised Review of Iodine, p. 206 Doc. No. 592-033 (published); Section A6.6.7/04	
1.2	**Data protection**	[redacted]		
1.2.1	Data owner	[redacted]		
1.2.2	Companies with letter of access	[redacted]		
1.2.3	Criteria for data protection	[redacted]		
		2	**GUIDELINES AND QUALITY ASSURANCE**	
2.1	**Guideline study**	[redacted]		X1
		Transformation assay [redacted]		
2.2	**GLP**	[redacted]		
2.3	**Deviations**	Not applicable. [redacted]		
		3	**MATERIALS AND METHODS**	
3.1	**Test material**	(1) Iodine (2) Potassium iodine (3) Polyvinylpyrrolidone iodine		

Section A6.6.7/01-04 Further testing if metabolites of concern are formed in mammals

Annex Point IIA VI.6.6.7

Transformation assay

3.1.1	Lot/Batch number	[redacted]	
3.1.2	Specification	[redacted]	
3.1.3	Description	[redacted]	
3.1.4	Purity	[redacted]	X2
3.1.5	Stability	[redacted]	X3
3.2	**Study Type**	Transformation assay	
3.2.1	Organism/cell type	Balb/c 3T3 cells	
3.2.2	Deficiencies / Proficiencies	[redacted]	
3.2.3	Metabolic activation system	[redacted]	
3.2.4	Positive control	[redacted]	
3.3	**Administration / Exposure; Application of test substance**		
3.3.1	Concentrations	[redacted]	
3.3.2	Way of application	[redacted]	
3.3.3	Incubation time	[redacted]	
3.3.4	Number of cells incubated	[redacted]	
3.3.5	Other modifications	[redacted]	
3.4	**Examinations**	[redacted]	
3.4.1	Number of cells evaluated	[redacted]	

Section A6.6.7/01-04 **Further testing if metabolites of concern are formed in mammals**

Annex Point IIA VI.6.6.7

Transformation assay

4 RESULTS AND DISCUSSION

4.1 Genotoxicity / Carcinogenicity

4.1.1 without metabolic activation

[redacted]

4.1.2 with metabolic activation

[redacted]

4.2 Cytotoxicity

[redacted] X4

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted]

5.2 Results and discussion

[redacted] X5

Section A6.6.7/01-04 Annex Point IIA VI.6.6.7	**Further testing if metabolites of concern are formed in mammals** Transformation assay
5.3 Conclusion	Negative results or questionable were observed when the Transformation Assay were carried out on Iodine, Potassium Iodine and Polyvinylpyrrolidone iodine. [redacted] "Potassium iodide, I_2, and povidone-iodine (0.1–10 mg/mL) did not show ... in transforming activity in Balb/c 3T3 cells grown in culture [redacted] "Povidone iodine, iodine and potassium iodide were negative ... No significant transforming activity was shown by povidone iodine, iodine or potassium iodide in the Balb/c 3T3 transformation [redacted] Both panels came to the conclusion "that stable iodine has been tested for genotoxicity in a variety of eukaryotic cell systems and has been found to be without mutagenic activity" [redacted] or "The mutagenicity data for iodine are generally negative" [redacted]
5.3.1 Reliability	[redacted]
5.3.2 Deficiencies	[redacted]

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

Section A6.6.7/01-04 *In-vitro* gene mutation in mammalian cells

Annex Point IIA VI.6.6 Transformation assay

Table A6.6.7/01-04-1: Table for Transformation Assay

Section A6.6.7/05 Further genotoxicity testing *in vivo*

Annex Point IIA VI.6.6.7

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible [ ]** **Scientifically unjustified [X]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification:	[redacted]	
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	
Conclusion	[redacted]	
Remarks		

Section A6.7/01-02 Carcinogenicity (rat)

Annex Point IIA VI.6.7 Oral

[redacted]

Official use only

1 REFERENCE

1.1	**Reference**	[1] Takegawa, K. et al (1998). Induction of Squamous Cell Carcinomas in the Salivary Glands of Rats by Potassium Iodide. Japanese Journal of Cancer Research, 89, 105-109. Doc. No. 592-082 (published); Section A6.7/01 Reference citing this study: [2] Expert Group on Vitamins and Minerals (2002): Revised Review of Iodine, p. 40, 41, 46 Doc. No. 681-001 (published); Section A6.7/02
1.2	**Data protection**	[redacted]
1.2.1	**Data owner**	[redacted]
1.2.2	**Companies with letter of access**	[redacted]
1.2.3	**Criteria for data protection**	[redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	[redacted]
2.2	**GLP**	[redacted]
2.3	**Deviations**	Not applicable

3 MATERIALS AND METHODS

3.1	**Test material**	Potassium iodide (CAS No. 7681-11-0)
3.1.1	Lot/Batch number	[redacted]
3.1.2	Specification	[redacted]
3.1.2.1	Description	[redacted]
3.1.2.2	Purity	[redacted]
3.1.2.3	Stability	[redacted]
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain	F344/DuCrj

Section A6.7/01-02 Carcinogenicity (rat)

Annex Point IIA VI.6.7 Oral

3.2.3	Source	[redacted]
3.2.4	Sex	Male, female
3.2.5	Age/weight at study initiation	[redacted]
3.2.6	Number of animals per group	[redacted]
3.2.6.1	at interim sacrifice	[redacted]
3.2.6.2	at terminal sacrifice	[redacted]
3.2.7	Control animals	[redacted]
3.3	**Administration/ Exposure**	Oral
3.3.1	Duration of treatment	[redacted]
3.3.2	Interim sacrifice(s)	[redacted]
3.3.3	Final sacrifice	[redacted]
3.3.4	Frequency of exposure	[redacted]
3.3.5	Post-exposure period	[redacted]
3.3.6	Type	[redacted]
3.3.7	Concentration	[redacted]
3.3.8	Vehicle	[redacted]
3.3.9	Concentration in vehicle	[redacted]
3.3.10	Total volume applied	[redacted]
3.3.11	Controls	[redacted]

Section A6.7/01-02 Carcinogenicity (rat)

Annex Point IIA VI.6.7 Oral

3.4 Examinations

3.4.1 Body weight

3.4.2 Food consumption

3.4.3 Water consumption

3.4.4 Clinical signs

3.4.5 Makroskopic investigations

3.4.6 Ophthalmoscopic examination

3.4.7 Haematology

3.4.8 Clinical Chemistry

3.4.9 Urinalysis

3.4.10 Pathology

3.4.10.1 Organ Weights

3.4.11 Histopathology

3.4.12 Other examinations

3.5 Statistics

3.6 Further remarks

4 RESULTS AND DISCUSSION

4.1 Body weight

4.2 Food consumption

4.3 Water consumption

4.4 Clinical signs

4.5 Macroscopic investigations

4.6 Ophthalmoscopic examination

4.7 Haematology

4.8 Clinical Chemistry

4.9 Urinalysis

4.10 Pathology

Section A6.7/01-02 Carcinogenicity (rat)

Annex Point IIA VI.6.7 Oral

4.11 Organ Weights

4.12 Histopathology

4.13 Other examinations

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

5.2 Results and discussion X1

Section A6.7/01-02 Carcinogenicity (rat)

Annex Point IIA VI.6.7 Oral

5.3 Conclusion

Squamous metaplasia of ductules or ducts observed at high Iodine doses [redacted] lower doses [redacted] clearly indicates the lack of mutagenicity *in vivo* and that the effects noted in the salivary glands are not due to genotoxic effects.

Thus, the development of squamous cell carcinomas (SCCs) following the chronic oral exposure to Iodine (1000 ppm) - [redacted] - is thought to occur through a non-genotoxic proliferation dependent mechanism, linked to the irritative nature of Iodine.

[redacted] As the effects are likely be linked to the irritative nature of Iodine, a risk of humans considering the recommended daily intake (150-200 µg/day) or the Upper Intake Level (600 µg/day) is not expected.

5.3.1 Reliability [redacted]

5.3.2 Deficiencies [redacted]

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date [redacted]

Materials and Methods [redacted]

Results and discussion [redacted]

Conclusion [redacted]

Reliability [redacted]

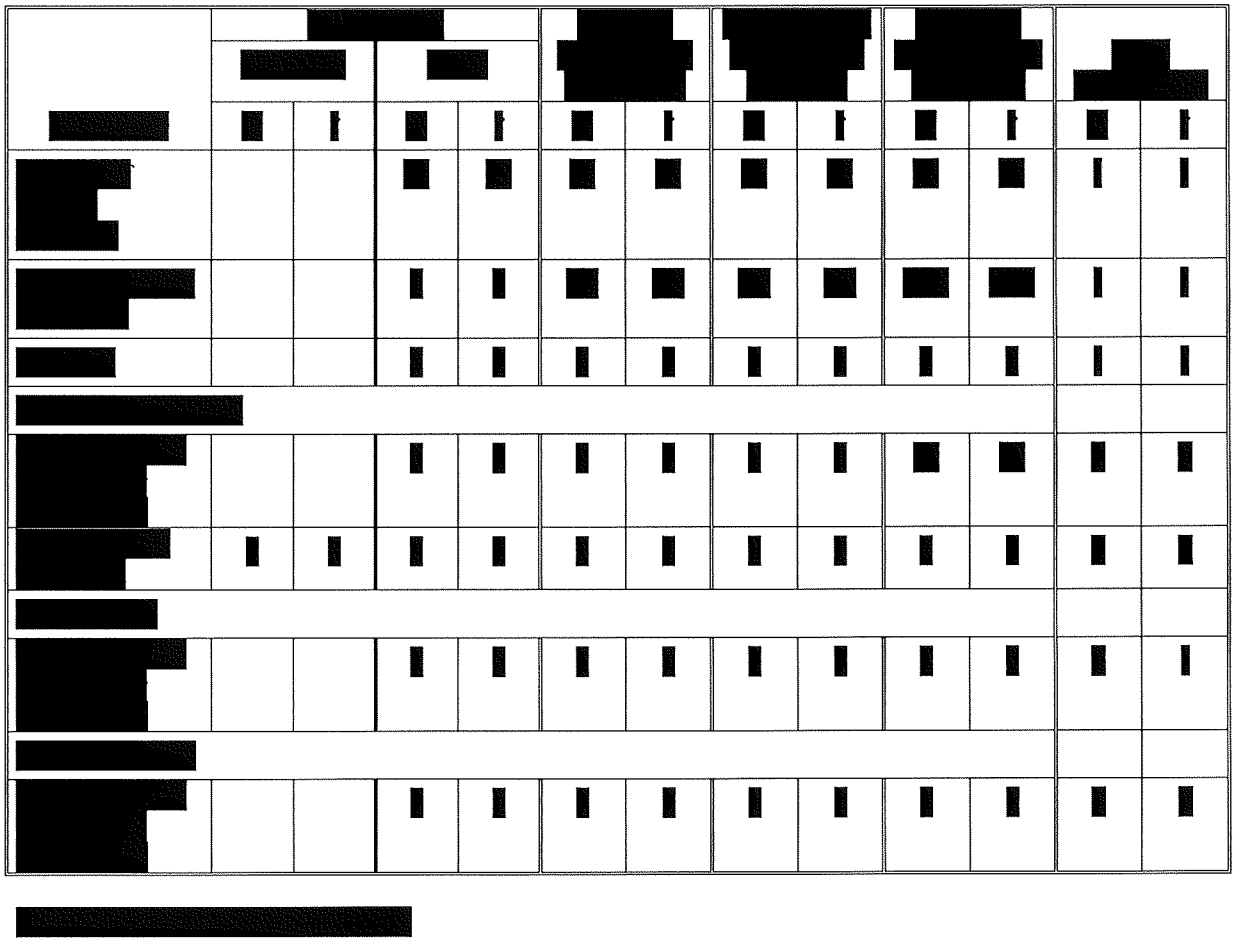
Acceptability [redacted]

Remarks

Section A6.5/01 Chronic toxicity / Carcinogenicity (rat)
Section A6.7/01 Oral

Annex Point IIA VI.6.5
Annex Point IIA VI.6.7

Table A6.5/01-1 Results of Chronic toxicity / Carcinogenicity study



Section A6.8.1/01 Teratogenicity Study
Annex Point IIA VI.6.8.1 Rabbit

[redacted]

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1 REFERENCE

1.1 Reference

Siegemund B., Weyers, W. (1987): Teratologische Untersuchungen eines niedermolekularen Polyvinylpyrrolidon-Jod-Komplexes an Kaninchen (Teratological studies of a low-molecular polyvinyl-pyrrolidone-Iodine complex in rabbits); Arzneimittel-Forschung (Arzneim.-Forsch.), vol. 37, no3, pp. 340-341;

Doc. No. 592-066 (published); Section A6.8.1/01

[redacted]

1.2 Data protection

[redacted]

1.2.1 Data owner

[redacted]

1.2.2 Companies with letter of access

[redacted]

1.2.3 Criteria for data protection

[redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study

[redacted]

The respective guideline, e.g. OECD 414 (2001) was not yet available when the study was performed.

2.2 GLP

[redacted]

2.3 Deviations

Not applicable [redacted]

3 MATERIALS AND METHODS

3.2 Test material

PVP-iodine [redacted]

3.2.1 Lot/Batch number [redacted]

3.2.2 Specification [redacted]

3.2.3 Description [redacted]

3.2.4 Purity [redacted]

3.2.5 Stability [redacted]

3.3 Test Animals

3.3.1 Species rabbit

3.3.2 Strain New Zealand White

Section A6.8.1/01 Teratogenicity Study
Annex Point IIA VI.6.8.1 Rabbit

3.3.3	Source	[redacted]
3.3.4	Sex	Female (nonparous)
3.3.5	Age/weight at study initiation	[redacted]
3.3.6	Number of animals per group	[redacted]
3.3.7	Control animals	[redacted]
3.3.8	Mating period	[redacted]
3.4	**Administration/ Exposure**	[redacted]
3.4.1	Duration of exposure	[redacted]
3.4.2	Postexposure period	[redacted]
3.4.3	Type	injection
3.4.4	Concentration	[redacted]
3.4.5	Vehicle	[redacted]
3.4.6	Concentration in vehicle	[redacted]
3.4.7	Total volume applied	[redacted]
3.4.8	Controls	[redacted]
3.5	**Examinations**	
3.5.1	Body weight	[redacted]
3.5.2	Food consumption	[redacted]
3.5.3	Clinical signs	[redacted]

Section A6.8.1/01 Teratogenicity Study
Annex Point IIA VI.6.8.1 Rabbit

3.5.4 Examination of uterine content

3.5.5 Examination of foetuses

3.5.5.1 General

3.5.5.2 Skelet

3.5.5.3 Soft tissues

3.6 Further remarks

3.7 Statistic

4 RESULTS AND DISCUSSION

4.1 Maternal toxic Effects

4.2 Teratogenic / embryotoxic effects

4.3 Conclusion

There was some evidence for a dose-response relation concerning bodyweight gain in dams (potentially indicating a slight systemic toxicity in dams at least at the top dose investigated) and absolute placenta weight (**Table A6.8.1/01-1** and **Table A6.8.1/01-2**). No dose related malformations of skeleton and organs of the foetuses were noted. No teratogenic effect due to the treatment of rabbits with PVP-Iodine was observed even at doses revealing slight indication of systemic toxic effects in dams.

5 APPLICANT'S SUMMARY AND CONCLUSION

Section A6.8.1/01 Teratogenicity Study
Annex Point IIA VI.6.8.1 Rabbit

5.1	**Materials and methods**	[redacted]
5.2	**Results and discussion**	[redacted]
5.3	**Conclusion**	The tested concentrations are representing disinfecting solutions or ointments for dermal applications in humans[redacted] Even under these stringent test conditions when doses of more than 700 times of the Upper Intake level for Iodine of 10 µg/kg bw/day were applied and some potential toxicity was revealed, no indications for teratogenic effects were noted. The negative findings of this study in context with those of the rat study [redacted] do not justify a further animal study because of animal welfare reasons. [redacted]
5.3.1	LO(A)EL maternal toxic effects	75 mg PVP-iodine /kg bw/[redacted]
5.3.2	NO(A)EL maternal toxic effects	35 mg PVP-iodine/kg bw/day [redacted]
5.3.3	LO(A)EL embryotoxic / teratogenic effects	> 75 mg PVP-iodine /kg bw/day
5.3.4	NO(A)EL embryotoxic / teratogenic effects	≥ 75 mg PVP-iodine/kg bw/day, [redacted]
5.3.5	Reliability	[redacted]
5.3.6	Deficiencies	[redacted]

Section A6.8.1/01 Teratogenicity Study

Annex Point IIA VI.6.8.1 **Rabbit**

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

Table A6.8.1/01-1: Table for Teratogenic effects

Maternal effects

[redacted]

Section A6.8.1/01 **Teratogenicity Study**

Annex Point IIA VI.6.8.1 **Rabbit**

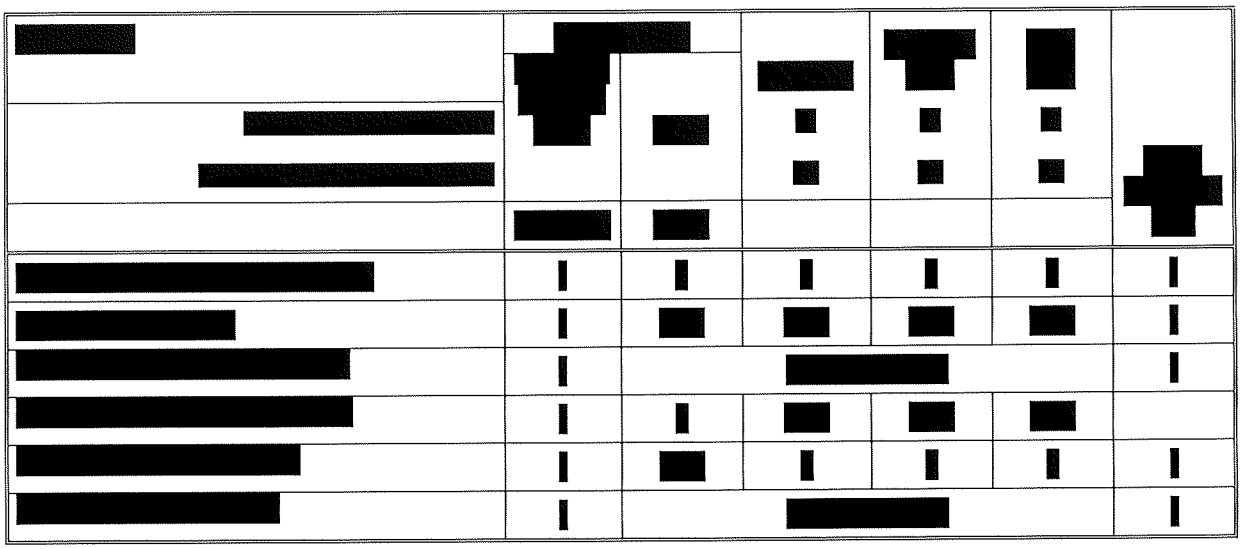
Table A6.8.1/01-2: Table for Teratogenic effects (separate data for all dosage groups)
Litter response (Caesarean section data)

Section A6.8.1/01 **Teratogenicity Study**

Annex Point IIA VI.6.8.1 **Rabbit**

Table A6.8.1/01-3: Table for Teratogenic effects (separate data for all dosage groups)

Examination of the foetuses



Section A6.8.1/02 **Combined Teratogenicity/Reprotoxicity Study**
Section A6.8.2/04 **Feeding study in rat**
Annex Point IIA VI.6.8.1

[redacted]

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1 REFERENCE

1.1	**Reference**	Ammerman, C.B., et al. (1964): Reproduction and lactation in rats fed excessive iodine; J Nutrition, 84, 107-112; Doc. No. 592-011 (published); Section A.6.8.1/02
1.2	**Data protection**	[redacted]
1.2.1	Data owner	[redacted]
1.2.2	Companies with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	[redacted] The respective guidelines, e.g. OECD 414 (2001), were not yet available when the study was performed.
2.2	**GLP**	[redacted]
2.3	**Deviations**	Not applicable [redacted] Compared to OECD guideline 414 the most relevant deviations are that the substance was administered as one dose level only and not to pregnant animals only but already 12 days before mating.

3 MATERIALS AND METHODS

3.1	**Test material**	Potassium iodide [redacted]
3.1.1	Lot/Batch number	[redacted]
3.1.2	Specification	[redacted]
3.1.3	Description	[redacted]
3.1.4	Purity	[redacted]
3.1.5	Stability	[redacted]
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain	Long-Evans
3.2.3	Source	[redacted]
3.2.4	Sex	Female (nonparous): treated

Section A6.8.1/02 **Combined Teratogenicity/Reprotoxicity Study**
Section A6.8.2/04 **Feeding study in rat**
Annex Point IIA VI.6.8.1

		Males (see point 3.3.1):
		-
3.2.5	Age/weight at study initiation	
3.2.6	Number of animals per group	
3.2.7	Mating	
3.2.8	Mating period	
3.2.9	Age/weight at study initiation	
3.2.10	Control animals	
3.3	**Administration/ Exposure**	
3.3.1	Duration of exposure	
3.3.2	Sacrificed	
3.3.3	Postexposure period	
3.3.4	Type	Via diet
3.3.5	Concentration	
3.3.6	Vehicle	
3.3.7	Concentration in vehicle	
3.3.8	Total volume applied	
3.3.9	Controls	

Section A6.8.1/02 **Combined Teratogenicity/Reprotoxicity Study**
Section A6.8.2/04 **Feeding study in rat**
Annex Point IIA VI.6.8.1

3.4	**Examinations**	
3.4.1	Body weight	[redacted]
3.4.2	Food consumption	[redacted]
3.4.3	Clinical signs	[redacted]
3.4.4	Examination of uterine content	[redacted]
3.4.5	Examination of foetuses (teratogenic effects)	
3.4.5.1	General	[redacted]
3.4.5.2	Skelet	[redacted]
3.4.5.3	Soft tissue	[redacted]
3.4.6	Others (reprotoxic effects)	[redacted]
3.4.7	Skelet	[redacted]
3.4.8	Soft tissue	[redacted]
3.5	**Further remarks**	[redacted]
3.6	**Statistic**	[redacted]

Section A6.8.1/02 **Combined Teratogenicity/Reprotoxicity Study**
Section A6.8.2/04 **Feeding study in rat**

Annex Point IIA VI.6.8.1

4 RESULTS AND DISCUSSION

4.1 Maternal toxic Effects

[redacted]

4.2 Teratogenic / embryo-toxic / reprotoxic effects

[redacted]

4.3 Other effects

[redacted]

Section A6.8.1/02 **Combined Teratogenicity/Reprotoxicity Study**
Section A6.8.2/04 **Feeding study in rat**
Annex Point IIA VI.6.8.1

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted]

5.2 Results and discussion

[redacted]

5.3 Conclusion

Section A6.8.1/02 Combined Teratogenicity/Reprotoxicity Study
Section A6.8.2/04 Feeding study in rat

Annex Point IIA VI.6.8.1

5.3.1	LO(A)EL maternal toxic effects	2500 ppm [redacted]
5.3.2	NO(A)EL maternal toxic effects	Not applicable [redacted]
5.3.3	LO(A)EL embryotoxic / teratogenic / reprotoxic effects	No LO(A)EL for embryotoxic / teratogenic toxic effects can be established [redacted]
5.3.4	NO(A)EL embryotoxic /	2500 ppm [redacted] No effects on foetuses noted.
5.3.5	NO(A)EL reprotoxic	2500 ppm [redacted] Based on numbers of pregnancies, litters and implantation sites no adverse effects are reported.
5.3.6	Reliability	[redacted]
5.3.7	Deficiencies	[redacted]

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

Section A6.8.2/01 Reproduction Toxicity Study
Annex Point IIA VI.6.8.2 **Feeding study in rat**

[redacted]

			Official use only
		1 REFERENCE	
1.1	**Reference**	Ammerman, C.B., et al. (1964): Reproduction and lactation in rats fed excessive Iodine; J Nutrition, 84, 107-112; Doc. No. 592-011; Section A6.8.2/01	
1.2	**Data protection**	[redacted]	
1.2.1	Data owner	[redacted]	
1.2.2	Companies with letter of access	[redacted]	
1.2.3	Criteria for data protection	[redacted]	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	[redacted]	
2.2	**GLP**	[redacted]	
2.3	**Deviations**	Not applicable [redacted] Compared with OECD guideline 415 there are several deviations, e.g. the test substance was administered only as one dose. The treatment of males is not explicitly indicated. This experiment can be considered as a limit test.	
		3 MATERIALS AND METHODS	
3.1	**Test material**	Potassium iodide [redacted]	
3.1.1	Lot/Batch number	[redacted]	
3.1.2	Specification	[redacted]	
3.1.3	Description	[redacted]	
3.1.4	Purity	[redacted]	
3.1.5	Stability	[redacted]	
3.2	**Test Animals**		
3.2.1	Species	Rat	
3.2.2	Strain	Long-Evans	
3.2.3	Source	[redacted]	
3.2.4	Sex	Female (nonparous)	
3.2.5	Age/weight at study initiation		
3.2.6	Number of animals per group	[redacted]	
3.2.7	Mating	[redacted]	
3.2.8	Duration of mating	[redacted]	
3.2.9	Deviations from standard protocol	[redacted]	

Section A6.8.2/01 Reproduction Toxicity Study
Annex Point IIA VI.6.8.2 Feeding study in rat

3.2.10	Control animals	[redacted]
3.3	**Administration/ Exposure**	Oral
3.3.1	Animal assignment to dosage groups	[redacted]
3.3.2	Duration of exposure before mating	[redacted]
3.3.3	Duration of exposure in general P, F1, F2 males, females	[redacted]
3.3.4	Type	[redacted]
3.3.5	Concentration	[redacted]
3.3.6	Vehicle	[redacted]
3.3.7	Concentration in vehicle	[redacted]
3.3.8	Total volume applied	[redacted]
3.3.9	Controls	[redacted]
3.4	**Examinations**	
3.4.1	Clinical signs	[redacted]
3.4.2	Body weight	[redacted]
3.4.3	Food/water consumption	[redacted]
3.4.4	Oestrus cycle	[redacted]
3.4.5	Sperm parameters	[redacted]

Section A6.8.2/01 **Reproduction Toxicity Study**
Annex Point IIA VI.6.8.2 **Feeding study in rat**

3.4.6	Offspring	Yes, [redacted]
3.4.7	Organ weights P and F1	[redacted]
3.4.8	Histopathology P and F1	[redacted]
3.4.9	Histopathology F1 not selected for mating, F2	[redacted]
3.5	**Further remarks**	[redacted]
3.6	**Statistic**	[redacted]

4 RESULTS AND DISCUSSION

4.1	**Parental effects**	
4.1.1	F0 animals	[redacted]
4.1.2	F1 parents	[redacted]
4.2	Litter observations	
4.2.1	Number and sexes of pups born	[redacted]
4.2.2	Pup body weight	[redacted]
4.2.3	Litter development observations	[redacted]
4.2.4	Pup clinical observation and necropsy findings during lactation	[redacted]
4.2.5	Necropsy findings of weaned pups	[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

Section A6.8.2/01 Reproduction Toxicity Study
Annex Point IIA VI.6.8.2 **Feeding study in rat**

5.2 Materials and methods

[redacted]

5.3 Results and discussion

[redacted]

5.4 Conclusion

5.4.1	LO(A)EL	
5.4.1.1	Parent males	Not applicable
5.4.1.2	Parent females	2500 ppm [redacted] to reduced or absent lactation X1
5.4.1.3	F1 males	Not [redacted]
5.4.1.4	F1 females	Not [redacted]
5.4.1.5	F1 both sexes	<2500 ppm [redacted] X2
5.4.1.6	F2 males	Not applicable
5.4.1.7	F2 females	Not applicable
5.4.2	NO(A)EL	

Section A6.8.2/01 Reproduction Toxicity Study
Annex Point IIA VI.6.8.2 **Feeding study in rat**

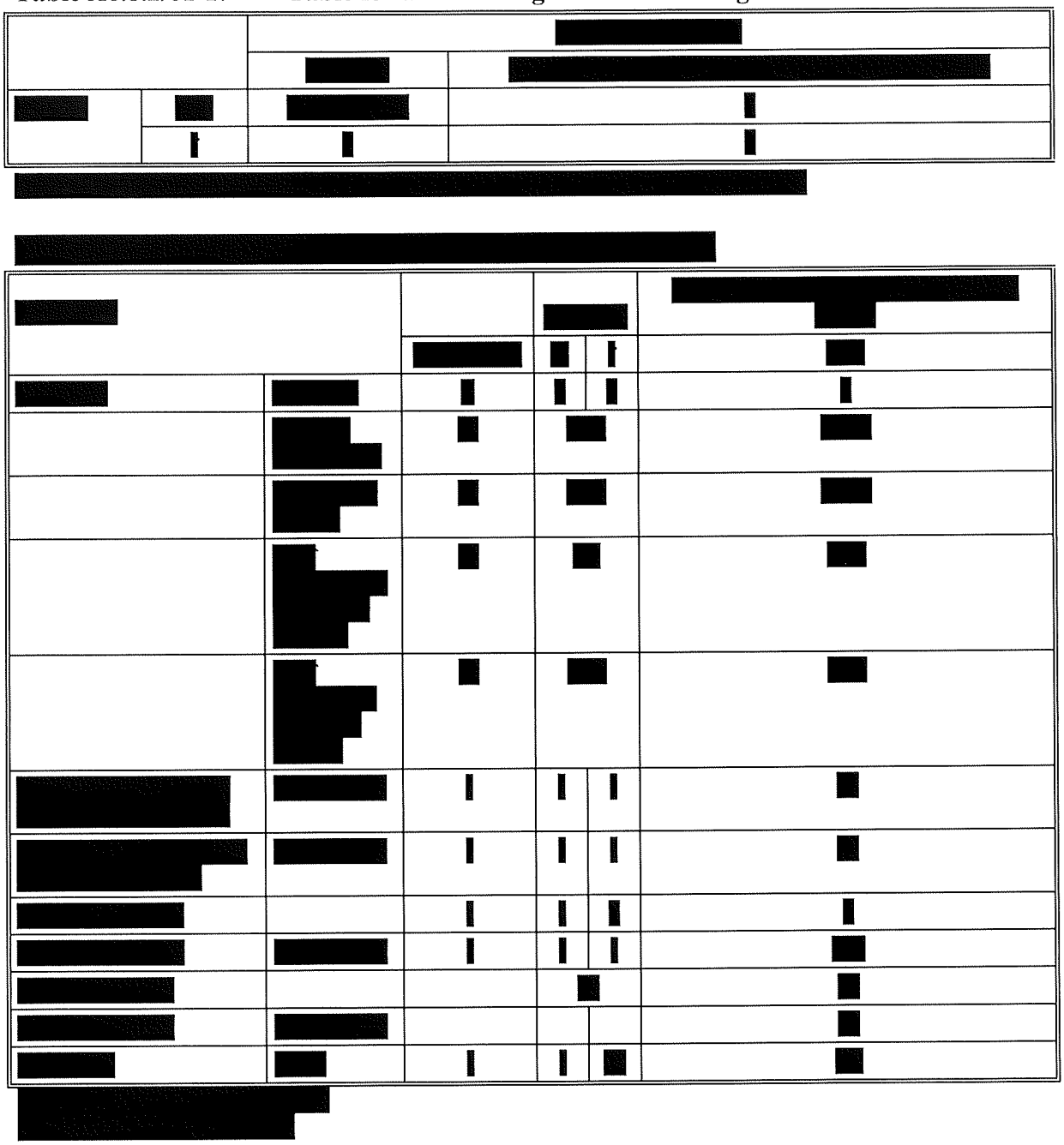
5.4.2.1	Parent males	Not applicable [redacted])
5.4.2.2	Parent females	<2500 ppm ([redacted]to reduced or absent lactation
5.4.2.3	F1 males	Not applicable [redacted]
5.4.2.4	F1 females	Not applicable [redacted]
5.4.2.5	F1 both sexes	<2500 ppm [redacted]
5.4.2.6	F2 males	Not applicable [redacted]
5.4.2.7	F2 females	Not applicable [redacted]
5.4.3	Reliability	[redacted]
5.4.4	Deficiencies	[redacted]

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

Table A6.8.2/01-1: Table for animal assignment for mating



Section A6.8.2/02 Reproduction Toxicity Study
Annex Point IIA VI.6.8.2 Feeding study in rat

[redacted]

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1 REFERENCE

1.1	**Reference**	Ammerman, C.B., et al. (1964): Reproduction and lactation in rats fed excessive Iodine; J Nutrition, 84, 107-112; Doc. No. 592-011; Section A6.8.2/02
1.2	**Data protection**	[redacted]
1.2.1	Data owner	[redacted]
1.2.2	Companies with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	[redacted]
2.2	**GLP**	[redacted]
2.3	**Deviations**	Not applicable [redacted]

3 MATERIALS AND METHODS

3.1	**Test material**	Potassium iodide [redacted]
3.1.1	Lot/Batch number	[redacted]
3.1.2	Specification	[redacted]
3.1.3	Description	[redacted]
3.1.4	Purity	[redacted]
3.1.5	Stability	[redacted]
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain	Long-Evans
3.2.3	Source	[redacted]
3.2.4	Sex	Female (nonparous)
3.2.5	Age/weight at study initiation	
3.2.6	Number of animals per group	[redacted]
3.2.7	Mating	[redacted]
3.2.8	Duration of mating	[redacted]
3.2.9	Deviations from standard protocol	[redacted]
3.2.10	Control animals	[redacted]

Section A6.8.2/02 Reproduction Toxicity Study
Annex Point IIA VI.6.8.2 **Feeding study in rat**

3.3	**Administration/ Exposure**	Oral
3.3.1	Animal assignment to dosage groups	[redacted]
3.3.2	Duration of exposure before mating	[redacted]
3.3.3	Duration of exposure in general P, F1, F2 males, females	[redacted]
3.3.4	Type	[redacted]
3.3.5	Concentration	[redacted]
3.3.6	Vehicle	[redacted]
3.3.7	Concentration in vehicle	[redacted]
3.3.8	Total volume applied	[redacted]
3.3.9	Controls	[redacted]
3.4	**Examinations**	
3.4.1	Clinical signs	[redacted]
3.4.2	Body weight	[redacted]

Section A6.8.2/02 **Reproduction Toxicity Study**
Annex Point IIA VI.6.8.2 **Feeding study in rat**

3.4.3 Food/water consumption

3.4.4 Oestrus cycle

3.4.5 Sperm parameters

3.4.6 Offspring

Yes,

3.4.7 Organ weights P and F1

3.4.8 Histopathology P and F1

3.4.9 Histopathology F1 not selected for mating, F2

3.5 Further remarks

3.6 Statistic

4 RESULTS AND DISCUSSION

4.1 Parental effects

4.1.1 F_0 animals

4.1.2 F1 parents

4.2 Litter observations

Section A6.8.2/02 **Reproduction Toxicity Study**
Annex Point IIA VI.6.8.2 **Feeding study in rat**

4.2.1 Number and sexes of pups born

4.2.2 Pup body weight

4.2.3 Litter development observations

4.2.4 Pup clinical observation and necropsy findings during lactation

4.2.5 Necropsy findings of weaned pups

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

Section A6.8.2/02 Reproduction Toxicity Study
Annex Point IIA VI.6.8.2 Feeding study in rat

5.2 Results and discussion

[redacted]

X1

[redacted]

5.3 Conclusion

5.3.1	LO(A)EL	
5.3.1.1	Parent males	Not applicable [redacted]
5.3.1.2	Parent females	≥500 ppm (≥ 28 mg Iodine /kg bw/ [redacted]
5.3.1.3	F1 males	Not applicable [redacted]
5.3.1.4	F1 females	Not applicable [redacted]
5.3.1.5	F1 both sexes	< 28 mg Iodine /kg bw/day [redacted] X2
5.3.1.6	F2 males	Not applicable [redacted]
5.3.1.7	F2 females	Not applicable [redacted]
5.3.2	NO(A)EL	
5.3.2.1	Parent males	Not applicable [redacted]
5.3.2.2	Parent females	< 28 mg Iodine /kg bw
5.3.2.3	F1 males	Not applicable [redacted]
5.3.2.4	F1 females	Not applicable [redacted]
5.3.2.5	F1 both sexes	< 28 mg Iodine /kg bw/day
5.3.2.6	F2 males	Not applicable [redacted]
5.3.2.7	F2 females	Not applicable [redacted]
5.3.3	Reliability	[redacted]

Section A6.8.2/02 **Reproduction Toxicity Study**
Annex Point IIA VI.6.8.2 **Feeding study in rat**

5.3.4 Deficiencies [redacted]

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

Table A6.8.2/02-1: Table for animal assignment for mating

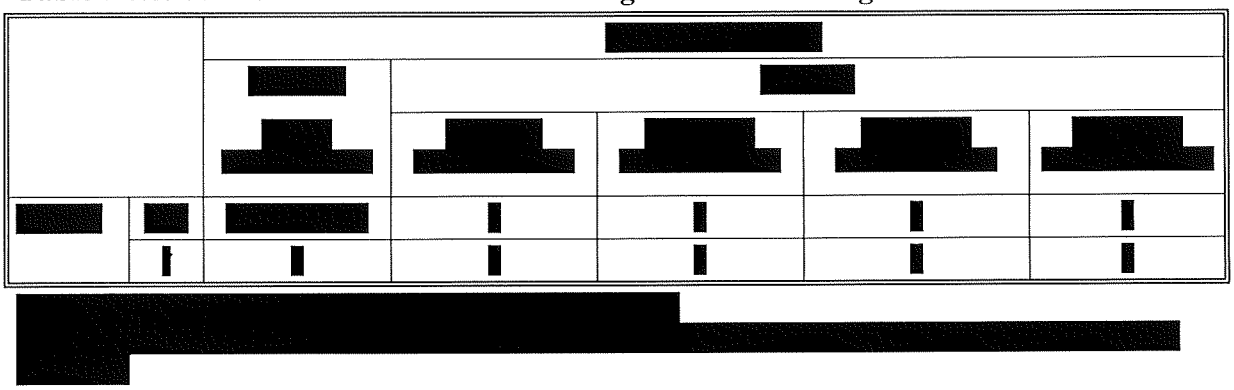
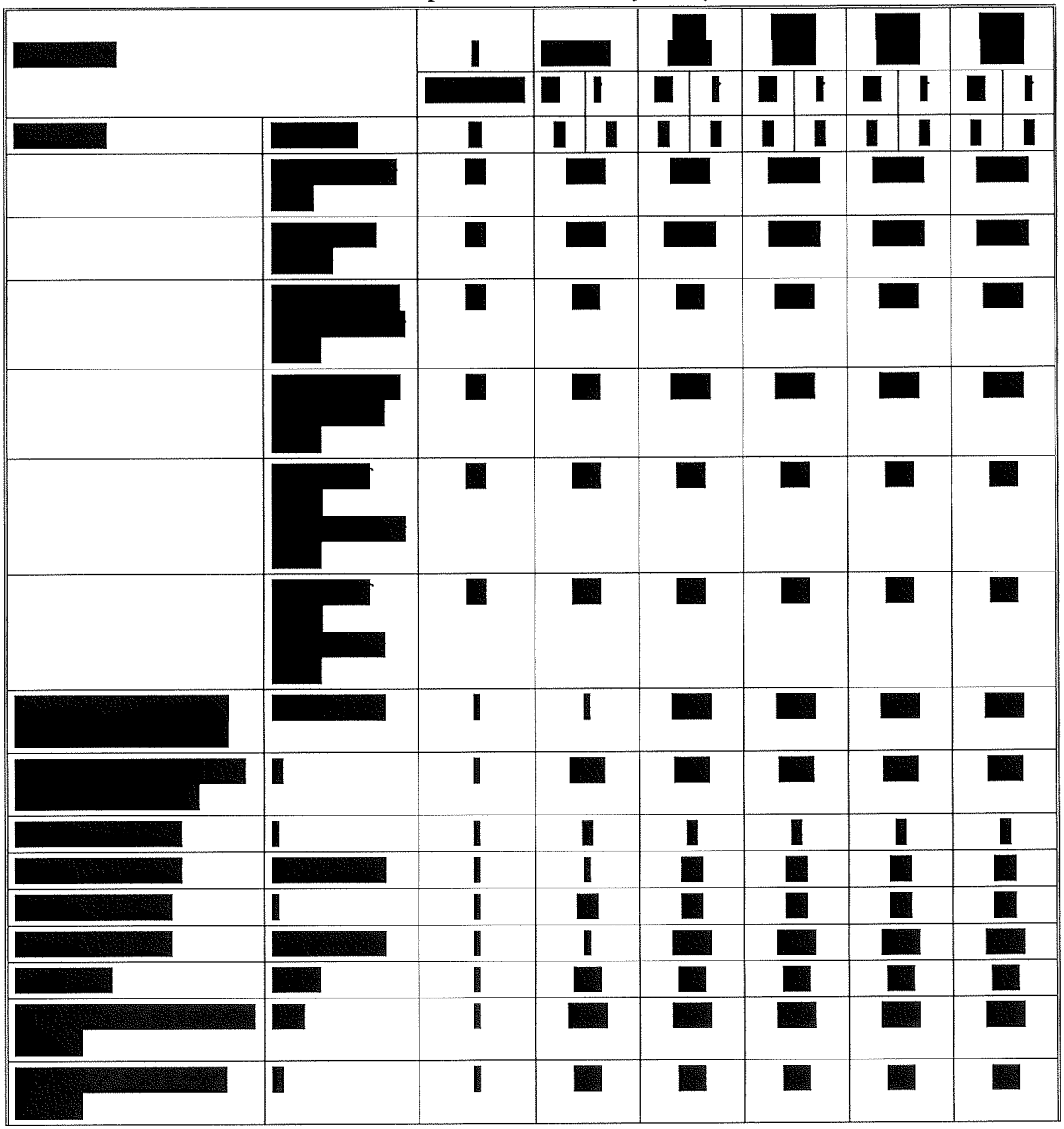


Table A6.8.2/02-2: Table for reproductive toxicity study



[redacted]

Section A6.8.2/03 Reproduction Toxicity Study
Annex Point IIA VI.6.8.2 Feeding study in rat

[redacted]

			Official use only
		1 REFERENCE	
1.1	**Reference**	Ammerman, C.B., et al. (1964): Reproduction and lactation in rats fed excessive iodine; J Nutrition, 84, 107-112; Doc. No. 592-011; Section A6.8.2/03	
1.2	**Data protection**	[redacted]	
1.2.1	Data owner	[redacted]	
1.2.2	Companies with letter of access	[redacted]	
1.2.3	Criteria for data protection	[redacted]	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	[redacted]	
2.2	**GLP**	[redacted]	
2.3	**Deviations**	Not applicable [redacted]	
		3 MATERIALS AND METHODS	
3.1	**Test material**	Potassium iodide [redacted]	
3.1.1	Lot/Batch number	[redacted]	
3.1.2	Specification	[redacted]	
3.1.3	Description	[redacted]	
3.1.4	Purity	[redacted]	
3.1.5	Stability	[redacted]	
3.2	**Test Animals**		
3.2.1	Species	Rat	
3.2.2	Strain	Long-Evans	
3.2.3	Source	[redacted]	
3.2.4	Sex	female (nonparous), male	
3.2.5	Age/weight at study initiation		
3.2.6	Number of animals per group	[redacted]	
3.2.7	Mating	[redacted]	
3.2.8	Duration of mating	[redacted]	
3.2.9	Deviations from standard protocol	[redacted]	

Section A6.8.2/03 Annex Point IIA VI.6.8.2		Reproduction Toxicity Study Feeding study in rat
3.2.10	Control animals	[redacted]
3.3	**Administration/ Exposure**	Oral
3.3.1	Animal assignment to dosage groups	[redacted]
3.3.2	Duration of exposure before mating	[redacted]
3.3.3	Duration of exposure in general P, F1, F2 males, females	[redacted]
3.3.4	Type	[redacted]
3.3.5	Concentration	[redacted]
3.3.6	Vehicle	[redacted]
3.3.7	Concentration in vehicle	[redacted]
3.3.8	Total volume applied	[redacted]
3.3.9	Controls	[redacted]
3.4	**Examinations**	
3.4.1	Clinical signs	[redacted]
3.4.2	Body weight	[redacted]
3.4.3	Food/water consumption	[redacted]
3.4.4	Oestrus cycle	[redacted]
3.4.5	Sperm parameters	[redacted]
3.4.6	Offspring	[redacted]
3.4.7	Organ weights P and F1	[redacted]
3.4.8	Histopathology P and F1	[redacted]
3.4.9	Histopathology F1 not selected for mating, F2	[redacted]
3.5	**Further remarks**	[redacted]

Section A6.8.2/03 **Reproduction Toxicity Study**
Annex Point IIA VI.6.8.2 **Feeding study in rat**

3.6 Statistic

[redacted]

4 RESULTS AND DISCUSSION

4.1 Parental effects

4.1.1 F_0 animals

[redacted]

4.1.2 F1 parents

[redacted]

4.2 Litter observations

4.2.1 Number and sexes of pups born

[redacted]

4.2.2 Pup body weight

[redacted]

4.2.3 Litter development observations

[redacted]

4.2.4 Pup clinical observation and necropsy findings during lactation

[redacted]

4.2.5 Necropsy findings of weaned pups

[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted]

5.2 Results and discussion

[redacted]

5.3 Conclusion

[redacted]

Consequently, for female rats, not the duration of exposure but the dose level and the time of exposure during gestation are likely to cause the reduced or absent lactation with the secondary effect of mortality of offspring.

5.3.1 LO(A)EL 2500 ppm Iodine [redacted]

Section A6.8.2/03 Annex Point IIA VI.6.8.2	Reproduction Toxicity Study Feeding study in rat
5.3.1.1 Parent males	Not applicable
5.3.1.2 Parent females	2500 ppm Iodine [redacted]
5.3.1.3 F1 males	Not applicable
5.3.1.4 F1 females	Not applicable
5.3.1.5 F1 both sexes	<2500 ppm Iodine [redacted]
5.3.1.6 F2 males	Not applicable
5.3.1.7 F2 females	Not applicable
5.3.2 NO(A)EL	<2500 ppm Iodine [redacted]
5.3.2.1 Parent males	Not applicable
5.3.2.2 Parent females	Not applicable
5.3.2.3 F1 males	Not applicable
5.3.2.4 F1 females	Not applicable
5.3.2.5 F1 both sexes	<2500 ppm Iodine [redacted]
5.3.2.6 F2 males	Not indicated
5.3.2.7 F2 females	Not indicated
5.3.3 Reliability	[redacted]
5.3.4 Deficiencies	[redacted]

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

Section A6.9.1/01 Neurotoxicity

Annex Point IIIA VI.1 Acute, subchronic and chronic

[redacted]

Official use only

1 REFERENCE

1.1 Reference

[1] TOXICOLOGICAL PROFILE FOR IODINE (April 2004); U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, Public Health Service, Agency for Toxic Substances and Disease Registry
http://www.atsdr.cdc.gov/toxprofiles/tp158.pdf
Doc. No. 581-009 (published); Section A6.9.1/01

1.2 Data protection [redacted]

1.2.1 Data owner [redacted]

1.2.2 Companies with letter of access [redacted]

1.2.3 Criteria for data protection [redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study Not applicable.
[redacted]

2.2 GLP [redacted]

2.3 Deviations Not applicable [redacted]

3 MATERIALS AND METHODS

3.1 Test material As given in section 2

4 RESULTS AND DISCUSSION

4.1 Assessment on neurological effects (general and per exposure route) [redacted]

Section A6.9.1/01 Neurotoxicity

Annex Point IIIA VI.1 Acute, subchronic and chronic

[redacted]

[redacted]

[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted]

5.2 Results and discussion

[redacted]

5.3 Conclusion

Excessive oral Iodine intake by the mother may cause Iodine-induced hypothyroidism and potentially secondary neurological effects in foetus or newborn infants because thyroid hormones are essential to the development of the neuromuscular system and brain. Such effects in older children or adults are not likely. Even at high doses no such effects have been noted so far.

5.3.1 Reliability

[redacted]

5.3.2 Deficiencies

[redacted]

Section A6.9.1/01 Neurotoxicity

Annex Point IIIA VI.1 Acute, subchronic and chronic

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

Section A6.10/01
Annex Point IIIA VI.7

Mechanistic study – any studies necessary to clarify effects reported in toxicity studies

Official use only

1 REFERENCE

1.1 Reference

[1] TOXICOLOGICAL PROFILE FOR IODINE (April 2004); U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, Public Health Service, Agency for Toxic Substances and Disease Registry
http://www.atsdr.cdc.gov/toxprofiles/tp158.pdf
Doc. No. 581-009 (published); Section A6.10/01

1.2 Data protection [redacted]

1.2.1 Data owner [redacted]

1.2.3 Criteria for data protection [redacted]

2 GUIDELINES AND QUALITY ASSURANCE

Not applicable, [redacted]

3 MATERIALS AND METHODS

3.1 Test material

Iodine [redacted]

3.2 Test method

Not applicable.

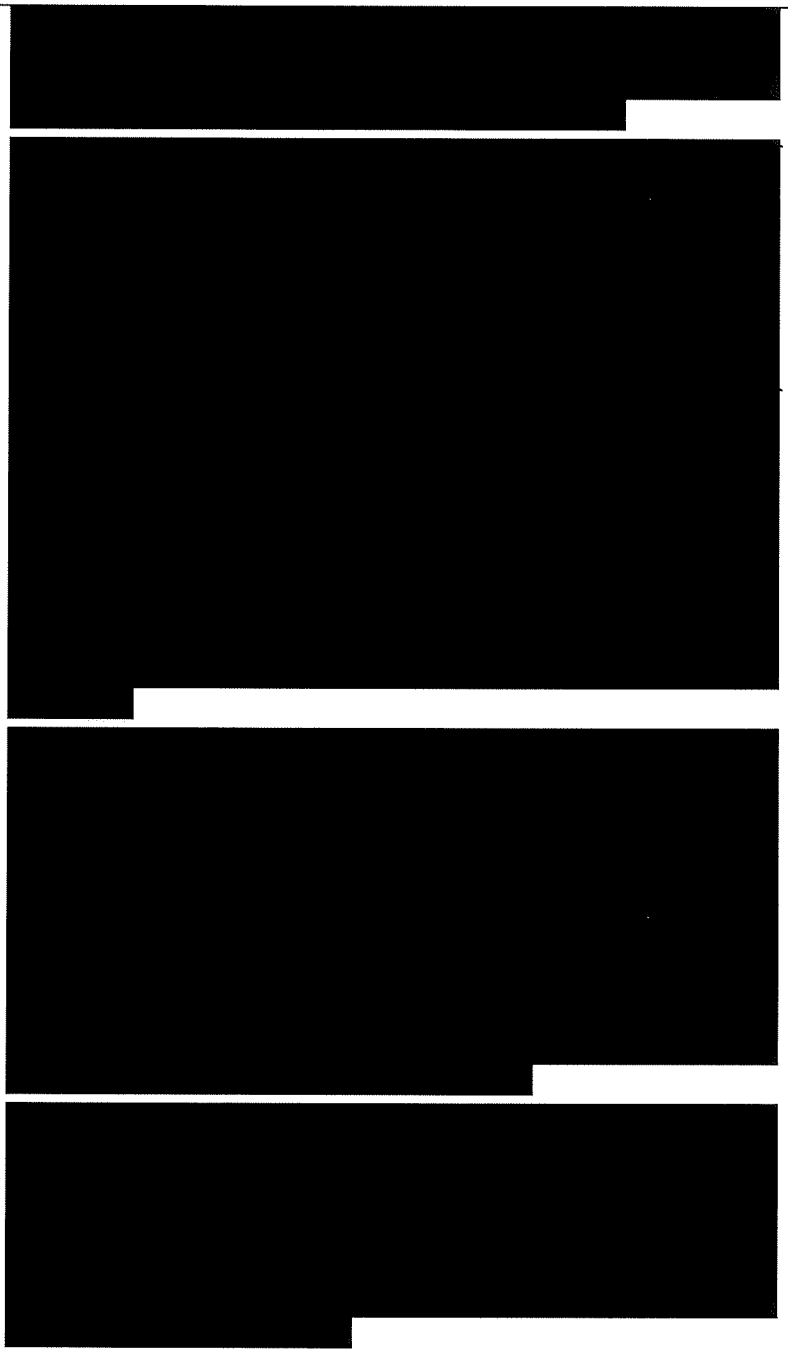
4 RESULTS AND DISCUSSION

4.1 Results

[redacted]

Section A6.10/01
Annex Point IIIA VI.7

Mechanistic study – any studies necessary to clarify effects reported in toxicity studies



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Section A6.10/01 Mechanistic study – any studies necessary to clarify effects reported in toxicity studies
Annex Point IIIA VI.7

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Section A6.10/01
Annex Point IIIA VI.7

Mechanistic study – any studies necessary to clarify effects reported in toxicity studies

	5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	Not applicable [redacted]	
5.2 Results and discussion	[redacted]	
5.3 Conclusion	Further mechanistic studies are not relevant for the hazard risk assessment of the uses of Iodine in biocidal products..	
5.3.1 Reliability	[redacted]	
5.3.2 Deficiencies	[redacted]	
	Evaluation by Competent Authorities	

EVALUATION BY RAPPORTEUR MEMBER STATE

Date	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	

Section A6.11 Studies on other routes of administration

Annex Point IIA6.1

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	Technically not feasible [ ] Scientifically unjustified [ ]	
Limited exposure [ ]	Other justification [X]	
Detailed justification:	[redacted]	

	Evaluation by Competent Authorities
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Evaluation of applicant's justification	[redacted]
Conclusion	[redacted]
Remarks	

Section A6.12.1/01 Medical data in anonymous form
Annex Point IIA, VI.6.9. Dermal exposure

Official use only

1 REFERENCE

1.1 Reference

[1] TOXICOLOGICAL PROFILE FOR IODINE (April 2004); U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, Public Health Service, Agency for Toxic Substances and Disease Registry; pp. 75-79
http://www.atsdr.cdc.gov/toxprofiles/tp158.pdf
Doc. No. 581-009 (published); Section A6.12.1/01

1.2 Data protection

[redacted]

2 GUIDELINES AND QUALITY ASSURANCE (NOT APPLICABLE)

3 MATERIALS AND METHODS

3.1 Substance

PVP-iodine [redacted]

[redacted]

4 RESULTS

4.1 Endocrine effects

[redacted]

Section A6.12.1/01 Medical data in anonymous form

Annex Point IIA, VI.6.9. Dermal exposure

[redacted]

[redacted]

[redacted]

[redacted]

Section A6.12.1/01 **Medical data in anonymous form**

Annex Point IIA, VI.6.9. **Dermal exposure**

[redacted]

Section A6.12.1/01 Medical data in anonymous form

Annex Point IIA, VI.6.9. **Dermal exposure**

4.2 Immunological and lymphoreticular effects

[redacted]

4.3 Others

[redacted]

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5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

PVP-iodine [redacted]

Section A6.12.1/01 Medical data in anonymous form
Annex Point IIA, VI.6.9. **Dermal exposure**

5.2 Results and discussion

[redacted]

5.3 Conclusion

Long-time experiences with PVP-iodine, [redacted], have shown that after regular and intensive exposure to intact skin a slight elevation of thyroid hormone levels may occur, in general without any adverse effects. This effect may be elevated if high PVP-iodine amounts come in contact with wounds or mucous membranes or is applied with Iodine containing drugs, but normally all thyroid hormone values return to baseline values when the exposure is discontinued.

Considering the wide-spread and frequent use of Povidone iodine / PVP-iodine for skin treatment, only single cases of skin reactions potentially indicating a skin sensitivity effect have been reported until today and all are associated with application of high concentrated solutions to open wound or mucous membranes (vaginal applications). No such effects have been reported with biocidal applications [redacted]

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]

Section A6.12.1/01 Medical data in anonymous form

Annex Point IIA, VI.6.9. **Dermal exposure**

Remarks	[redacted]

Section A6.12.2/01-03 Direct observations, e.g. clinical cases, poisoning incidents

Annex Point IIA, VI.6.9.2

Acute oral exposure in humans
(corresponding to Section A6.1.1/01-06)

Official use only

1 REFERENCE

1.1 Reference

[1] EUROPEAN COMMISSION, HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL, SCF, Scientific Committee on Food: Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Iodine (expressed on 26 September 2002), p.15
http://europa.eu.int/comm/food/fs/sc/scf/out146_en.pdf
Doc. No. 592-031 (published); Section A.6.12.2/01

[2] Moore, M. (1938): Attempted Suicide, The Ingestion of Iodine as a Method of Attempted Suicide; N Eng J Med, p. 384
Doc. No. 592-007 (published); Section A.6.12.2/02

[3] Registry of Toxic Effects of Chemical Substances (RTECS), p. 1
Doc. No. 591-002 (published); Section A.6.12.2/03

1.2 Data protection [redacted]

1.2.1 Data owner [redacted]

1.2.3 Criteria for data protection [redacted]

2 GUIDELINES AND QUALITY ASSURANCE

Not applicable, [redacted]

3 MATERIALS AND METHODS

3.1 Test material Iodine [redacted]

3.2 Test method Not applicable. [redacted]

4 RESULTS AND DISCUSSION

4.1 Results [redacted]

Section A6.12.2/01-03 Direct observations, e.g. clinical cases, poisoning incidents

Annex Point IIA, VI.6.9.2

Acute oral exposure in humans
(corresponding to Section A6.1.1/01-06)

[redacted]

4.2 Discussion

[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted]

5.2 Results and discussion

[redacted] X

5.3 Conclusion

[redacted]

5.3.1 Reliability

[redacted]

5.3.2 Deficiencies

[redacted]

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

Section A6.12.2/04-06

Annex Point IIA, VI.6.9.2

Direct observations, e.g. clinical cases, poisoning incidents

Acute dermal exposure in humans
(corresponding to Section A6.1.2/01)

Official use only

1 REFERENCE

1.1 Reference

[1] TOXICOLOGICAL PROFILE FOR IODINE (April 2004); U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, Public Health Service, Agency for Toxic Substances and Disease Registry, p. 75
http://www.atsdr.cdc.gov/toxprofiles/tp158.pdf
Doc. No. 581-009 (published), Section A.6.12.2/04

[2] INCHEM: Poison Information Monograph on Iodine (PIM 280, p. 20 of PIM 280, i.e. p. 63 of the whole document, point 9.1.3)
http://www.inchem.org/documents/pims/pharm/iodine.htm
Doc. No. 591-008 (published); Section A.6.12.2/05

[3] GESTIS-database on hazardous substances of the German institutions for statutory accident insurance and prevention ("Berufsgenossenschaften"), p. 2
www.hvbg.de/bgia/gestis-database
Doc. No. 592-050 (published); Section A.6.12/06

1.2 Data protection [redacted]

1.2.1 Data owner [redacted]

1.2.3 Criteria for data protection [redacted]

2 GUIDELINES AND QUALITY ASSURANCE

Not applicable, [redacted]

3 MATERIALS AND METHODS

3.1 Test material Iodine [redacted]

3.2 Test method Not applicable. [redacted]

4 RESULTS AND DISCUSSION

4.1 Results [redacted]

4.2 Discussion [redacted]

Section A6.12.2/04-06 **Direct observations, e.g. clinical cases, poisoning incidents**

Annex Point IIA, VI.6.9.2

Acute dermal exposure in humans
(corresponding to Section A6.1.2/01)

[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods [redacted]

5.2 Results and discussion [redacted]

5.3 Conclusion Deaths associated with dermal (intact skin) exposure to Iodine is very unlikely.

5.3.1 Reliability [redacted]

5.3.2 Deficiencies [redacted]

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

Section A6.12.2/07

Annex Point IIA, VI.6.9.2

Direct observations, e.g. clinical cases, poisoning incidents

Repeated exposure in humans following surgery

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1 REFERENCE

1.1 Reference

[1] California Environmental Protection Agency, Department of Pesticide Regulation, Medical Toxicology Branch (2005), Summary of Toxicology Data, Iodine and related Iodine Complexes
http://www.cdpr.ca.gov/docs/toxsums/pdfs/718c.pdf
Doc. No. 581-013 (published); Section A.6.12.2/07

1.2 Data protection [redacted]

1.2.1 Data owner [redacted]

1.2.3 Criteria for data protection [redacted]

2 GUIDELINES AND QUALITY ASSURANCE

Not applicable, [redacted]

3 MATERIALS AND METHODS

3.1 Test material

Iodine [redacted]

3.2 Test method

Not applicable.
[redacted]

4 RESULTS AND DISCUSSION

4.1 Results

[redacted]

4.2 Discussion

[redacted]

Section A6.12.2/07
Annex Point IIA, VI.6.9.2

Direct observations, e.g. clinical cases, poisoning incidents
Repeated exposure in humans following surgery

5 APLICANT'S SUMMARY AND CONCLUSION

5.1	Materials and methods	Not applicable [redacted]
5.2	Results and discussion	[redacted]
5.3	Conclusion	[redacted]
5.3.1	Reliability	[redacted]
5.3.2	Deficiencies	[redacted]

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

Section A6.12.3/01 Health records

Annex Point IIA, VI.6.9. On the use of teat dips, provided by the manufacturer

Official use only

1 REFERENCE

1.1	**Reference**	Matthies, W. (2006): Safety Update Report – P3-cide-plus as a teat dip [redacted]
1.2	**Data protection**	[redacted]

2 GUIDELINES AND QUALITY ASSURANCE (NOT APPLICABLE)

3 MATERIALS AND METHODS

3.1	**Test item**	Iodine [redacted]
3.2	**Persons exposed**	Farmers / milkers
3.3	**Exposure**	Dermal, via inhalation,
3.3.1	Reason of exposure	Occupational
3.3.2	Frequency of exposure	[redacted]
3.3.3	Overall time period of exposure	[redacted]
3.3.4	Duration of single exposure	[redacted]
3.3.5	Exposure concentration/dose	[redacted]
3.3.6	Other information	[redacted]
3.4	**Tools**	[redacted]

4 RESULTS

4.1	**Results**	[redacted]

Section A6.12.3/01 Health records

Annex Point IIA, VI.6.9. On the use of teat dips, provided by the manufacturer

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	Materials and methods	[redacted]
5.2	Results and discussion	[redacted]
5.3	Conclusion	The safety margin for this product is considered to be very high.

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Remarks	

Section A6.12.4/01-03 Epidemiological Study

Annex Point IIA VI.6.9

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1 REFERENCE

1.1 Reference

[1] EUROPEAN COMMISSION, HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL, SCF, Scientific Committee on Food: Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Iodine (expressed on 26 September 2002).
http://europa.eu.int/comm/food/fs/sc/scf/out146_en.pdf
Doc. No. 592-031 (published); Section A6.12.4/01

[2] Federal Institute for Risk assessment (BfR, 2006): Use of Minerals in Food; Toxicological and nutritional-physiological aspects; Part II; p. 198
ISBN 3-938163-11-9
http://www.bfr.bund.de/cm/238/use_of_minerals_in_foods.pdf
Doc. No. 592-080 (published); Section A6.12.4/02

[3] TOXICOLOGICAL PROFILE FOR IODINE (April 2004); U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, Public Health Service, Agency for Toxic Substances and Disease Registry
http://www.atsdr.cdc.gov/toxprofiles/tp158.pdf
Doc. No. 581-009 (published); Section A6.12.4/03

1.2 Data protection [redacted]

1.2.1 Data owner [redacted]

1.2.2 Companies with letter of access [redacted]

1.2.3 Criteria for data protection [redacted]

2 RESULTS AND DISCUSSION

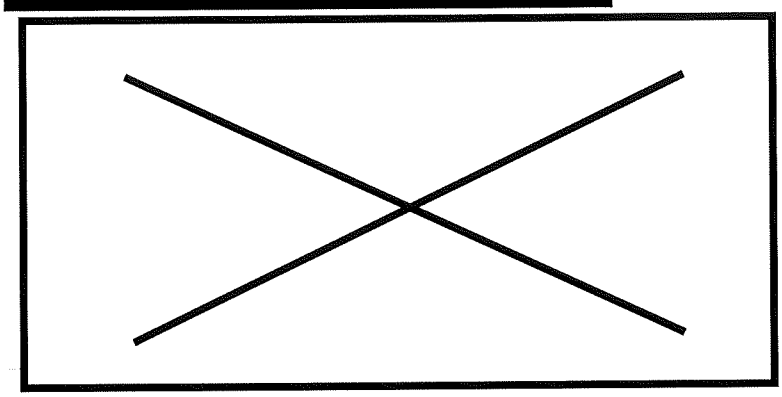
2.1 Results [redacted]

Section A6.12.4/01-03 Epidemiological Study

Annex Point IIA VI.6.9

[redacted]

[redacted]



[redacted]

[redacted]

[redacted]

[redacted]

3 APPLICANT'S SUMMARY AND CONCLUSION

3.1	Materials and methods	Not applicable
3.2	Results and discussion	[redacted]

Section A6.12.4/01-03 Epidemiological Study

Annex Point IIA VI.6.9

[redacted]

3.3	**Conclusion**	Some regions in Europe have a deficient nutritional status of Iodine. The positive effects due to additional Iodine uptake by iodinated salt prevail.
3.3.1	Reliability	[redacted]
3.3.2	Validity	[redacted]
3.3.3	Deficiencies	[redacted]

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

Section A6.12.6 Sensitisation/Allergenicity Observations

Annex Point IIA, VI.6.9.6

Section A6.12.3/01 (health records), A6.14/12(b)-13 (exposure to humans) and Section A6.12.1 (medical data in an anonymous form).

No ECB template is available. This template was supplemented based on published DAR's.

JUSTIFICATION FOR NON-SUBMISSION OF DATA			Official use only
Other existing data [X]	Technically not feasible [ ]	Scientifically unjustified [ ]	
Limited exposure [ ]	Other justification [ ]		

Detailed justification:

[redacted]

Evaluation by Competent Authorities
EVALUATION BY RAPPORTEUR MEMBER STATE
Date [redacted]

Section A6.12.6 Sensitisation/Allergenicity Observations

Annex Point IIA, VI.6.9.6

Evaluation of applicant's justification	[redacted]
Conclusion	[redacted]
Remarks	

Section A6.12.7/01-02 Specific treatment in case of an accident or poisoning: First aid measures, antidotes and medical treatment

Annex Point IIA, VI.6.9.7

No ECB template is available. This template was supplemented based on published DAR's.

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		1	**REFERENCE**
1.1	**Reference**	[1]	GESTIS-database on hazardous substances of the German institutions for statutory accident insurance and prevention ("Berufsgenossenschaften") www.hvbg.de/bgia/gestis-database Doc. No. 592-050 (published); Section A.6.12.7/01
		[2]	TOXICOLOGICAL PROFILE FOR IODINE (April 2004); U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, Public Health Service, Agency for Toxic Substances and Disease Registry http://www.atsdr.cdc.gov/toxprofiles/tp158.pdf Doc. No. 581-009 (published); Section A6.12.7/02
1.2	**Data protection**	[redacted]	
		2	**GUIDELINES AND QUALITY ASSURANCE (NOT APPLICABLE)**
		3	**FIRST AID AND INFORMATION FOR THE PHYSICIAN**
3.1	**Substance**	Iodine	
3.2	**First aid**		
3.2.1	First aid, eyes	[redacted]	
3.2.2	First aid, skin	[redacted]	
3.2.3	First aid, respiratory tract	[redacted]	

Section A6.12.7/01-02 Specific treatment in case of an accident or poisoning: First aid measures, antidotes and medical treatment

Annex Point IIA, VI.6.9.7

3.2.4	First aid, swallowing	[redacted]
3.2.5	Recommendations for the first aider	[redacted]
3.3	**Information for physicians**	
3.3.1	Symptoms of acute poisoning	[redacted]

Section A6.12.7/01-02 **Specific treatment in case of an accident or poisoning:**
Annex Point IIA, VI.6.9.7 **First aid measures, antidotes and medical treatment**

3.3.2 Medical advice

[redacted]

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1	Materials and methods	Not applicable [redacted]
4.2	Results and discussion	[redacted]
4.3	Conclusion	ditto

Section A6.12.7/01-02 Specific treatment in case of an accident or poisoning: First aid measures, antidotes and medical treatment

Annex Point IIA, VI.6.9.7

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

Section A6.12.8/01 Prognosis following poisoning (expected effects and the duration of these effects must be described)

Annex Point IIA, VI.6.9

Please refer also to Document IIIA, Section A6.3.2, Section A6.4.2, Section A6.12., Section A6.12.7, and Section A6.1.1/01-06.

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1 REFERENCE

1.1 Reference

[1] TOXICOLOGICAL PROFILE FOR IODINE (April 2004); U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, Public Health Service, Agency for Toxic Substances and Disease Registry
http://www.atsdr.cdc.gov/toxprofiles/tp158.pdf
Doc. No. 581-009 (published); Section A6.12.8/01

1.2 Data protection

[redacted]

2 GUIDELINES AND QUALITY ASSURANCE (NOT APPLICABLE)

3 MATERIALS AND METHODS

3.1 Substance

Iodine in various forms [redacted]

4 RESULTS

4.1 Prognosis

[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted]

5.2 Results and discussion

[redacted]

5.3 Conclusion

Lethal effects due to poising with single doses of Iodine are not likely. Furthermore, recovery is expected when exposure is discontinued and proper medication is applied.

Section A6.12.8/01 Prognosis following poisoning (expected effects and the duration of these effects must be described)

Annex Point IIA, VI.6.9

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

Section A6.13/01-07 Annex Point IIIA, VI.2	Toxic effects on livestock and pets In horses, cows, pigs and hens with focus on reproductive and developmental effects	
	1 REFERENCE	Official use only
1.1 Reference	[1] World Health Organization and Food and Agriculture Organization of the United Nations (2004): Vitamin and mineral requirements in human nutrition (Second edition). Table of content: http://whqlibdoc.who.int/publications/2004/9241546123.pdf Text: http://whqlibdoc.who.int/publications/2004/9241546123_chap16.pdf Doc. No. 692-033 (published); Section A. 6.13/01 [2] EUROPEAN COMMISSION, HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL, SCF, Scientific Committee on Food: Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Iodine (expressed on 26 September 2002). http://europa.eu.int/comm/food/fs/sc/scf/out146_en.pdf Doc. No. 592-031 (published); Section A.6.13/02 [3] Subcommittee on Mineral Toxicity in Animals, Committee on Animal Nutrition, Board on Agricultures and Renewable Resources, Committee on Natural Resources, National Research Council: Mineral Tolerance of Domestic Animals (1980) ISBN 0309030226 http://www.nap.edu/books/0309030226/html/ Doc. No. 592-020 (published); Section A.6.13/03 [4] Silva, CA; Merkt, H, Bergamo PN, Barros SS, Barros CS, Santos MN, Hoppen HO, Heidemann P, Meyer H, (Faculty of Veterinary Medicine, Federal University of Santa Maria, Brazil), Journal of Reproduction and Fertility Supplements, 35, 529-533 (1987): Consequence of excess Iodine supply in a Thoroughbred stud in southern Brazil; Doc. No. 592-045 (published); Section A.6.13/04 [5] Grimminger, S.P. (2005): Zum Iodbedarf und zur Iodversorgung der Haus- und Nutztiere und des Menschen http://edoc.ub.uni-muenchen.de/archive/00004322/01/Grimminger_Susan_P.pdf Doc. No. 592-040 (published); Section A.6.13/05 [6] Johanson, K.J. (December 2000); Department of Forest Mycology and Pathology; The Swedish University of Agricultural Sciences, Uppsala (Technical Report; TR-00-21): Iodine in soil http://www.skb.se/upload/publications/pdf/TR-00-21webb.pdf Doc. No. 781-002 (published); Section A.6.13/06 [7] Arrington L.R., Taylor R.N. Jr, Ammerman C.B.; Shirley R.L. (1965): Effects of excess dietary Iodine upon rabbits, hamsters, rats and swine; J Nutr. 1965 Dec; Vol. 87(4), pp 394-398 Doc No 592-012 (published); Section A.6.13/07	
1.2 Data protection	[redacted]	
1.2.1 Data owner	[redacted]	