Section A1 Applicant

Annex Point IIA1

1.1 Applicant

Name: Detia Freyberg GmbH
Address: Dr.-Werner-Freyberg-Str. 11
D-69514 Laudenbach
Telephone: [redacted]
Fax number: [redacted]
E-mail address: [redacted]

1.2 Manufacturer of Active Substance (if different)

Name: Degesch de Chile Ltda.
Address: Casilla 2404 C.C., Santiago
Camino Antiguo a Valparaiso 1321
Padre Hurtado - Talagante
Santiago
Chile
Telephone: [redacted]
Fax number: [redacted]
E-mail address: [redacted]
Location of manufacturing plant: Chile

1.3 Manufacturer of Product(s) (if different)

Same as "Applicant"

1) Product 1

2) Product n

Section A1 Applicant

Annex Point IIA1

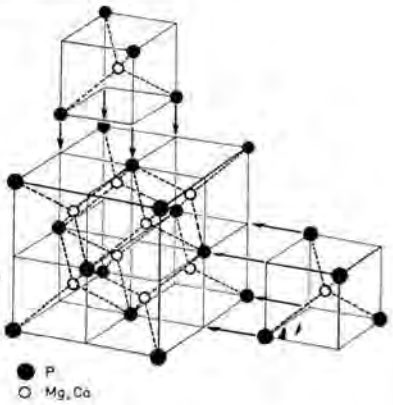
Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss 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*

Section A2 Identity of Active Substance

Subsection (Annex Point)

Official use only

2.1	**Common name (IIA2.1)**	Magnesium phosphide
2.2	**Chemical name (IIA2.2)**	IUPAC: Magnesium phosphide EINECS: Trimagnesium diphosphide CA: Magnesium phosphide
2.3	**Manufacturer's development code number(s) (IIA2.3)**	Not applicable, since manufacturer's code numbers are not routinely assigned.
2.4	**CAS No and EC numbers (IIA2.4)**	
2.4.1	**CAS-No**	12057-74-8
	Isomer 1	
	Isomer n	
2.4.2	**EC-No**	235-023-7
	Isomer 1	
	Isomer n	
2.4.3	**Other**	
2.5	**Molecular and structural formula, molecular mass (IIA2.5)**	
2.5.1	**Molecular formula**	Mg_3P_2
2.5.2	**Structural formula**	Antifluorite lattice



2.5.3	**Molecular mass**	134.9
2.6	**Method of manufacture of the active substance (IIA2.1)**	[redacted]

Section A2 Identity of Active Substance

2.7	Specification of the purity of the active substance, as appropriate (IIA2.7)	[redacted]
2.8	Identity of impurities and additives, as appropriate (IIA2.8)	[redacted]
2.8.1	Isomeric composition	[redacted]
2.9	The origin of the natural active substance or the precursor(s) of the active substance (IIA2.9)	[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	[redacted]
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	
Acceptability	[redacted]
Remarks	
	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 A3 Physical and Chemical Properties of Active Substance

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.1 Melting point, boiling point, relative density (IIA3.1)								
3.1.1 Melting point	92/69/EEC, A.1 OECD 102 (Melting point/ Melting range)	[redacted]	**result: Melting point > 500° C pressure:**	[redacted]	Y	1	[redacted] Magnesium phosphide technical: MELTING POINT/MELTING RANGE, BOILING POINT/BOILING RANGE, VAPOUR PRESSURE, [redacted]	x
3.1.2 Boiling point	92/69/EEC, A.2 OECD 103 (Boiling point/ Boiling range)	[redacted]	**result: Boiling point > 500° C pressure: 1013.3 hPa**	[redacted]	Y	1	[redacted] Magnesium phosphide technical: MELTING POINT/MELTING RANGE, BOILING POINT/BOILING RANGE, VAPOUR PRESSURE, [redacted]	x
3.1.3 Bulk density/ relative density	92/69/EEC, A.3 OECD 109	[redacted]	Temperature: 23.5°C Density: 1.47 g/cm³		Y	1	[redacted] Magnesium phosphide:	x

Section A3 Physical and Chemical Properties of Active Substance

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
	(Density of liquids and soils)	[redacted]	Relative density : D^{R}_{4}: 1.47	-			Relative density. [redacted]	
3.2 Vapour pressure (IIA3.2)	92/69/EEC, A.4 OECD 104 (Screening test for thermal stability and stability on air)	[redacted]	**temperature:20°, 25°, 30° C result: P << 1.0 x 10^{-7} hPa**	[redacted]	Y	1	Magnesium phosphide technical: MELTING POINT/MELTING RANGE, BOILING POINT/BOILING RANGE, VAPOUR PRESSURE. [redacted]	x
3.2.1 Henry´s Law Constant (Pt. I-A3.2)			**measured/calculated: result:**	justification for non-submission is provided	n.a.	n.a.		
3.3 Appearance (IIA3.3)								
3.3.1 Physical state	solid							
3.3.2 Colour	grey							
3.3.3 Odour	"foul, fishy, garlicky" (technical phosphine)							

Section A3 Physical and Chemical Properties of Active Substance

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.4 Absorption spectra (IIA3.4) **UV/VIS** **IR** **NMR** **MS**	n.a.	n.a.	n.a.	[redacted]	n.a.	n.a.	[redacted] Statement of the evaluation of UV/Vis, IR and NMR spectra of aluminium and magnesium phosphide, [redacted]	
3.5 Solubility in water (IIA3.5) Water solubility 1 Water solubility 2	*including effects of pH (5-9)* n.a.	n.a.	**result:** **temperature:** **pH:** n.a.	[redacted]	n.a.	n.a.	[redacted] Statement of the performance of the following tests according to EU Test Guideline 92/69/EWG: A6 Solubility in water, A8 Distribution coefficient, A17 Fire enhancing properties, C7 Hydrolysis abiotic decomposition, [redacted]	
3.6 Dissociation constant (-)	n.a.	n.a.	n.a.	[redacted]	n.a.	n.a.	[redacted] Statement of the performance of the following tests according to EU Test Guideline 92/69/EWG: A6 Solubility in water, A8 Distribution	

Section A3 Physical and Chemical Properties of Active Substance

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
							coefficient, A17 Fire enhancing properties, C7 Hydrolysis abiotic decomposition, [redacted]	
3.7 Solubility in organic solvents, including the effect of temperature on solubility (IIIA3.1)	n.a.	n.a.	**result: temperature: n.a.**	[redacted]	n.a.	n.a.	[redacted] Statement of the performance of the following tests according to CIPAC Method MT 181: Solubility in organic solvents, [redacted]	
3.8 Stability in organic solvents used in b.p. and identity of relevant breakdown products (IIIA3.2)	n.a.	n.a.	n.a.	[redacted]	n.a.	n.a.	[redacted] Statement of the performance of the following tests according to CIPAC Method MT 181: Solubility in organic solvents, [redacted]	

Section A3 Physical and Chemical Properties of Active Substance

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.9 Partition coefficient n-octanol/water (IIA3.6) log Pow 1 log Pow 2	*including effects of pH (5-9)* n.a.	n.a.	n.a. **result:** **temperature:** **pH:**	[redacted]	n.a.	n.a.	[redacted] Statement of the performance of the following tests according to EU Test Guideline 92/69/EWG: A6 Solubility in water, A8 Distribution coefficient, A17 Fire enhancing properties, C7 Hydrolysis abiotic decomposition. [redacted]	
3.10 Thermal stability, identity of relevant breakdown products (IIA3.7)	OECD 113 (Screening test for thermal stability and stability in air)	[redacted]	The test substance shows neither endothermic nor exothermic effects up to the highest test temperature of 500°C	-	Y	1	[redacted] MELTING POINT/MELTING RANGE, BOILING POINT/BOILING RANGE, VAPOUR PRESSURE. [redacted]	x
3.11 Flammability, including auto-flammability and identity of	96/69/EEC A.10 Flammability (solids) A.12 Flammability (substances and	[redacted]	Flammability The test substance is not a readily combustible solid in the sense of Guideline	-	Y	1	Magnesium phosphide technical: FLAMMABILITY (SOLIDS).	x

Section A3 Physical and Chemical Properties of Active Substance

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
combustion products (IIA3.8)	preparations which, in contact with water evolve highly flammable gases in dangerous quantities) A.16 Auto-flammability (solids – determination of relative self-ignition temperature)	[redacted]	92/69/EEC, A.10 Flammability (substances and preparations which, in contact with water or damp air, evolve highly flammable gases in dangerous quantities) The test substance is hazardous in the sense of Guideline 92/69/EEC, method A.12. In contact with water the test substance evolves highly flammable gases in dangerous quantities. The gas ignites spontaneously.				FLAMMABILITY (SUBSTANCES AND PREPARATIONS WHICH, IN CONTACT WITH WATER OR DAMP AIR, EVOLVE HIGHLY FLAMMABLE GASES IN DANGEROUS QUANTITIES). [redacted] Magnesium phosphide technical: EXPLOSIVE PROPERTIES, AUTO-FLAMMABILITY (SOLIDS – DETERMINATION OF RELATIVE SELF-IGNITION TEMPERATURE). Siemens Axiva GmbH [redacted]	

Section A3 Physical and Chemical Properties of Active Substance

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
							[redacted]	
3.12 Flash-point (IIA3.9)	n.a.	n.a.	n.a.	[redacted]	n.a.	n.a.		
3.13 Surface tension (IIA3.10)	n.a.	n.a.	Determination of the surface tension is technically not feasible	n.a.	n.a	n.a.	[redacted] Statement of the performance of the following tests according to EU Test Guideline 92/69/EWG: A6 Solubility in water, A8 Distribution coefficient, A17 Fire enhancing properties, C7 Hydrolysis abiotic decomposition, [redacted]	
3.14 Viscosity (-)	n.a.	n.a.	n.a.	only required for liquids	n.a.			
3.15 Explosive properties (IIA3.11)	96/69/EEC A14 Explosive properties	[redacted]	The test substance has no danger of explosion according to the explosive properties in the sense of Guideline 96/69/EEC, A. 14.	-	Y	1	[redacted] Magnesium phosphide technical: EXPLOSIVE PROPERTIES, AUTO-FLAMMABILITY (SOLIDS – DETERMINATION OF RELATIVE SELF-IGNITION	

Section A3 Physical and Chemical Properties of Active Substance

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
							TEMPERATURE). [redacted]	
3.16 **Oxidizing properties (IIA3.12)**	n.a.	n.a	Determination of the oxidizing properties is scientifically unjustified	-	n.a.	n.a.	[redacted] Statement of the performance of the following tests according to EU Test Guideline 92/69/EWG: A6 Solubility in water, A8 Distribution coefficient, A17 Fire enhancing properties, C7 Hydrolysis abiotic decomposition. [redacted]	X
3.17 **Reactivity towards container material (IIA3.13)**	After a two years storage stability test the containers (aluminium bottles) were checked for visible defects (deformation, change in colour).	[redacted]	Containers (aluminium bottles) are resistant and do not react with Magnesium phosphide	-	n.a.	n.a.	Determination of the Storage Stability of Magtoxin. [redacted]	

Section A3 Physical and Chemical Properties of Active Substance
Annex point IIA, III 3

Section A3 **Physical and Chemical Properties of Active Substance**
Annex point IIA, III 3

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

Evaluation by Rapporteur Member State

Date	2006/08/14
3.1.1 Melting point (IIA, III 3.1)	The method is quoted as follows: 92/69/EEC, A.1 (DSC) [redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2006/08/14
3.1.2 Boiling point (IIA, III 3.1)	The method is quoted as follows: 92/69/EEC, A.2 (DSC) [redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2006/08/14
3.1.3 Bulk density/ relative density (IIA, III 3.1)	[redacted]
Reliability	[redacted]
Acceptability	[redacted]

Section A3 Physical and Chemical Properties of Active Substance

Annex point IIA, III 3

Remarks	
Date	2006/08/14
3.2 Vapour pressure (IIA, III 3.2)	The method is quoted as follows: 92/69/EEC, A.4 (vapour pressure balance) [redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2006/08/14
3.10 Thermal stability, identity of relevant breakdown products (IIA3.7)	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
Date	2007/05/10
3.11 Flammability, including auto-flammability and identity of combustion products (IIA3.8)	EEC, A.13 (Pyrophoric properties of solids and liquids)
Reliability	[redacted]
Acceptability	[redacted]

Section A3 Physical and Chemical Properties of Active Substance

Annex point IIA, III 3

Remarks	[redacted]
Date	2007/05/10
3.11 Flammability, including auto-flammability and identity of combustion products (IIA3.8)	EEC, A.16 (Auto-flammability, solids-Determination of relative self-ignition temperature):
Reliability	
Acceptability	[redacted]
Remarks	[redacted]
Date	2007/05/10
3.16 Oxidizing properties (IIA3.12)	EEC, A.17 (Oxidising properties)
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

Section A3
Annex point IIA, III 3

Physical and Chemical Properties of Active Substance

	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 A3 Physical and Chemical Properties of Phosphine (CAS 7803-51-2)

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.1 Melting point, boiling point, relative density (IIA3.1)								
3.1.1 Melting point	Not stated	[redacted]	**result: Melting point** - 133.5° C **pressure:**	published	n.a.	n.a.	Phosphine and Selected Metal Phospides, WHO, Geneva, 1988, p. 17 -19	x
3.1.2 Boiling point	Not stated	[redacted]	**result: Boiling point** – 87.4° C	published	n.a.	n.a.	Phosphine and Selected Metal Phospides, WHO, Geneva, 1988, p. 17 -19	x
3.1.3 Bulk density/ relative density	n.a	[redacted]	n.a.	A.s. is gaseous.	n.a.	n.a.		x
Vapour density	not stated	[redacted]	1.17 (air = 1)	published	n.a.	n.a.	Phosphine and Selected Metal Phospides, WHO, Geneva, 1988, p. 17 -19	
3.2 Vapour pressure (IIA3.2)	Not stated	[redacted]	34600 hPa (20°C)	published	n.a.	n.a.	Dräger Werk AG (1993): Dräger-Röhrchen-Handbuch, Lübeck, 1993, p. 343	

Section A3 Physical and Chemical Properties of Phosphine (CAS 7803-51-2)

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.2.1 Henry´s Law Constant (Pt. I-A3.2)	calculated	[redacted]	**calculated result:** 33269 Pa x m^3 x mol^{-1}	n.a.	n.a.	n.a.	Calculated: Application for registration of "Detia Gas-Ex-B forte", Detia Freyberg GmbH, Laudenbach, B/7, 16.12.94	x
3.3 Appearance (IIA3.3)								
3.3.1 Physical state	gaseous							
3.3.2 Colour	colorless							
3.3.3 Odour	"foul, fishy, garlicky" (technical phosphine)							
3.4 Absorption spectra (IIA3.4)			For the results please see the referenced spectra				Phosphine and Selected Metal Phospides, WHO, Geneva, 1988, p. 17 –19	
UV/VIS	n.a	[redacted]		published	n.a.	n.a.	Gmelins Handbuch der Anorganischen Chemie 16, Phosphor Teil C (1965), p.17 –19	
IR	n.a.	[redacted]		published	n.a.	n.a.		
NMR	n.a.	[redacted]		published	n.a.	n.a.	E. Fluck, The Chemistry of Phosphine, Fortschr. D. chem.. Forschung; Springer Verlag (1973). Reprint form Vol. 35, p.8 - 11	
MS	n.a.	[redacted]		published	n.a.	n.a.		

Section A3 Physical and Chemical Properties of Phosphine (CAS 7803-51-2)

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.5 Solubility in water (IIA3.5) Water solubility 1 Water solubility 2	*including effects of pH (5-9)* n.a.	[redacted]	**result:** 22.8 ml in 100 ml water **temperature:** 17°C **pH:** Solubility is little affected by the pH.	[redacted]	n.a.	n.a.	E. Fluck, The Chemistry of Phosphine, Fortschr. D. chem.. Forschung; Springer Verlag (1973). Reprint form Vol. 35, p. 12	x
3.6 Dissociation constant (-)	n.a.	[redacted]	pK (B) = 27.4 pK (S) = 28.8 (27°C)	[redacted]	n.a.	n.a.	Application for registration of "Detia Gas-Ex-B forte", Detia Freyberg GmbH, Laudenbach, B/7, 16.12.94	
3.7 Solubility in organic solvents, including the effect of temperature on solubility (IIIA3.1)	Not stated	[redacted]	Solubility is measured by the volume of phosphine dissolved in one volume of solvent under a partial pressure of 1 atmosphere and varies between 2.8 (Aniline) and 15.9 (Trifluoroacetic acid).	[redacted]	n.a.	n.a.	Phosphine and Selected Metal Phospides, WHO, Geneva, 1988, p. 17 –19	x
3.8 Stability in organic solvents used in b.p. and identity of relevant breakdown products (IIIA3.2)	n.a.	[redacted]	n.a.	[redacted]	n.a.	n.a.		

Section A3 Physical and Chemical Properties of Phosphine (CAS 7803-51-2)

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.9 Partition coefficient n-octanol/water (IIA3.6)	OECD (1981) 107	[redacted]	Log Pow = 0.9 +/- 0.3 Temperature: 21 °C	[redacted]	N	2	[redacted] Untersuchungsbereicht Octanol-Wasser-Verteilungskoeffizient von PH_3, [redacted]	x
3.10 Thermal stability, identity of relevant breakdown products (IIA3.7)	n.a.	[redacted]	Thermal decomposition at 550°C	[redacted]	n.a.	n.a.	Application for registration of "Detia Gas-Ex-B forte", Detia Freyberg GmbH, Laudenbach, B/7, 16.12.94	
3.11 Flammability, including auto-flammability and identity of combustion products (IIA3.8)	n.a.	[redacted]	Pure Phosphine has an autoignition temperature of 38°C.	[redacted]	n.a.	n.a.	Phosphine and Selected Metal Phospides, WHO, Geneva, 1988, p. 17 –19	
3.12 Flash-point (IIA3.9)	n.a.	[redacted]	n.a.	[redacted]	n.a.	n.a.		

Section A3 Physical and Chemical Properties of Phosphine (CAS 7803-51-2)

Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.13 Surface tension (IIA3.10)	n.a.	[redacted]	n.a.	[redacted]	n.a	n.a.		
3.14 Viscosity (-)	n.a.	[redacted]	n.a.	[redacted]	n.a.	n.a.		x
3.15 Explosive properties (IIA3.11)	n.a.	[redacted]	Phosphine forms explosive mixtures with air concentrations greater than 1.8%	[redacted]	n.a.	n.a.	Phosphine and Selected Metal Phospides. WHO, Geneva. 1988. p. 17 –19	
3.16 Oxidizing properties (IIA3.12)	n.a.	[redacted]	n.a.	[redacted]	n.a.	n.a.		
3.17 Reactivity towards container material (IIA3.13)	After a two years storage stability test the containers (aluminium bottles) were checked for visible defects (deformation, change in colour).	[redacted]	Containers are resistant and do not react with Magnesium phosphide and the released Phosphine (see II A 3.13, Magnesium phosphide related part)	-	n.a.	n.a.	[redacted] Determination of the Storage Stability of Magtoxin. [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 [redacted]

Reliability [redacted]

Acceptability [redacted]

Remarks [redacted]

Date [redacted]

Reliability [redacted]

Acceptability [redacted]

Remarks [redacted]

Date [redacted]

[redacted]


Date
Reliability
Acceptability
Remarks
Date
Reliability
Acceptability
Remarks
Date
Reliability
Acceptability
Remarks

Date

3.9 Partition coefficient

Section A3 Annex Point 3.2.1	Henry's Law Constant	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [X]** **Scientifically unjustified [ ]** **Other justification [ ]**	
Detailed justification: [redacted]		
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	
Conclusion	The applicant´s version is acceptable.	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A3 **Annex Point 3.4.4**	**Absorption spectra** [redacted]	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data [ ]	**Technically not feasible [X]** **Scientifically unjustified [X]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	
Conclusion	[redacted]	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A3 **Annex Point 3.4**	**Absorption spectra** [redacted]	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [X]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification: [redacted]		
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	
Conclusion	[redacted]	

Section A3 **Annex Point 3.4**	**Absorption spectra** [redacted]
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A3 Annex Point 3.5	Solubility in water [redacted]	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [X]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification: [redacted]		
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Evaluation of applicant's justification	[redacted]
Conclusion	[redacted]
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A3 Annex Point 3.6	Dissociation constant [redacted]	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [X]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification: [redacted]		
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Evaluation of applicant's justification	[redacted]
Conclusion	[redacted]
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A3 **Annex Point 3.7**	**Solubility in organic solvents, including the effect of temperature on solubility** [redacted]	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [X]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Evaluation of applicant's justification	[redacted]
Conclusion	[redacted]
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A3 **Annex Point 3.8**	**Stability in organic solvents used in b.p. and identity of relevant breakdown products**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [X]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification: [redacted]		
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	
Conclusion	[redacted]	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A3 **Annex Point 3.9**	**Partition coefficient n-octanol/water** [redacted]	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [X]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification: [redacted]		
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Evaluation of applicant's justification	[redacted]
Conclusion	[redacted]
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A3 **Annex Point 3.13**	**Surface tension** [redacted]	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [X]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification: [redacted]		
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Evaluation of applicant's justification	[redacted]
Conclusion	[redacted]
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A4 (4.1-4.3) **Analytical Methods for Detection and Identification**

Annex Point IIA4.1.1 (b) *Routine analysis of the technical active substance Magnesium Phosphide*

Official use only

1. REFERENCE

1.1 Reference	[redacted] Determination of Magnesium Phosphide and Four Impurities in Five Batches of Magnesium Phosphide Technical. [redacted]
1.2. Data protection	Yes
1.2.1. Data owner	Detia Freyberg GmbH
1.2.3 Criteria for data protection	[redacted]
2 Guideline:	[redacted]
	GLP: yes (certified laboratory)
3 Test substance	[redacted]
Materials and Methods (principle of analyses)	[redacted]

[redacted]

3.3 Linearity

[redacted]

3.3.2 Number of measurements [redacted]

3.7 Precision

3.7.1 Repeatability

[redacted]

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

[redacted]

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods

[redacted]

4.2 Conclusion

[redacted]

4.2.1 Reliability

[redacted]

4.2.2 Deficiencies

[redacted]

Section A4 (4.1-4.3) Analytical Methods for Detection and Identification

Annex Point IIA4.1.1 (b) *Routine analysis of the technical active substance Magnesium Phosphide*

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	
Acceptability	[redacted]
Remarks	
	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 A4 (4.1-4.3) Analytical Methods for Detection and Identification

Annex Point IIA4.1.1 *Routine analysis of the technical active substance*

Official use only

1. REFERENCE

1.1 Reference [redacted] Determination of Hydrogen Phosphide and Magnesium Phosphide respectively [redacted]

1.2. Data protection [redacted]

1.2.1. Data owner Detia Freyberg GmbH

2 Guideline: [redacted]

3 Materials and Methods (principle of analyses) [redacted]

Recheck of the method: [redacted]

[redacted]	[redacted]	[redacted]

Section A4 (4.1-4.3) **Analytical Methods for Detection and Identification**

Annex Point IIA4.1.1 *Routine analysis of the technical active substance*

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods

[redacted]

4.2 Conclusion

[redacted]

4.2.1 Reliability

[redacted]

4.2.2 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	[redacted]
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	
Acceptability	[redacted]
Remarks	
	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 A4 (4.1-4.3) Analytical Methods for Detection and Identification

Annex Point IIA4.2 (a) *Residues in soil*

Official use only

1. REFERENCE

1.1	**Reference**	[redacted]EXAMINATION OF THE DECOMPOSITION BEHAVIOUR OF HYDROGEN PHOSPHIDE (PHOSPHINE) IN STANDARD SOILS.[redacted]
1.2	**Data protection**	[redacted]
1.2.1	Data owner	Detia Freyberg GmbH
	GLP	[redacted]
	Materials and Methods	[redacted]
3.3/3.4/3.6	**Linearity/ Specificity/ Limit of quantification**	[redacted]
3.3/3.7.1	**Recovery rate/ Reproduceability**	[redacted]

[redacted]

3.7.2	**Independent laboratory validation**	[redacted]
		2. APPLICANT'S SUMMARY AND CONCLUSION
4.1	**Materials and methods**	[redacted]ed by pure N_2 and directed through Dräger-tubes for measurement.
4.2	**Conclusion**	[redacted]
4.2.1	Reliability	[redacted]
4.2.2	Deficiencies	[redacted]

Section A4 (4.1-4.3) Analytical Methods for Detection and Identification

Annex Point IIA4.2 (a) *Residues in soil*

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

Section A4 (4.1-4.3) Analytical Methods for Detection and Identification

Annex Point IIA4.2 (b) *Detection in air*

Official use only

		1. REFERENCE
1.1	**Reference**	Kettrup, A. ; Angerer, J. (1994): Luftanalysen, Sonderdruck aus DFG – Deutsche Forschungsgemeinschaft. Band 1, Ed. Greim, H., published
1.2	**Data protection**	No
1.2.1	Data owner	published
2.1	**Guideline**	Modified method of NIOSH, Manual of analytical methods, No. S332 "Phosphine", vol. 5, 1980
2.2	**GLP**	not applicable
3	**Materials and Methods**	Test item and reference substance: phosphine gas, purity 99.999 %, Messer Griesheim, Germany Analytical determination: Phosphine containing air samples were conducted through silica gel adsorption tubes impregnated with mercury cyanide. Desorption was carried out with a potassium permanganate solution by oxidation of the formed mercury phosphine complex to phosphate. Following various steps of preparation involving incubation at 65-70°C, addition of $FE(NH_4)_2(SO_4)_2$, water and molybdate, isobutyl alcohol/toluene (1/1) was added and the organic phase separated. Following further addition of sulphuric acid in methanol and $SnCl_2$, the resulting blue hetero-polymolybdate complex was quantified by photometric determination at 625 nm. Remark: As an alternative to the standard calibration with phosphine gas, a standard curve was prepared with K_2HPO_4 as reference substance. The results of this calibration were in good agreement with the phosphine standard, but are not reported specifically in this summary.
3.3	**Linearity**	For calibration purposes, phosphine gas with sample volumes of 10, 30, 50, 80 and 100 µl was adsorbed and further processed as described above. The calibration curve was found to be linear between 0.5 µg and 20 µg PH_3 (equivalent to approximately 0.0125 mg/m^3 sample air and 0.5 mg/m^3 sample air) with a correlation coefficient of 0.9958.
3.4	**Specificity**	Existing orthophosphates in air, and compounds forming molybdate complexes and being soluble in isobutene/toluene may interfere.
3.5	**Recovery**	The recovery was not explicitly stated. However, due to the results of the precision determination above, the recovery was calculated to be in the range of 100% ± 5-7% (RSD).
3.6	**Limit of quantification**	The limit of quantification was stated as 0.5 µg PH_3 (absolute) corresponding to 100 ml sample volume with a phosphine concentration of 0.0125 mg/m^3.
3.7.1	**Precision (repeatability of the method):**	Air samples with a debit content of 0.025 – 0.25 µg/m^3 phosphine were prepared form phosphine gas and air. The phosphine content at each fortification level was determined in 10 replicates. The relative standard deviations (RSD) are summarised in the following table:

Section A4 (4.1-4.3) **Analytical Methods for Detection and Identification**

Annex Point IIA4.2 (b) *Detection in air*

Concentration µg/m³	RSD (%)
0.025	6.7
0.15	5.1
0.25	6.2

3.7.2 Independent laboratory validation

not stated

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods

Test item and reference substance: phosphine gas, purity 99.999 %, Messer Griesheim, Germany

Analytical determination: Phosphine containing air samples were conducted through silica gel adsorption tubes impregnated with mercury cyanide. Desorption was carried out with a potassium permanganate solution by oxidation of the formed mercury phosphine complex to phosphate. Following various steps of preparation involving incubation at 65-70°C, addition of $FE(NH_4)_2(SO_4)_2$, water and molybdate, isobutyl alcohol/toluene (1/1) was added and the organic phase separated. Following further addition of sulphuric acid in methanol and $SnCl_2$, the resulting blue hetero-polymolybdate complex was quantified by photometric determination at 625 nm.

4.2 Conclusion

According to the data presented above, the established method was found feasible for the monitoring of phosphine residues in air.

4.2.1 Reliability

1

4.2.2 Deficiencies

No

Section A4 (4.1-4.3) Analytical Methods for Detection and Identification

Annex Point IIA4.2 (b) *Detection in air*

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	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 A4 (4.1-4.3) Analytical Methods for Detection and Identification

Annex Point IIA4.2 (c) *Residues in water*

Official use only

1. REFERENCE

1.1	**Reference**	[redacted]Method validation for the determination of residues of phosphine in surface water and potable water.[redacted]
1.2	**Data protection**	Yes
1.2.1	Data owner	[redacted]
1.2.3	Criteria for data protection	[redacted]
	GLP	yes (certified laboratroy)
		[redacted]
	Materials and Methods	[redacted]
		[redacted]
3.3	**Linearity**	[redacted]
		[redacted]
3.4	**Specificity**	[redacted]

Section A4 (4.1-4.3) Analytical Methods for Detection and Identification

Annex Point IIA4.2 (c) *Residues in water*

3.5 Recovery

[redacted]

			Recovery rates [%]		
[redacted]					

3.6 Limits of quantification and detection

[redacted]

3.7.1 Precision (repeatability of the analytical system):

[redacted]

[redacted]	

3.7.2 Independent laboratory validation

[redacted]

2. APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods

[redacted]

4.2 Conclusion

[redacted]

4.2.1 Reliability

[redacted]

4.2.2 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	[redacted]
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	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 A4 (4.1-4.3) Analytical Methods for Detection and Identification

Annex Point IIA4.2 (d) *Residues in animal and human body fluids and tissues*

Official use only

1. REFERENCE

1.1	**Reference**	L.T.F. Chan, R.J. Crowley, D. Delliou, R.Geyer (1983): Phosphine Analysis in Post Mortem Specimens Following Ingestion of Aluminium Phosphide; Journal of Analytical Toxicology, Vol. 7, July/August 1983
1.2	**Data protection**	No
1.2.1	Data owner	published
2.1	**Guideline**	not stated
2.2	**GLP**	not stated
3	**Materials and Methods**	In this study post mortem specimens from the body of a 27-year-old man who had ingested an unknown quantity of Phostoxin tablets (Degesch) were analysed. A simple and rapid headspace procedure is outlined for the analysis of phosphine in post mortem specimens using GC/NPD procedures.

Method description:

Reagents: A primary gravimetric standard gas mixture of 5.1 $\pm$ 0.1 ppm of phosphine in nitrogen (certified) was obtained from Commonwealth Industrial Gases Ltd.. A 10% sulphuric acid solution was prepared using analytical grade concentrated sulphuric acid and deionised water.
Glassware: Glass headspace vials (75.5 mm x 23 mm) were obtained from Perkin Elmer. The sealed vials had a capacity of 24 ml. Two graduated glass gas-tight syringes, one 1 ml and one 5 ml were used for transferring and injecting the standard gas mixture and headspace gases.
Instrumentation: Analysis was carried out on a Hewlett-Packard Model 5730A GC/NPD, Model 18789A. Porapak Q, 100/120 mesh column packing was used in a 1.4 m x 4 mm i.d. glass column. The flow rate of the nitrogen carrier gas was 30ml/min. The hydrogen and air flow rates to the detector were 4 ml/min and 50 ml/min, respectively. The temperature settings of the chromatograph were: injector 150°C, detector 200°C and column 80°C.
Sample Preparation for Tissues and Blood: The homogenized sample, either 1 g or 1 ml, was placed in a headspace vial that had been flushed with nitrogen. Two millilitres of 10% sulphuric acid was added. The vial was immediately sealed and shaken on a vortex mixer for 30 seconds. A 1 ml aliquot of the headspace was then injected into the gas chromatograph.
Phosphine standards: Standards of 500 pg/ml and 1000 pg/ml concentration were prepared by adding 1 ml of deionised water and 2 ml of 10% sulphuric acid to two headspace vials that had been flushed with nitrogen and sealed. Using a 5 ml syringe, 1.5 ml and 3.0 ml aliquots of the standard gas mixture were transferred to the prepared vials. The vials were shaken on a vortex mixer for 30 seconds and 2 ml aliquots of the headspace were injected into the gas chromatograph.
Quantitation of the post mortem specimens for phosphine was performed by peak height measurements relative to those of the standards. Under the conditions described, the retention time of phosphine was 2.9 min.

Section A4 (4.1-4.3) **Analytical Methods for Detection and Identification**

Annex Point IIA4.2 (d) *Residues in animal and human body fluids and tissues*

Findings

The results are shown in the following table:

Phosphine Levels in Post Mortem Specimens Liberated after Acidification:

Sample	Concentration
Blood	0.5 ng/ml
Liver	3 ng/g
Stomach and contents	3000 ng/g
Urine	Insufficient sample

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods

Headspace GC/NPD procedure.

4.2 Conclusion

A rapid and sensitive headspace method has been described for the analysis of post mortem samples from a death involving aluminium phosphide.

4.2.1 Reliability 2

4.2.2 Deficiencies No

Section A4 (4.1-4.3) Analytical Methods for Detection and Identification

Annex Point IIA4.2 (d) *Residues in animal and human body fluids and tissues*

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

Section A4 (4.1-4.3)

Annex Point IIA4.1/4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification of Phosphine which is evolvable from Human Blood

Official use only

1 REFERENCE

1.1 Reference

[redacted] Residue analysis of Zinc Phosphide in human blood, [redacted]

1.2 Data protection

Yes

(indicate if data protection is claimed)

1.2.1 Data owner: Zinc phosphide pool

1.2.2

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

[redacted]

3 MATERIALS AND METHODS

3.1 Preliminary treatment

[redacted]

3.1.1 Enrichment

[redacted]

Give data on e.g. extraction procedure (solvent, technique etc.)

3.1.2 Cleanup

[redacted]

Give data on purification of the enriched sample

3.2 Detection

Non-entry field

3.2.1 Separation method

[redacted]

Section A4 (4.1-4.3)

Annex Point IIA4.1/4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification of Phosphine which is evolvable from Human Blood

		Give type and conditions
3.2.2	Detector	[redacted]
3.2.3	Standard(s)	[redacted]
3.2.4	Interfering substance(s)	[redacted]
3.3	**Linearity**	Non-entry field
3.3.1	Calibration range	[redacted]
3.3.2	Number of measurements	[redacted]
3.3.3	Linearity	
3.4	**Specifity: interfering substances**	[redacted]
3.5	**Recovery rates at different levels**	*Give mean value and range of data; specify levels*
3.5.1	Relative standard deviation	
3.6	**Limit of determination**	[redacted]
3.7	**Precision**	Non-entry field
3.7.1	Repeatability	[redacted]
3.7.2	Independent laboratory	

validation

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods

[redacted]

4.2 Conclusion

[redacted]

4.2.1 Reliability

[redacted]

Based on the assessment of the method include appropriate reliability indicator 0, 1, 2, 3, 4

4.2.2 Deficiencies

[redacted]

Section A4 (4.1-4.3)

Annex Point IIA4.1/4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification of Phosphine which is evolvable from Human Blood

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

Gelöscht: 7
Gelöscht: -
Gelöscht: 01
Gelöscht: -
Gelöscht: 25

Section A4 (4.1-4.3)

Annex Point IIA4.1/4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification of Phosphine which is evolvable from Milk, Liver and Muscle

Official use only

1 REFERENCE

1.1 Reference [redacted]

1.2 Data protection Yes

1.2.1 Data owner Zinc phosphide Pool

1.2.2

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 [redacted]

3 MATERIALS AND METHODS

3.1 Preliminary treatment [redacted]

3.1.1 Enrichment [redacted]

3.1.2 Cleanup [redacted]

3.2 Detection [redacted]

3.2.1 Separation method [redacted]

3.2.2 Detector [redacted]

3.2.3 Standard(s) [redacted]

Section A4 (4.1-4.3)

Annex Point IIA4.1/4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification of Phosphine which is evolvable from Milk, Liver and Muscle

3.2.4	Interfering substance(s)	
3.3	**Linearity**	Non-entry field
3.3.1	Calibration range	
3.3.2	Number of measurements	
3.3.3	Linearity	
3.4	**Specifity: interfering substances**	
3.5	**Recovery rates at different levels**	

Give mean value and range of data; specify levels

3.5.1	Relative standard deviation	

Section A4 (4.1-4.3)

Annex Point IIA4.1/4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification of Phosphine which is evolvable from Milk, Liver and Muscle

[redacted]

3.6 Limit of determination

[redacted]

3.7 Precision

3.7.1 Repeatability

[redacted]

Give statistical data

3.7.2 Independent laboratory validation

[redacted]

Section A4 (4.1-4.3)

Annex Point IIA4.1/4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification of Phosphine which is evolvable from Milk, Liver and Muscle

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods

[redacted]

4.2 Conclusion

[redacted]

4.2.1 Reliability

[redacted]

4.2.2 Deficiencies

[redacted]

Section A4 (4.1-4.3)

Annex Point IIA4.1/4.2 & IIIA-IV.1

Analytical Methods for Detection and Identification of Phosphine which is evolvable from Milk, Liver and Muscle

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Materials and methods	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	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 A4 (4.1-4.3) Annex Point IIA4.1/4.2 & IIIA-IV.1	Analytical Methods for Detection and Identification of Magnesium phosphide in Blood, Milk, Liver and Muscles	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [x] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [ ]** **Other justification [ ]**	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]	No data submission intended	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	

Section A4 (4.1-4.3) **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**Analytical Methods for Detection and Identification of Magnesium phosphide in Blood, Milk, Liver and Muscles**
Conclusion	[redacted]
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A4 (4.1-4.3) Analytical Methods for Detection and Identification

Annex Point IIA4.3 *Residues of the active substance in food or feed stuffs*

Official use only

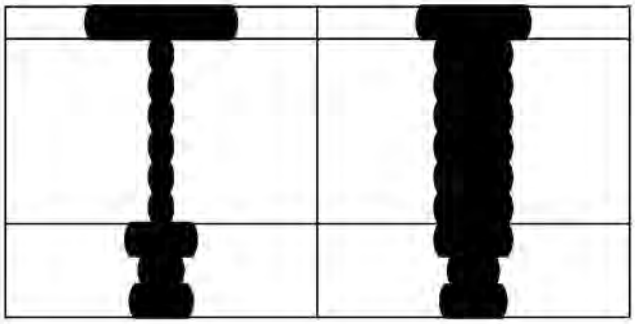
1. REFERENCE

1.1	**Reference**	[redacted] Determination of Residues of Detia Gas-EX-B, MAGTOXIN and PHOSTOXIN Tablets after Fumigation of Different Storage Goods, [redacted]
1.2	**Data protection**	Yes
1.2.1	Data owner	Detia Freyberg GmbH
1.2.3	Criteria for data protection	[redacted]
	GLP	yes
	Materials and Methods	[redacted]
	Analytical determination	Into a three-neck round-bottomed flask about 10 – 100 g of the [redacted]
	Detector response, injection precision and recovery	[redacted]

Section A4 (4.1-4.3) **Analytical Methods for Detection and Identification**

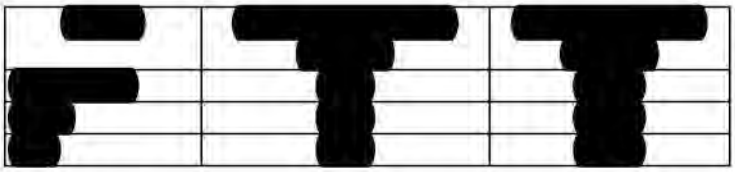
Annex Point IIA4.3 *Residues of the active substance in food or feed stuffs*

[redacted]



Quantitation Limit and Detection Limit (LOQ)

[redacted]



2. APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods

[redacted]

4.2 Conclusion

[redacted]

4.2.1 Reliability

[redacted]

4.2.2 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	[redacted]
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	

Section A5 Effectiveness against target organisms and intended uses

Subsection (Annex Point)		Official use only
5.1	Function (IIA5.1)	
5.2	Organism(s) to be controlled and products, organisms or objects to be protected (IIA5.2)	
5.2.1	Organism(s) to be controlled (IIA5.2)	
5.2.2	Products, organisms or objects to be protected (IIA5.2)	
5.3	Effects on target organisms, and likely concentration at which the active substance will be used (IIA5.3)	
5.3.1	Effects on target organisms (IIA5.3)	

Section A5 **Effectiveness against target organisms and intended uses**

5.3.2 Likely concentrations at which the A.S. will be used (IIA5.3)

PT18 (Insecticide)

[redacted]

5.4 Mode of action (including time delay) (IIA5.4)

[redacted]

Section A5 **Effectiveness against target organisms and intended uses**

[redacted]

5.4.1 Mode of action

5.4.2 Time delay

5.5 Field of use envisaged (IIA5.5)

[redacted]

5.6 User (IIA5.6)

Industrial

[redacted]

Professional

[redacted]

General public

5.7 Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies (IIA5.7)

5.7.1 Development of resistance

[redacted]

5.7.2 Management strategies

[redacted]

Formatiert: Schriftart: 10 pt

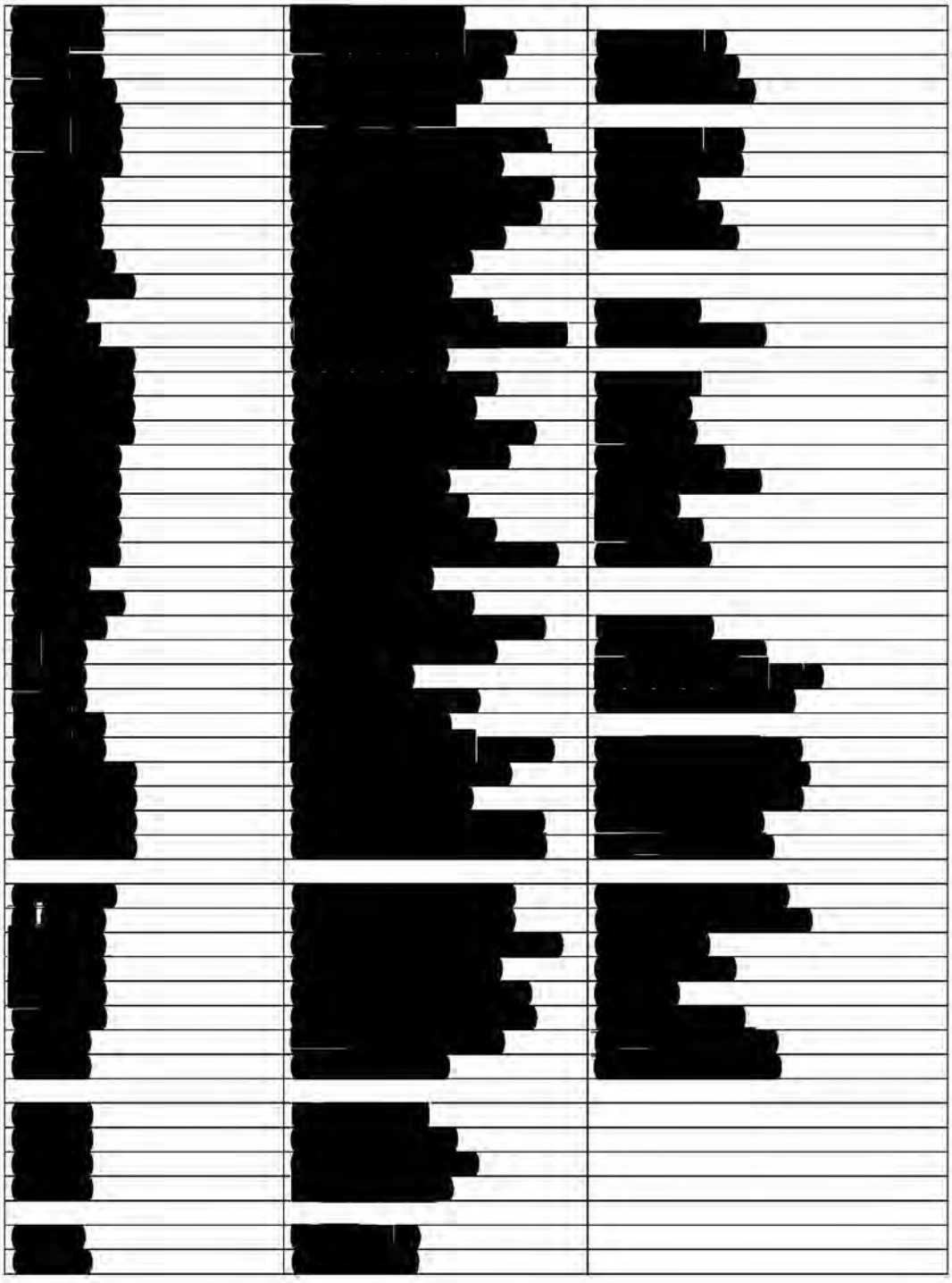
5.8 Likely tonnage to be

[redacted]

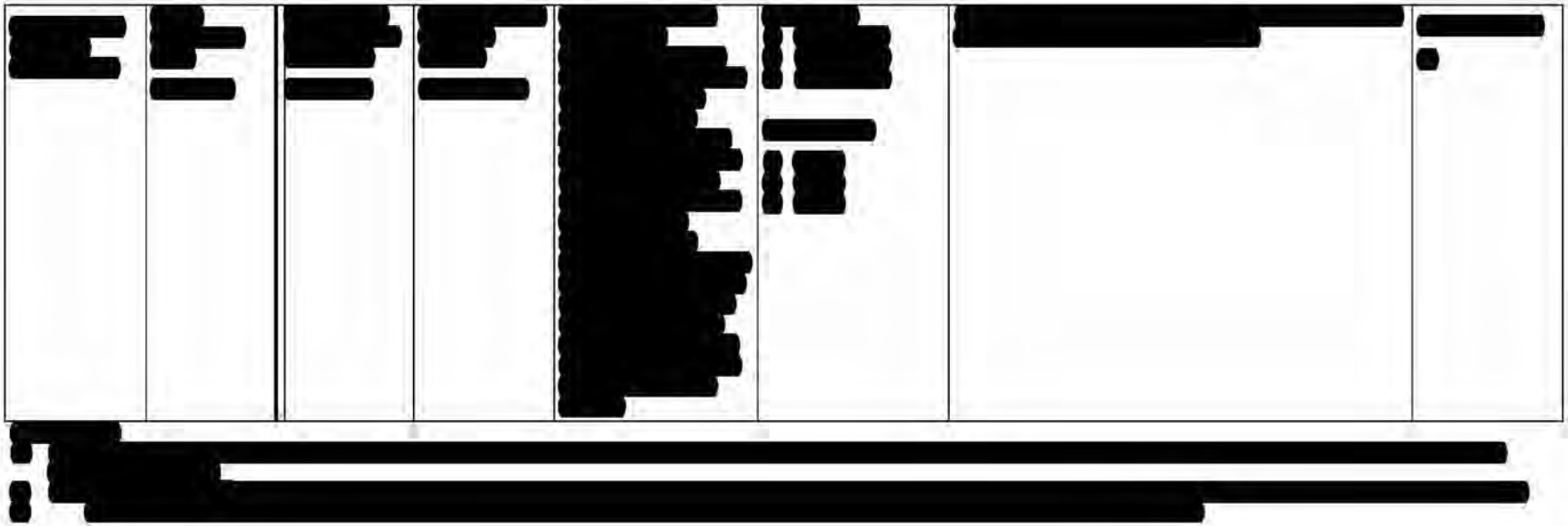
placed on the market per year (IIA5.8)

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

Table 5.2.1 Organism(s) to be controlled



Section 5.3: Summary table of experimental data on the effectiveness of the active substance against target organisms at different fields of use envisaged, where applicable



Annex 1: Evaluation by Rapporteur Member State, CA-Tables

Table1: Section 5.3: Summary table of experimental data on the effectiveness of the active substance against target organisms at different fields of use envisaged, where applicable

[redacted]

Section A6.1.1
Annex Point IIA6.1

Acute Toxicity
Oral (Mice)

Official use only

1. REFERENCE

1.1	**Reference**	[redacted]ACUTE TOXICITY STUDY OF ALUMINIUM PHOSPHIDE BY ORAL ADMINISTRATION TO NMRI MICE[redacted]
1.2	**Data protection**	[redacted]
1.2.1	Data owner	Detia Freyberg GmbH

2. GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline**	[redacted]
2.2	**GLP**	Yes

3. MATERIALS AND METHODS

[redacted]

Section A6.1.1 **Acute Toxicity**

Annex Point IIA6.1 *Oral (Mice)*

4. RESULTS AND DISCUSSION

[redacted]

4.4 **LD_{50}** [redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 **Materials and methods** [redacted]

5.2 **Results and discussion** [redacted]

5.3 **Conclusion**

5.3.1 Reliability [redacted]

5.3.2 Deficiencies [redacted]

Evaluation by Competent Authorities

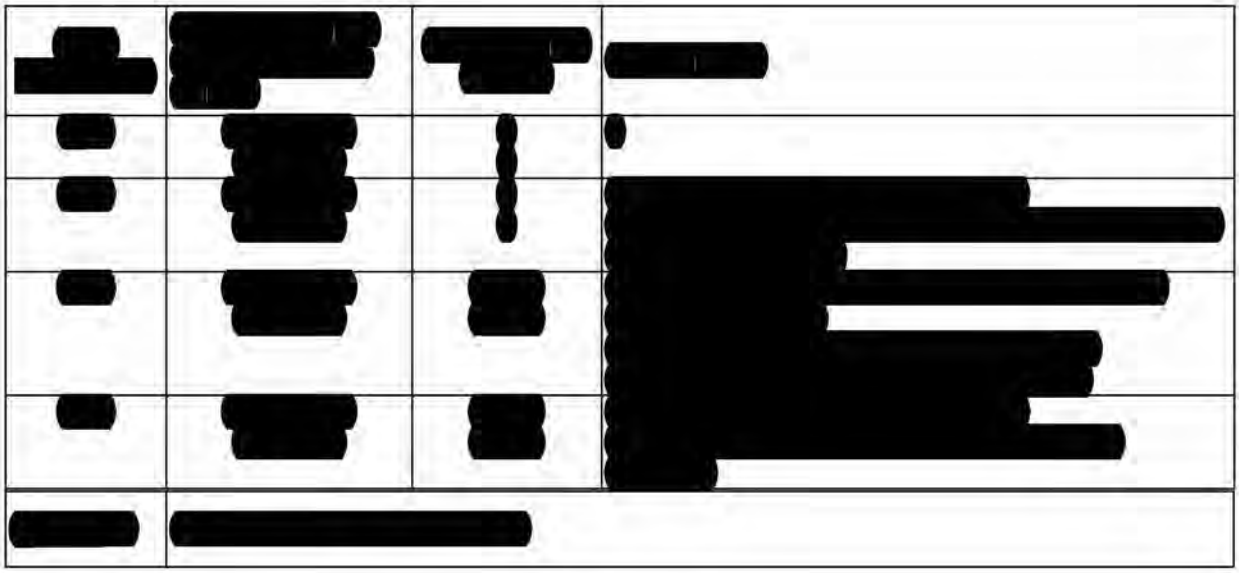
EVALUATION BY RAPPORTEUR MEMBER STATE

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

COMMENTS FROM ...

Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

[redacted]



Section A6.1.1 Acute Toxicity

Annex Point IIA6.1

Oral

Official use only

		1 REFERENCE
1.1	**Reference**	[redacted] Acute oral Toxicity of 1% Magnesiumphosphid in Vaseline in rats. [redacted]
1.2	**Data protection**	[redacted]
1.2.1	Data owner	Detia Freyberg GmbH
1.2.2		
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**	[redacted]
		3 MATERIALS AND METHODS
3.1	**Test material**	[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]
3.1.2.3	Stability	[redacted]
3.2	**Test Animals**	
3.2.1	Species	[redacted]
3.2.2	Strain	[redacted]
3.2.3	Source	[redacted]
3.2.4	Sex	[redacted]
3.2.5	Age/weight at study initiation	[redacted]
3.2.6	Number of animals per group	[redacted]
3.2.7	Control animals	[redacted]
3.3	**Administration/ Exposure**	[redacted]
3.3.1	Postexposure period	[redacted]
		Oral
3.3.2	Type	[redacted]

Section A6.1.1 Acute Toxicity

Annex Point IIA6.1 *Oral*

3.3.3	Concentration	[redacted]	X
3.3.4	Vehicle	[redacted]	X
3.3.5	Concentration in vehicle	[redacted]	X
3.3.6	Total volume applied	[redacted]	
3.3.7	Controls	[redacted]	
3.4	**Examinations**	[redacted]	
3.5	**Method of determination of LD_{50}**	[redacted]	
3.6	**Further remarks**	[redacted]	

4 RESULTS AND DISCUSSION

4.1	**Clinical signs**	[redacted]
4.2	**Pathology**	[redacted]
4.3	**Other**	[redacted]
[redacted]	[redacted]	[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	[redacted]
5.2	**Results and discussion**	The LD50 (for 24h and 14 days) for the rat was calculated as 11.2 mg/kg for males and females by oral administration.
5.3	**Conclusion**	
5.3.1	Reliability	[redacted]
5.3.2	Deficiencies	[redacted]

Section A6.1.1 Acute Toxicity

Annex Point IIA6.1

Oral

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	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

[redacted]

[redacted]	[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 A6.1.2 Acute Toxicity

Annex Point IIA6.1 *Percutaneous (Rats)*

Official use only

1. REFERENCE

1.1	**Reference**	[redacted]ACUTE TOXICOLOGICAL STUDY ON COMPOUND ALUMINIUMPHOSPHID AFTER DERMAL APPLICATION TO THE RAT[redacted]
1.2	**Data protection**	[redacted]
1.2.1	Data owner	Detia Freyberg GmbH

2. GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline**	[redacted]
2.2	**GLP**	Yes
2.3	**Deviations**	[redacted]

3. MATERIALS AND METHODS

[redacted]

4. RESULTS AND DISCUSSION

[redacted]

4.4 LD_{50}

[redacted]

LD_{50} (24 h) = 1824 mg/kg b.w. (males and females)

LD_{50} (14 d) = 1080 mg/kg b.w. (males and females)

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted]

5.2 Results and discussion

[redacted]

5.3 Conclusion

5.3.1 Reliability

[redacted]

5.3.2 Deficiencies

[redacted]

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date

Materials and Methods

Results and discussion

Conclusion

Reliability

Acceptability

Remarks

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

[redacted]

Section A6.1.3 Acute Toxicity

Annex Point IIA6.1 *Inhalation (Rats)*

Official use only

1. REFERENCE

1.1	**Reference**	[redacted] Acute Inhalation Toxicity Testing of Hydrogen Phosphide in Rats. [redacted]
1.2	**Data protection**	[redacted]
1.2.1	Data owner	Detia Freyberg GmbH

2. GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline**	[redacted]
2.2	**GLP**	[redacted]
2.3	**Deviations**	[redacted]

3. MATERIALS AND METHODS

[redacted]

4. RESULTS AND DISCUSSION

[redacted]

4.4	**LC_{50}**	204 ppm (confidence limits 195 – 213 ppm) for male rats and 179 ppm (confidence limits 170 – 188 ppm) for female rats

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	[redacted]
5.2	**Results and discussion**	[redacted]
5.3	**Conclusion**	
5.3.1	Reliability	[redacted]
5.3.2	Deficiencies	[redacted]

Section A6.1.3 Acute Toxicity

Annex Point IIA6.1

Inhalation (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	[redacted]
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	

ANNEX

[redacted]

Section A6.1.4 Acute Dermal Irritation

Annex Point IIA6.1.4 *Specify section no., heading and species as appropriate*

Official use only

1 REFERENCE

1.1	**Reference**	[redacted]IRRITANT EFFECTS OF ALUMINIUMPHOSPHID ON INTACT SKIN OF RABBITS. PHARMATOX,[redacted]
1.2	**Data protection**	No
1.2.1	Data owner	Detia Freyberg GmbH

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	[redacted]
2.2	**GLP**	Yes
2.3	**Deviations**	[redacted]

3 MATERIALS AND METHODS

[redacted]

4 RESULTS AND DISCUSSION

[redacted]

After 24 hours of contact all localizations at intact skin did show slight oedema, further 48 hours later there were no deviations at intact skin compared to normal skin.

5 APPLICANT'S SUMMARY AND CONCLUSION

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

Section A6.1.4 Acute Dermal Irritation

Annex Point IIA6.1.4 *Specify section no., heading and species as appropriate*

5.2.1	Reliability	[redacted]
5.2.2	Deficiencies	[redacted]

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2006-11-13
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	

[redacted]

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

Section 6.1.4 Acute Eye Irritation

Annex Point IIA6.1.4 *Specify section no., heading and species as appropriate*

Official use only

1 REFERENCE

1.1	**Reference**	[redacted] IRRITANT EFFECTS OF ALUMINIUMPHOSPHID ON RABBIT EYE. [redacted]
1.2	**Data protection**	[redacted]
1.2.1	Data owner	Detia Freyberg GmbH

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	[redacted]
2.2	**GLP**	Yes
2.3	**Deviations**	[redacted]

3 MATERIALS AND METHODS

[redacted]

4 RESULTS AND DISCUSSION

[redacted]

Post application and after washed out method slight conjunctival irritations occurred. Slightly increased reddening till 8 hours, chemosis for 1 hour only, and slightly increased secretion till 4 hours p.a.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	[redacted]
5.2	**Results and discussion**	[redacted]
5.3	**Conclusion**	
5.3.1	Reliability	[redacted]

Section 6.1.4 Acute Eye Irritation

Annex Point IIA6.1.4 *Specify section no., heading and species as appropriate*

5.3.2 Deficiencies [redacted]

Section 6.1.4 Acute Eye Irritation

Annex Point IIA6.1.4

Specify section no., heading and species as appropriate

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date

Materials and Methods

Results and discussion

Conclusion

Reliability

Acceptability

Remarks

Section 6.1.4 Acute Eye Irritation

Annex Point IIA6.1.4

Specify section no., heading and species as appropriate

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

[redacted]

[redacted]	[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 A6.1.5/01

Annex Point IIA6.1.5

Skin sensitisation

Buehler Test

			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted]Skin sensitization of DEGESCH-MAGPHOS-PASTILHAS de 0.6 g in Guinea Pigs (Cavia porcellus). [redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Detia Freyberg GmbH	
1.2.2	Criteria for data protection	[redacted]	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	[redacted]	
2.2	**GLP**	[redacted]	
2.3	**Deviations**	[redacted]	
		3 MATERIALS AND METHODS	
3.1	**Test material**	[redacted]	X
3.1.1	Batch number	[redacted]	
3.1.1	Specification	[redacted]	
3.1.1.1	Description	[redacted]	
3.1.1.2	Purity	[redacted]	
3.1.1.3	Stability	[redacted]	
3.1.1.4	Preparation of test substance for application	[redacted]	
3.1.1.5	Pretest performed on irritant effects	[redacted]	

Section A6.1.5/01

Annex Point IIA6.1.5

Skin sensitisation

Buehler Test

3.2	**Test Animals**		
3.2.1	Species	[redacted]	
3.2.2	Strain	[redacted]	
3.2.3	Source	[redacted]	
3.2.4	Sex	[redacted]	
3.2.5	Age/weight at study initiation	[redacted]	X
3.2.6	Number of animals per group	[redacted]	X
3.2.7	Control animals	[redacted]	
3.3	**Administration/ Exposure**	[redacted]	
3.3.1	Induction schedule	[redacted]	
3.3.2	Way of Induction	[redacted]	X
3.3.3	Concentrations used for induction	[redacted]	
3.3.4	Concentration Freunds Complete Adjuvant (FCA)	[redacted]	
3.3.5	Challenge schedule	[redacted]	
3.3.6	Concentrations used for challenge	[redacted]	
3.3.7	Rechallenge	[redacted]	
3.3.8	Scoring schedule	[redacted]	
3.3.9	Removal of the test substance	[redacted]	
3.3.10	Positive control substance	[redacted]	
3.4	**Examinations**		X
3.4.1	Pilot study	[redacted]	
3.5	**Further remarks**	[redacted]	
		4 RESULTS AND DISCUSSION	X
4.1	**Results of pilot studies**	[redacted]	
4.2	**Results of test**		
4.2.1	30h after challenge	[redacted]	
4.2.2	54h after challenge	[redacted]	

Section A6.1.5/01 **Skin sensitisation**
Buehler Test

Annex Point IIA6.1.5

4.2.3	Other findings	[redacted]	X
4.3	**Overall result**	[redacted]	

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	[redacted]
5.2	**Results and discussion**	[redacted]
5.3	**Conclusion**	According to the results the test-substance DEGESCH-MAGPHOS-PASTILHAS DE 0.6 g was classified as a substance that produces no sensitization.
5.3.1	Reliability	[redacted]
5.3.2	Deficiencies	[redacted]

Evaluation by Competent Authorities

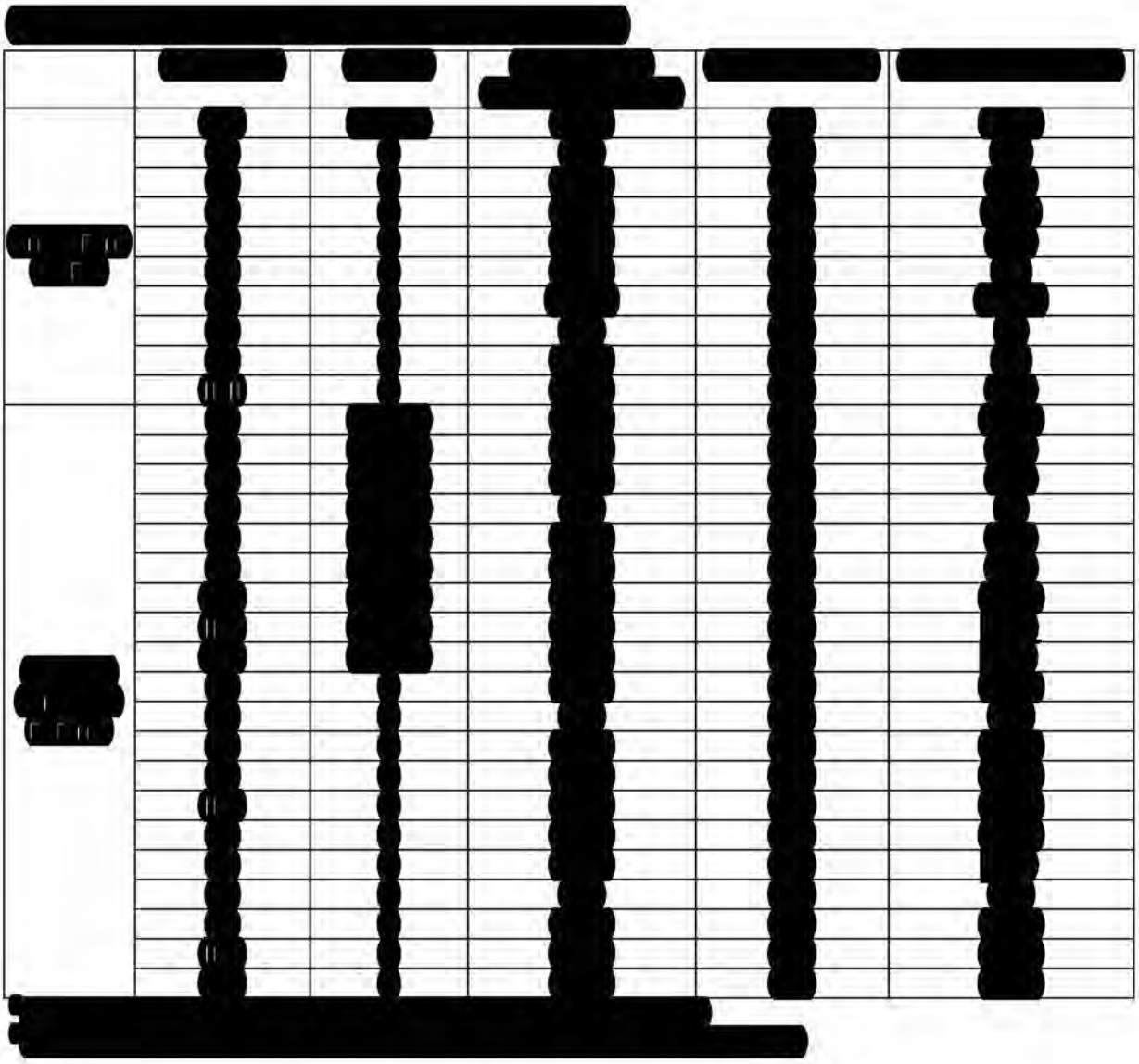
EVALUATION BY RAPPORTEUR MEMBER STATE

Date

Materials and Methods

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 A6.1.5/02 Skin sensitisation

Annex Point IIA6.1.5 (a)

Specify type of study:
Buehler Test

Official use only

1 REFERENCE

1.1 Reference

[redacted]Evaluation of Skin sensitization of test substance Detia Gas-Ex-T Pastilhas de 3 g.[redacted]

1.2 Data protection

Yes

1.2.1 Data owner

Detia Freyberg GmbH

1.2.2 Criteria for data protection

[redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study

[redacted]

2.2 GLP

[redacted]

2.3 Deviations

[redacted]

3 MATERIALS AND METHODS

[redacted]

Section A6.1.5/02 **Skin sensitisation**

Annex Point IIA6.1.5 (a) *Specify type of study:*
Buehler Test

4 RESULTS AND DISCUSSION

[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods [redacted]

5.2 Results and discussion According the results the test-substance Detia Gas-Ex-T Pastilhas 3 g was classified as a substance that produces no sensitization.

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	[redacted]
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 Metabolism studies in mammals

Annex Point IIA6.2/01

Official use only

1 REFERENCE

1.1	**Reference**	Curry, A.S.; et al. (1959): Absorption of Zinc phosphide particles; Nature 184, 642 – 643
1.2	**Data protection**	No
1.2.1	Data owner	published
1.2.2		
1.2.3	Criteria for data protection	No data protection claimed

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	not stated
2.2	**GLP**	No
2.3	**Deviations**	not stated

There are no studies available concerning adsorption, distribution, metabolism and excretion of ingested Magnesium phosphide. However, there exist respective studies with Zinc phosphide. Although these studies do not meet current standards, they nevertheless allow for a reasonable assessment. Following oral administration, the process initiating toxic action is the same in the above metal phosphides: they are hydrolysed rapidly in the stomach, forming the toxic agent phosphine and the respective inert metal cations. Therefore the results obtained with Zinc phosphide are transferable to Magnesium phosphide.

3 MATERIALS AND METHODS

3.1	**Test material**	Zinc phosphide
3.1.1	Lot/Batch number	not stated
3.1.2	Specification	Deviating from specification given in section 2 as follows:
3.1.2.1	Description	Zinc phosphide (^{32}P-labelled)
3.1.2.2	Purity	n. a.
3.1.2.3	Stability	n. a.
3.1.2.4	Radiolabelling	^{32}P
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain	Not stated
3.2.3	Source	Not stated
3.2.4	Sex	Not stated

Section A6.2 Metabolism studies in mammals

Annex Point IIA6.2/01

3.2.5	Age/weight at study initiation	Age not stated, weight approximately 250 g
3.2.6	Number of animals per group	6
3.2.7	Control animals	No
3.3	**Administration/ Exposure**	Oral (Suspension of Zinc phosphide (^{32}P-labelled) in commercially available evaporated milk was fed to adult rats)
3.3.1	Preparation of test site	n.a.
3.3.2	Concentration of test substance	Doses considered to be in excess of LD_{50} (40 mg/kg bw)
3.3.3	Specific activity of test substance	Phosphorus activity of 0.8mc
3.3.4	Volume applied	10 mgm.
3.3.5	Size of test site	n.a.
3.3.6	Exposure period	n.a.
3.3.7	Sampling time	n.a.
3.3.8	Samples	The livers from rats RA/2 and RA/1 were analysed separately; those from rats RA/3, 4, 5 and 6 were combined before analysis. Carbon dioxide was passed in the cold through suspensions of the cut-up livers in water and the resulting gases were passed through a filter paper soaked in silver nitrate, which was changed at half-hourly intervals. When the ß counts from the silver phosphide were low, or absent, dilute mineral acid was added and the procedure was repeated.
		4 RESULTS AND DISCUSSION
4.1	**Toxic effects, clinical signs**	Table 6_2-1 shows the results that were obtained.
4.2	**Dermal irritation**	n.a
4.3	**Recovery of labelled compound**	Not stated
4.4	**Percutaneous absorption**	n.a.

Section A6.2 Metabolism studies in mammals

Annex Point IIA6.2/01

4.5	**Results of further experiments**	The authors of the article have conducted further experiments, which are barely reported in this publication: They used the same suspension as mentioned above to feed it to rats and guinea pigs. In dilute acid, zinc phosphide rapidly liberates phosphine and they showed by experiments on rats that when these animals were fed a dose of zinc phosphide in excess of the LD_{50} then, if death resulted, it occurred rapidly and moreover phosphine was detectable in the liver. In lower doses, when animals were killed more than 24 hours after ingestion, no phosphine was detectable in the liver, but on adding acid to this tissue, however, a very faint brown stain was obtained when the gases were passed through a filter paper soaked in methanolic silver nitrate. Such small quantities were present that it was not possible to obtain confirmatory reduced phosphomolybdate blue colour. Further experiments showed that the main urinary excretion product in these poisoned rats and guinea pigs was hypophosphite and that on histological examination their gastric and intestinal mucosae were intact.	X
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	No guideline story, for material and methods see point 3 above.	
5.2	**Results and discussion**	The increase in counts following acidification in rats RA/1 and RA/3, 4, 5 and 6 shows that phosphide is to be found in liver following its oral administration. Rat RA/2 obviously died from phosphine poisoning, rat RA/1 had phosphine and phosphide present in its liver while the four other rats had recovered from the effects of phosphine and had none left in their livers but they had absorbed significant quantities of phosphide. The authors see evidence for particle absorption.	X
5.3	**Conclusion**		
5.3.1	Reliability	4	
5.3.2	Deficiencies	n.a.	

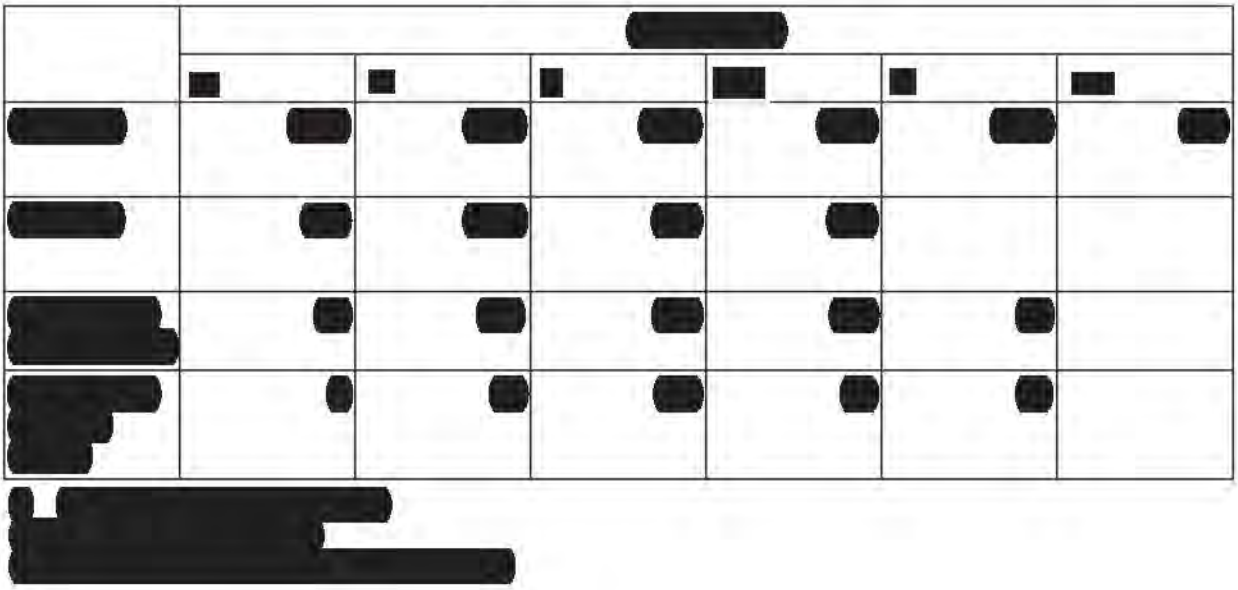
Section A6.2 Metabolism studies in mammals

Annex Point IIA6.2/01

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	

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

[redacted]



[redacted]

Section A6.2 Metabolism studies in mammals

Annex Point IIA6.2/02

Official use only

1 REFERENCE

1.1	**Reference**	Andreev, S.B. et al. (1959): Some results of the use of tracer techniques in the study of plant protection; 2nd Int. Conf. Peaceful Uses Atomic Energy 1958 (27), 85 – 92
1.2	**Data protection**	No
1.2.1	Data owner	published
1.2.2		
1.2.3	Criteria for data protection	No data protection claimed

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	not stated
2.2	**GLP**	No
2.3	**Deviations**	n. a.

3 MATERIALS AND METHODS

3.1	**Test material**	Zinc phosphide
3.1.1	Lot/Batch number	not stated
3.1.2	Specification	Deviating from specification given in section 2 as follows:
3.1.2.1	Description	Zinc phosphide (^{32}P-labelled)
3.1.2.2	Purity	no data
3.1.2.3	Stability	no data.
3.1.2.4	Radiolabelling	^{32}P The experiments were carried out on the grey rat, *Rattus norvegicus* Berk, to which were administered lethal doses (8 mg per 200 g live weight) of zinc phosphide (1) orally (pure substance), (2) subcutaneously (suspended in water) or (3) per rectum (suspended in water). In the subsequent dissection, ^{32}P content was analysed in samples of blood, liver, spleen, kidneys, lungs, muscles, bones, cortex and the medulla oblongata, plus stomach and intestine.

Section A6.2 Metabolism studies in mammals

Annex Point IIA6.2/02

4 RESULTS AND DISCUSSION

(1) Already 15 minutes after the oral administration of a lethal dose of Zinc phosphide to rats, radioactivity is detectable in blood, liver and the anterior section of the intestinal tract. 30 minutes post dosing, radioactivity was also found in the posterior part of the intestine, as well as in spleen, kidneys and lungs, whereas the level in blood and livers had already considerably decreased. One hour p.a., radioactivity was widely distributed within the body, lacking only in brain, bone and muscle. At the same time, some radioactivity could already be recovered from urine. Upon death (usually within 6 – 8 hours p.a.), the radioactivity was present in all organs and tissues with a predominant accumulation in liver. Levels in stomach and intestine had considerably decreased, though still higher than in any other organ. Swelling of the stomach and the small intestine was observed in poisoned animals, which was attribute to the presence of large amounts of PH_3 by analysis (silver phosphide precipitation). Radioactivity had also accumulated at the time of death in the medulla oblongata, correlating with disturbance of breathing and supporting the assumption that the toxicity of Zinc phosphide is related to a disruption of respiratory function.
(2) For the elucidation whether phosphine is formed from Zinc phosphide only in the stomach, Zinc phosphide was also administered per rectum at the same dose level as above. 24 hours p.a., radioactivity was detectable in blood, liver and kidney, apart from the material present in the large intestine. It was not verified whether this radioactivity was in the form of phosphine or Zinc phosphide.
(3) 24 hours after the subcutaneous administration, the radioactivity was detectable only at the site of injection, indicating that decomposition of the formation of mobile toxic compounds would not occur under these circumstances.

Following oral administration of (^{32}P)-Zinc phosphide to rats, radioactivity is rapidly absorbed and distributed. The limited absorption and diminished toxicity after administration per rectum demonstrates that hydrolysis in the acidic milieu of the stomach is the key process that mediates toxicity.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	see 3
5.2	**Results and discussion**	see 4
5.3	**Conclusion**	
5.3.1	Reliability	4
5.3.2	Deficiencies	No

Section A6.2 Metabolism studies in mammals

Annex Point IIA6.2/02

	Evaluation by Competent Authorities Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	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 Metabolism studies in mammals

Annex Point IIA6.2/03

Official use only

1 REFERENCE

1.1	**Reference**	WHO (1988), Environmental Health Criteria 73, pp. 48-51
1.2	**Data protection**	No
1.2.1	Data owner	published
1.2.2		
1.2.3	Criteria for data protection	No data protection claimed

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	not stated
2.2	**GLP**	No
2.3	**Deviations**	not stated

3 MATERIALS AND METHODS

3.1	**Test material**	Aluminium phosphide, Magnesium phosphide, Phosphine
3.1.1	Lot/Batch number	not stated
3.1.2	Specification	Deviating from specification given in section 2 as follows:
3.1.2.1	Description	not stated
3.1.2.2	Purity	not stated
3.1.2.3	Stability	not stated
3.1.2.4	Radiolabelling	no
3.2	**Test Animals**	
3.2.1	Species	Different species, see 5.2
3.2.2	Strain	Not stated
3.2.3	Source	Not stated
3.2.4	Sex	Not stated
3.2.5	Age/weight at study initiation	not stated
3.2.6	Number of animals per group	n. a.
3.2.7	Control animals	not stated
3.3	**Administration/ Exposure**	Oral, inhalation, dermal, see 5.2

Section A6.2 Metabolism studies in mammals

Annex Point IIA6.2/03

3.3.1	Preparation of test site	n.a.
3.3.2	Concentration of test substance	Different concentrations, see 5.2
3.3.3	Specific activity of test substance	n. a.
3.3.4	Volume applied	Different volumes, see 5.2
3.3.5	Size of test site	n.a.
3.3.6	Exposure period	n.a.
3.3.7	Sampling time	n.a.
3.3.8	Samples	See 5.2

4 RESULTS AND DISCUSSION

4.1	**Toxic effects, clinical signs**	See 5.2
4.2	**Dermal irritation**	n.a.
4.3	**Recovery of labelled compound**	Not stated
4.4	**Percutaneous absorption**	n.a.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

No guideline study, for material and methods see point 3 above.

5.2 Results and discussion

Absorption

Inhalation:
Because systemic toxic effects are detectable after short exposures to very low atmospheric concentrations of phosphine, inhaled phosphine is generally considered to be readily absorbed through the lungs. Hydrolysis suggests that aluminium or magnesium phosphides deposited on the moist surfaces of the respiratory tract would release absorbable phosphine.

Dermal:
Hydrolysis of aluminium and magnesium phosphides on the skin would lead to the evolution of gaseous phosphine, which could the be absorbed by inhalation. In general, dermal absorption of phosphine and metal phosphides is insignificant.

Oral:
The oral route is not relevant to the absorption of gaseous phosphine. Human ingestion of tablets containing aluminium phosphide yielded evidence of acidhydrolysable phosphide in blood and liver (Chan et al. 1983). These results indicate that metal phosphides can be absorbed directly.

Section A6.2 Metabolism studies in mammals

Annex Point IIA6.2/03

Distribution

Inhaled phosphine produces neurological and hepatic symptoms suggesting that it reaches the nervous system and liver (Childs & Coates, 1971). Ingested phosphides have been shown to reach the liver and blood in rats and human beings (Curry et al., 1959; Meredith, 1981; Chan et al.; 1983).

Metabolic Transformation

Metal phosphides are hydrolysed to phosphine and the corresponding metal cation (Van Wazer, 1982). In rats, phosphine that is not excreted in the expired air is oxidized and appears in the urine, chiefly as hypophosphite and phosphite (Curry et al., 1959; Meredith, 1981). Meredith (1981) also reported an unidentified metabolite, detectable by paper chromatography and distinct from pyrophosphate and metaphosphate. The fact that (a) phosphine is incompletely oxidized; and (b) the proportion of an administered dose that is eliminated as expired phosphine increases with the dose suggests that the oxidative pathway is slow.

Elimination and Excretion

Hypophosphite is the principal urinary excretion product (Curry et al., 1959).

Reaction with Body Components

Phosphine reacts with some haem- and copper-containing proteins in vitro. Insect cytochrome c oxidase is reduced and not reoxidizable in air (Rajak, 1971). Mammalian haemoglobin does not react with phosphine in the absence of oxygen, but oxyhaemoglobin is converted through Fe^{3+}-containing compounds to a verdichromogen-like material (Trimborn & Klimmer, 1962). The nature of the reaction between phosphine and these proteins is uncertain, but oxyhaemoglobin is denatured and a variety of enzymes are inhibited by reaction of phosphine.

5.3 Conclusion

5.3.1 Reliability 4

5.3.2 Deficiencies n.a.

Section A6.2 Metabolism studies in mammals

Annex Point IIA6.2/03

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	2006-12-07
Materials and Methods	Accepted.
Results and discussion	Accepted.
Conclusion	Accepted.
Reliability	2
Acceptability	Acceptable
Remarks	
	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_2-1. Table for Results (referring to point 4.1)

ß-RAY COUNTS AT VARIOUS TIMES

	Time [hours]					
	0	**½**	**1**	**1 ½**	**2**	**2 ½**
Rat RA/2	6500	5500	3200	1200	500*	200
Rat RA/1	450	300*	600	200		
Rat RA/3, 4, 5, and 6 (a)**	36	32*	300	110	64	
Rat RA/3, 4, 5, and 6 (b)***	0	0*	153	63	21	

* Time at which acid was added
** Background = 32 c.p.m.
*** Readings repeated, background = 1 c.p.m.

Section A 6.2 Annex Point IIA 6.2	Metabolism studies and toxicokinetics	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data [X] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [ ]** **Other justification [ ]**	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	

Section A 6.2 Annex Point IIA 6.2	Metabolism studies and toxicokinetics
Conclusion	[redacted]
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A 6.3.1 Annex Point IIA 6.3.1	Repeated dose toxicity (oral)	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data [X] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	
Conclusion	[redacted]	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A6.3.2 Annex Point IIA6.3.2	Repeated dose toxicity (dermal)	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data [X] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification: [redacted]		
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	
Conclusion	[redacted]	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA VI.6.3.3 (Inhalation)

Official use only

		1 REFERENCE
1.1	**Reference**	Omae, K. et al. (1996): Acute and sub-acute inhalation toxicity of highly purified phosphine (PH_3) in male ICR mice; J. Occup. Health 38, 36 - 42
1.2	**Data protection**	No
1.2.1	Data owner	published
1.2.2		
1.2.3	Criteria for data protection	No data protection claimed
		2 GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	not stated
2.2	**GLP**	not stated (It is not stated in this publication, if the original study was conducted according GLP, but since the investigations were carried out in 1996, it can be presumed that the study was conducted in compliance with the GLP regulations.)
2.3	**Deviations**	n. a.
		3 MATERIALS AND METHODS
3.1	**Test material**	Phosphine
3.1.1	Lot/Batch number	not stated
3.1.2	Specification	Purity: 99.995 %
3.1.2.1	Description	stable, colourless gas
3.1.2.2	Purity	99.995 %
3.1.2.3	Stability	stable
3.2	**Test Animals**	
3.2.1	Species	mouse
3.2.2	Strain	ICR
3.2.3	Source	Charles River
3.2.4	Sex	Male
3.2.5	Age/weight at study initiation	4 weeks old
3.2.6	Number of animals per group	10
3.2.7	Control animals	Yes
3.3	**Administration/ Exposure**	Inhalation

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA VI.6.3.3 (Inhalation)

3.3.1	Duration of treatment	14 days or 28 days	
3.3.2	Frequency of exposure	5 days per week	
3.3.3	Postexposure period	Duration of the observation period for the subacute experiment is not reported.	
3.3.4	**Oral**	**n. a.**	
3.3.5	**Inhalation**		
3.3.5.1	Concentrations	Nominal concentration	5 ppm
		Analytical concentration	4.9 ± 0.3 ppm
3.3.5.2	Particle size	no aerosol	
3.3.5.3	Type or preparation of particles	no study with particles	
3.3.5.4	Type of exposure	Whole body	
3.3.5.5	Vehicle	highly purified nitrogen	
3.3.5.6	Concentration in vehicle	not indicated	
3.3.5.7	Duration of exposure	6 h	
3.3.5.8	Controls	Exposed to filtered room air	
3.3.6	**Dermal**	**n. a.**	
3.3.7	**Intraperitoneal/ Intravenous/ Intratracheal instillation**	**n. a.**	
3.4	**Examinations**		
3.4.1	Observations		
3.4.1.1	Clinical signs	yes, time period not indicated	
3.4.1.2	Mortality	yes, time period not indicated	
3.4.2	Body weight	yes, time period not indicated	
3.4.3	Food consumption	not indicated	
3.4.4	Water consumption	not indicated	
3.4.5	Ophthalmoscopic examination	not indicated	
3.4.6	Haematology	yes, number of animals: all animals time points: end of study Parameters: Total count of red blood cells and white blood cells (WBC) and the differential count of WBC.	
3.4.7	Clinical Chemisty	yes, number of animals: all animals time points: end of study Parameters: blood urea nitrogen, alanine aminotransferase, aspartate	

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA VI.6.3.3 (Inhalation)

		aminotransferase, alkaline phosphatase, cholinesterase inhibition.
3.4.8	Urinalysis	no
3.5	**Sacrifice and pathology**	
3.5.1	Organ Weights	yes organs: liver, kidneys, testes, epididymides, spleen, brain, lung, pancreas
3.5.2	Gross and histopathology	yes all dose groups organs: Organs mentioned in 3.5.1 and additionally: The sciatic nerve, the skull for nasal cavity examination and the femoral bone for bone marrow analysis.
3.5.3	Other examinations	no
3.5.4	Statistics	Student's t-test of Welch's t-test was used for statistical testing of the differences in the mean effect variable for exposed and control mice.
3.6	**Further remarks**	

4 RESULTS AND DISCUSSION

4.1	**Observations**	
4.1.1	Clinical signs	In both the two- and four-week exposure groups, the animals exhibited a face washing movement and were extremely active in their cages in the initial period after the start of exposure. Approximately on hour after start of exposure, their spontaneous motor activity diminished and they gathered in the corners of the exposure cage. Except for mild piloerection, there were no other particularly noteworthy findings.
4.1.2	Mortality	One of the animals in the four-week exposure group died on day 12 after the start of exposure, and right ventricular dilation and pulmonary congestion were observed. All of the other animals survived until the day of necropsy.
4.2	**Body weight gain**	not reported
4.3	**Food consumption and compound intake**	not determined
4.4	**Ophtalmoscopic examination**	not determined
4.5	**Blood analysis**	
4.5.1	Haematology	see table A6_3_3_1
4.5.2	Clinical chemistry	see table A6_3_3_1
4.5.3	Urinalysis	not determined
4.6	**Sacrifice and pathology**	
4.6.1	Organ weights	see table A6_3_3_2
4.6.2	Gross and	see table A6_3_3_3

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA VI.6.3.3 (Inhalation)

	histopathology	
4.7	**Other**	no other significant effects

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	
5.2	**Results and discussion**	Exposure concentrations were 4.9 ± 0.3 ppm. Animals showed face-washing and were extremely active after the start of exposure, but approximately one hour after start of exposure, their spontaneous motor activity diminished. Expect for mild piloerection, there were no other particular findings. One animal of the 4-week exposure period died on day 12, and ventricular dilatation and pulmonary congestion were observed upon necropsy. Body weight gains were significantly different from control after 2 weeks of exposure, but in the 4-week exposure group only the absolute weight of kidneys was significantly decreased. The organ weights of liver, spleen, thymus and kidneys showed statistically significant effects, whereas weights of lungs, testes, heart and brain that did not show statistically significant difference to control. Histopathologic examinations revealed pulmonary congestion in one animal of the 4-week exposure group. Inflammatory changes in the mucosa of the nasal cavity were seen only in animals of the 4-week exposure group. Haematological investigations showed a significant decrease ($p \leq 0.05$) of monocytes after 2 weeks of exposure, and a significant increase ($p \leq 0.05$) of eosinophiles after 4 weeks. ALT and BUN were significantly increased ($p \leq 0.05$) in the 4-week exposure group. There were no differences in the mature sperm counts. Inhalation exposure for up to 4 weeks resulted in a mortality of only a single animal.
5.3	**Conclusion**	
5.3.1	LO(A)EL	not determined.
5.3.2	NO(A)EL	not determined
5.3.3	Other	
5.3.4	Reliability	2
5.3.5	Deficiencies	No

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date 2006-11-16

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA VI.6.3.3 (Inhalation)

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

	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A6_3_3_1. Hematological and serum biochemical examinations in the subacute exposure experiment

	Subacute exposure experiment			
	Control	2-weeks	Control	4-weeks
n	9	10	10	9
RBC (10^4/µl)	835.8 ± 34.6	836.3 ± 31.6	856.3 ± 27.5	857.0 ± 38.4
WBC (10^2/µl)	25.7 ± 3.2	26.0 ± 3.2	29.0 ± 7.3	29.2 ± 10.6
Stab (%)	2.4 ± 1.3	2.7 ± 0.8	2.2 ± 1.2	1.9 ± 0.9
Seg (%)	11.6 ± 3.1	9.3 ± 3.1	12.5 ± 2.3	10.7 ± 3.0
Eosino (%)	0.0	0.7 ± 1.0	0.1 ± 0.3	1.3 ± 0.7*
Mono (%)	1.7 ± 0.8	0.5 ± 0.5*	0.4 ± 0.5	1.1 ± 1.0
Lymph (%)	84.3 ± 4.3	86.8 ± 3.4	84.8 ± 2.3	85.0 ± 4.1
Ch-E (IU/l)	572.2 ± 95.5	586.9 ± 106.9	475.7 ± 52.2	489.2 ± 44.8
AST (IU/l)	77.0 ± 27.2	56.3 ± 16.5	66.4 ± 4.1	69.4 ± 9.0
ALT (IU/l)	20.6 ± 3.9	18.8 ± 6.7	22.3 ± 2.4	27.4 ± 4.0*
ALP (IU/l)	75.6 ± 17.7	80.7 ± 11.0	73.8 ± 7.1	70.2 ± 5.4

* $p < 0.05$ compared to control group

Table A6_3_3-2. Organ weight (gram) in subacute exposure experiment

	No	Liver	bl-Kidneys	Spleen	Lung	Bl-Testes	Heart	Brain	Thymus
Control	9	1.33 ± 0.05	0.47 ± 0.03	0.10 ± 0.02	0.30 ± 0.02	0.21 ± 0.02	0.16 ± 0.01	0.50 ± 0.02	0.06 ± 0.01
2-weeks	10	1.22 ± 0.10*	0.45 ± 0.07	0.07 ± 0.02*	0.26 ± 0.05	0.20± 0.01	0.15 ± 0.02	0.50 ± 0.01	0.05 ± 0.01*
Control	10	1.30 ± 0.13	0.56 ± 0.04	0.08 ± 0.02	0.26 ± 0.02	0.23 ± 0.03	0.17 ± 0.02	0.49 ± 0.02	0.03 ± 0.01
4-weeks	9	1.29 ± 0.08	0.52 ± 0.04*	0.09 ± 0.02	0.25 ± 0.02	0.22 ± 0.03	0.17 ± 0.02	0.49 ± 0.02	0.04 ± 0.01

* _ $p < 0.05$ compared to control group

Table A6_3_3-3. Incidence number of histopathological lesion in the liver, lung, heart and nasal cavity in the acute and subacute exposure experiments

	Acute exposure experiment					Subacute exposure experiment			
	Cont	1 hr	2 hrs	4 hrs	8 hrs*	Cont	2-wks	Cont	4-wks
n	10	10	10	10	10	10	10	10	10
Lung									
Inflamation	0	0	0	0	2	0	0	0	0
Bleeding	2	3	2	1	1	1	0	0	0
Congestion	0	2	1	3	10	0	0	0	1
Liver									
Fatty degeneration of the hepatic cells	2	2	2	2	3	3	2	4	3
Microvacuole in the hepatic cells	0	0	0	0	7	2	1	2	8
Accumulation of cells in the sinusoid	6	5	2	5	0	3	3	0	4
Congestion	0	0	0	0	9	0	0	0	0
Heart									
Inflamation	1	0	1	0	0	0	0	0	0
Edema	0	0	0	0	1	0	0	0	0
Papillary muscle necrosis	0	0	0	0	1	0	0	0	
Nasal cavity									
Exucate	0	0	1	10	5	0	0	0	2
Necrotic epithelial cells and cell infiltration	0	0	3	10	3	0	0	0	2

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA VI.6.4

(Subchronic oral toxicity test)

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1 REFERENCE

1.1	**Reference**	[redacted]Untersuchungen zur subchronischen Toxizität von Aluminiumphosphid, 90-Tage-Test an wachsenden Wistarratten[redacted] (Translation: "Study on the Subchronical toxicity of Aluminium phosphide, 90-day-test on growing wistar rats)
1.2	**Data protection**	No
1.2.1	Data owner	Detia Freyberg GmbH
1.2.2		
1.2.3	Criteria for data protection	No data protection claimed

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	[redacted]

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA VI.6.4

(Subchronic oral toxicity test)

[redacted]

2.2 GLP

2.3 Deviations

3 MATERIALS AND METHODS

3.1 Test material

3.1.1 Lot/Batch number

3.1.2 Specification

3.1.2.1 Description

3.1.2.2 Purity

3.1.2.3 Stability

3.2 Test Animals

3.2.1 Species

3.2.2 Strain

3.2.3 Source

3.2.4 Sex

3.2.5 Age/weight at study initiation

3.2.6 Number of animals per group

3.2.7 Control animals

3.3 Administration/ Exposure

3.3.1 Duration of treatment

3.3.2 Frequency of exposure

3.3.3 Postexposure period

3.3.4 Oral

3.3.4.1 Type

3.3.4.2 Concentration

3.3.4.3 Vehicle

3.3.4.4 Concentration in vehicle

3.3.4.5 Total volume applied

3.3.4.6 Controls

3.4 Examinations

3.4.1 Observations

3.4.1.1 Clinical signs

3.4.1.2 Mortality

3.4.2 Body weight

3.4.3 Food consumption

3.4.4 Water consumption

3.4.5 Ophthalmoscopic examination

3.4.6 Haematology

3.4.7 Clinical Chemisty

3.4.8 Urinalysis

3.5 Sacrifice and pathology

3.5.1 Organ Weights

3.5.2 Gross and histopathology

3.5.3 Other examinations

3.5.4 Statistics

3.6 Further remarks

4 RESULTS AND DISCUSSION

4.1 Observations

4.1.1 Clinical signs

4.1.2 Mortality

4.2 Body weight gain

4.3 Food consumption and compound intake

4.4 Ophtalmoscopic examination

4.5 Blood analysis

4.5.1 Haematology

4.5.2 Clinical chemistry

[redacted]

4.5.3 Urinalysis

[redacted]

4.6 Sacrifice and pathology

4.6.1 Organ weights

[redacted]

4.6.2 Gross and histopathology

[redacted]

4.7 Other

[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted]

5.2 Results and discussion

[redacted]

5.3 Conclusion

5.3.1	LO(A)EL	not calculated
5.3.2	NO(A)EL	0.1 mg/kg
5.3.3	Other	
5.3.4	Reliability	1
5.3.5	Deficiencies	No

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

	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

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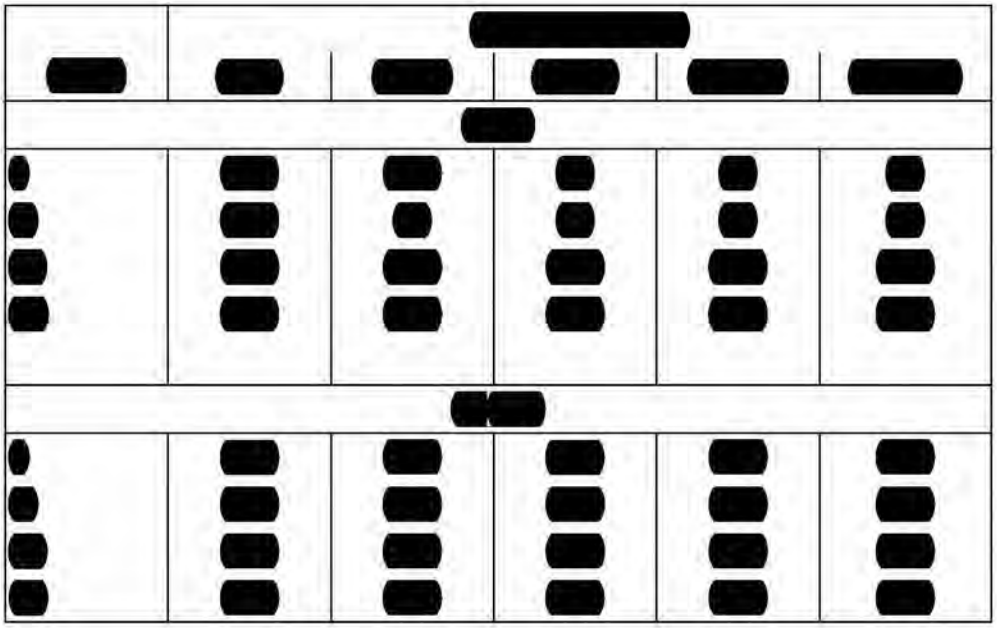

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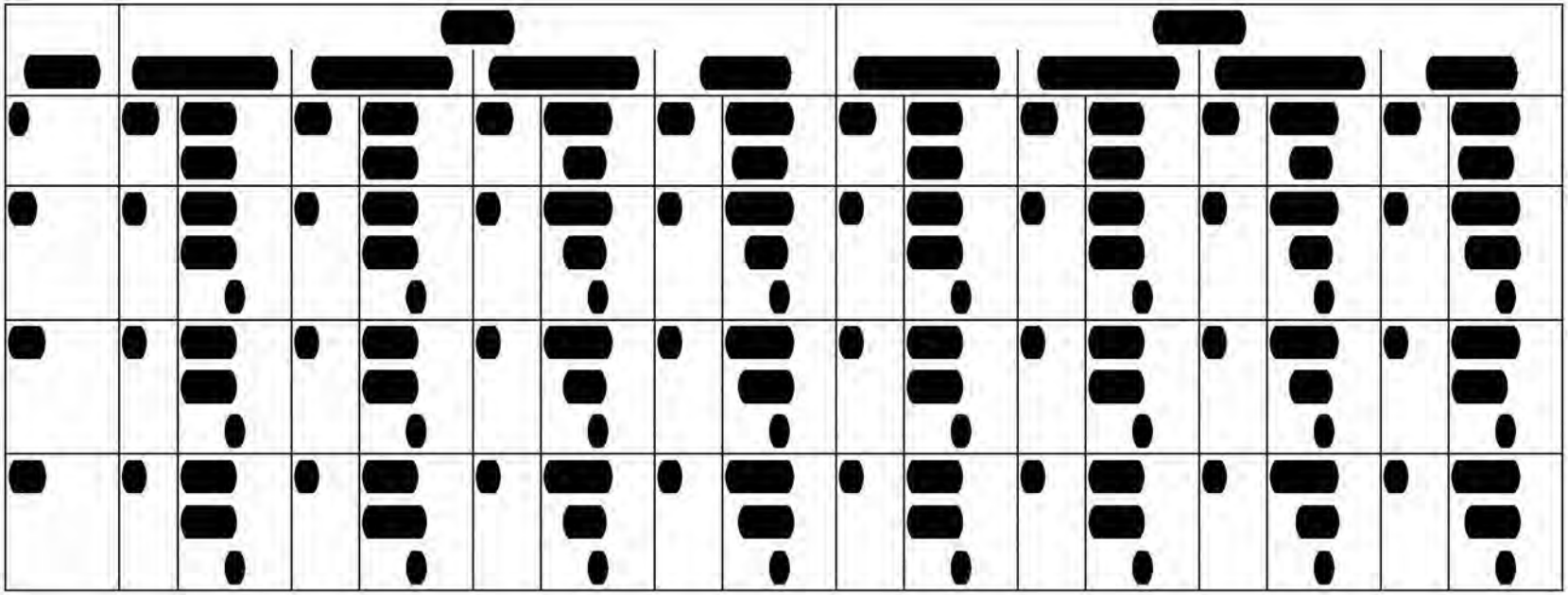

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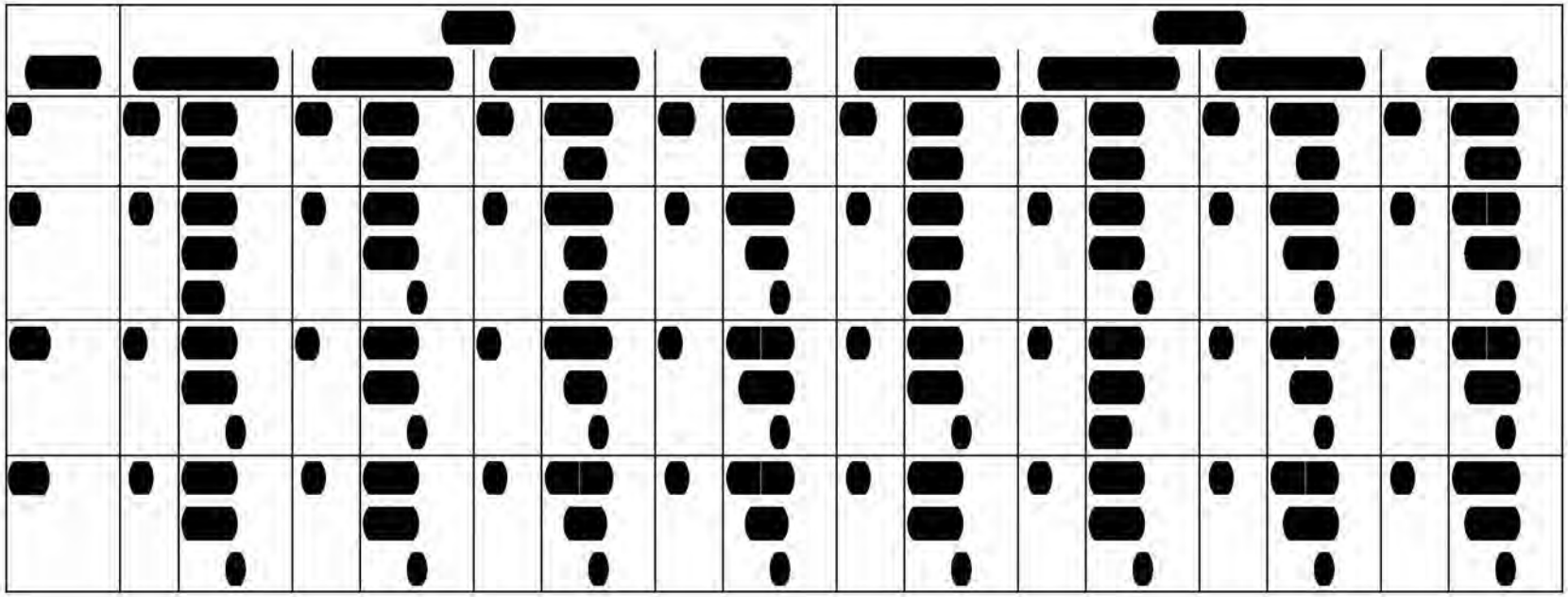

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[redacted]	[redacted]		[redacted]		[redacted]		[redacted]		[redacted]		[redacted]		[redacted]		[redacted]	
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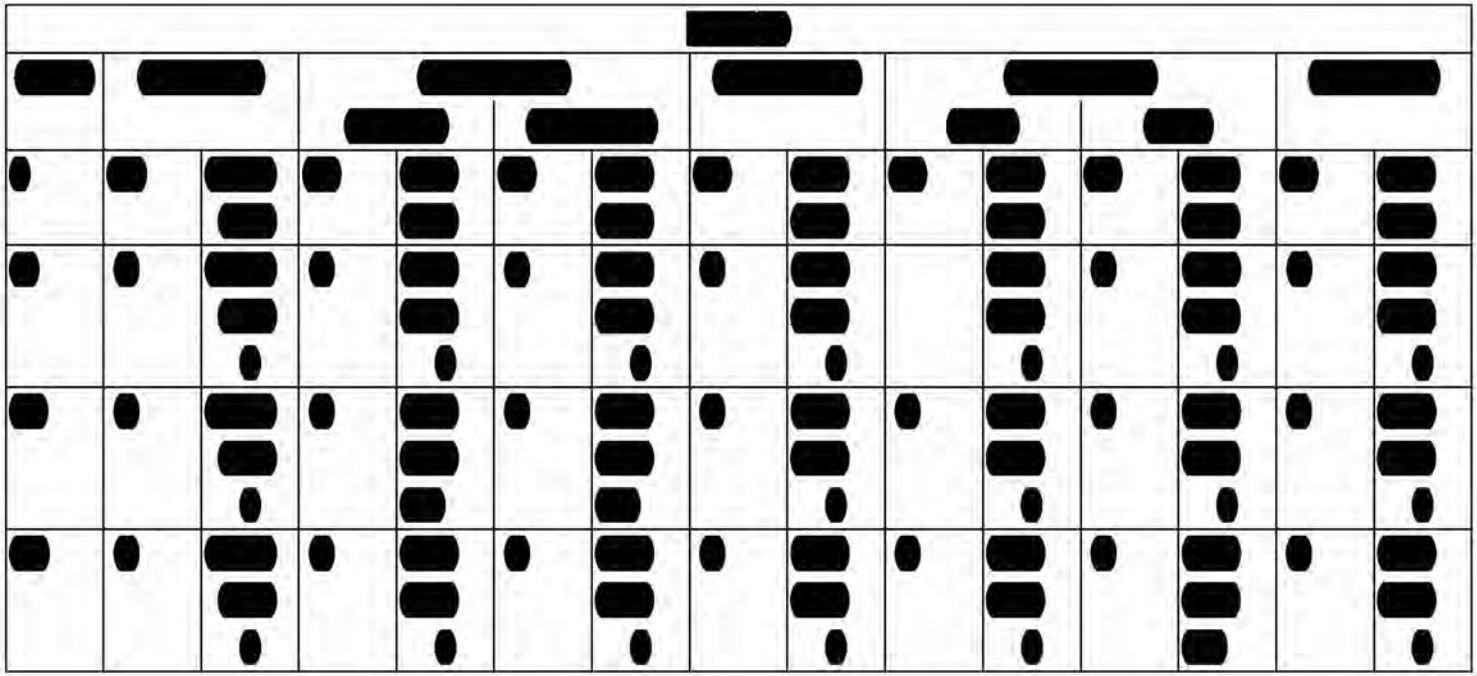

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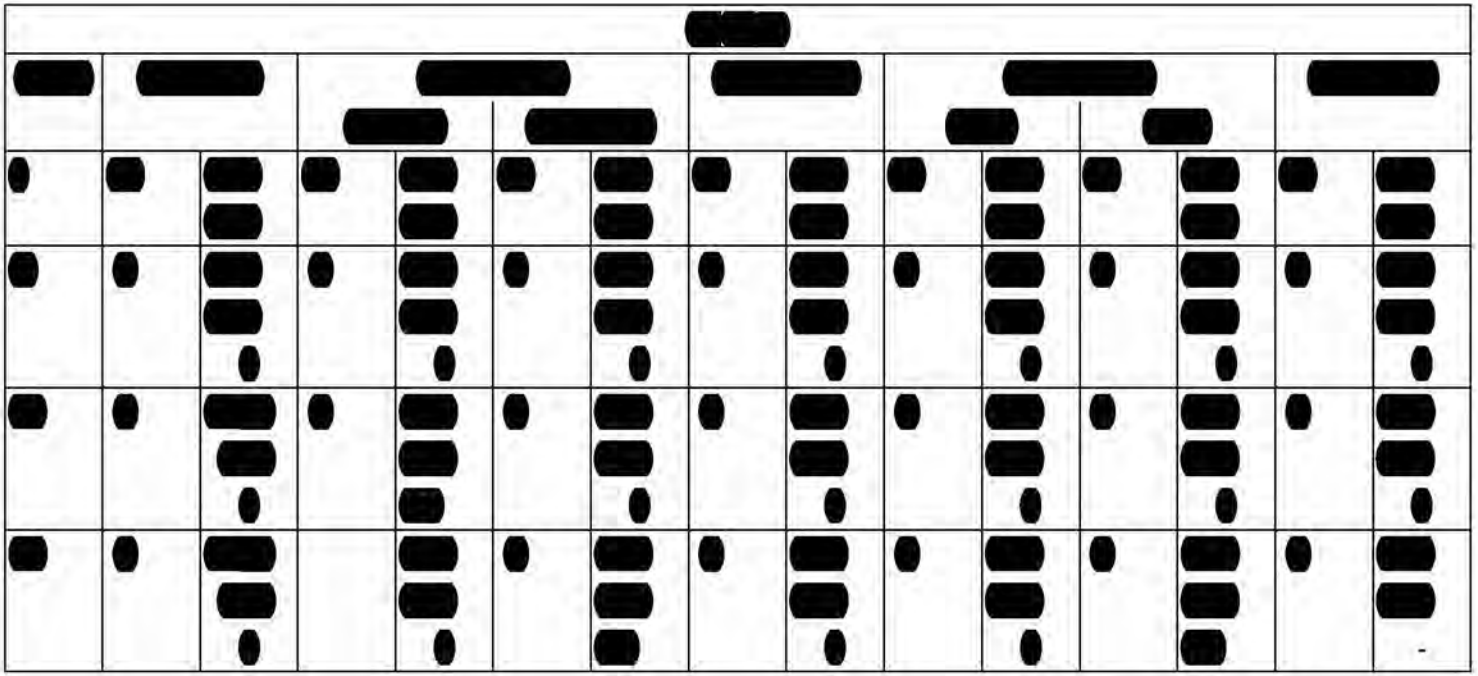

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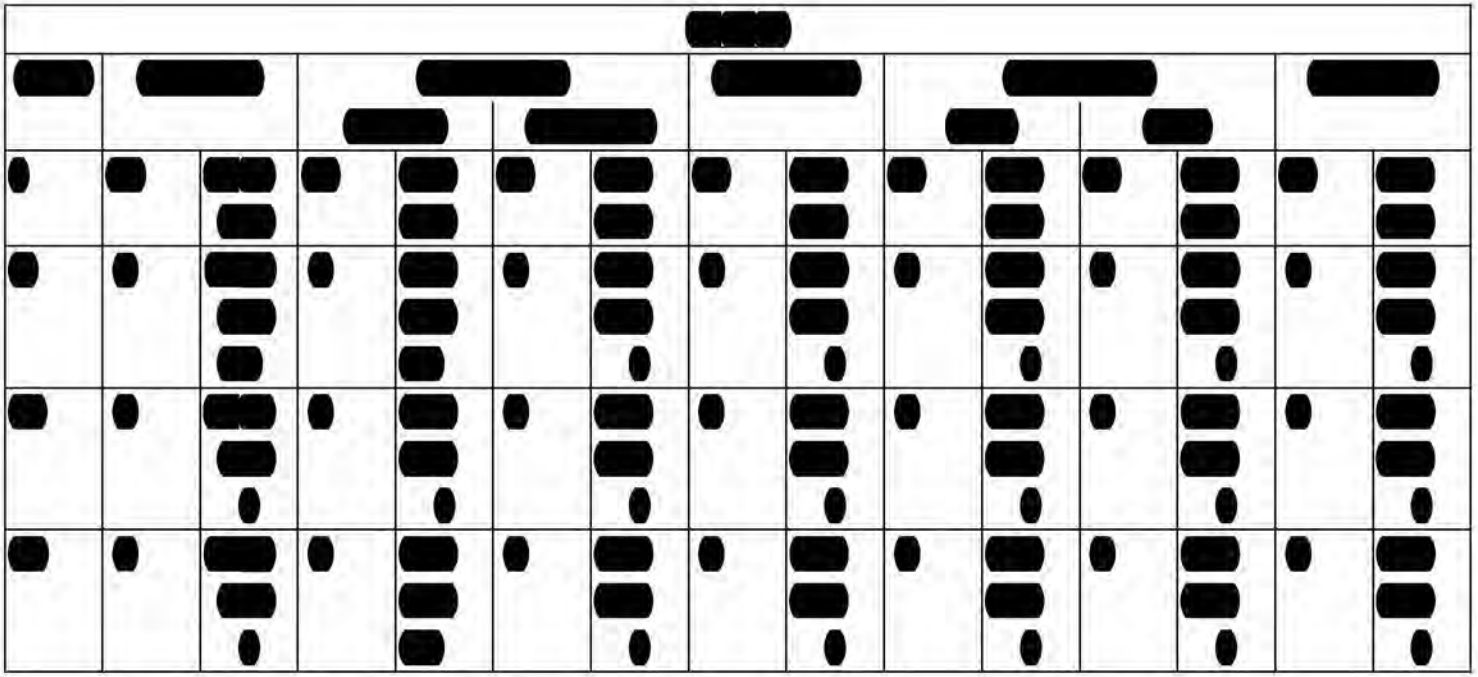

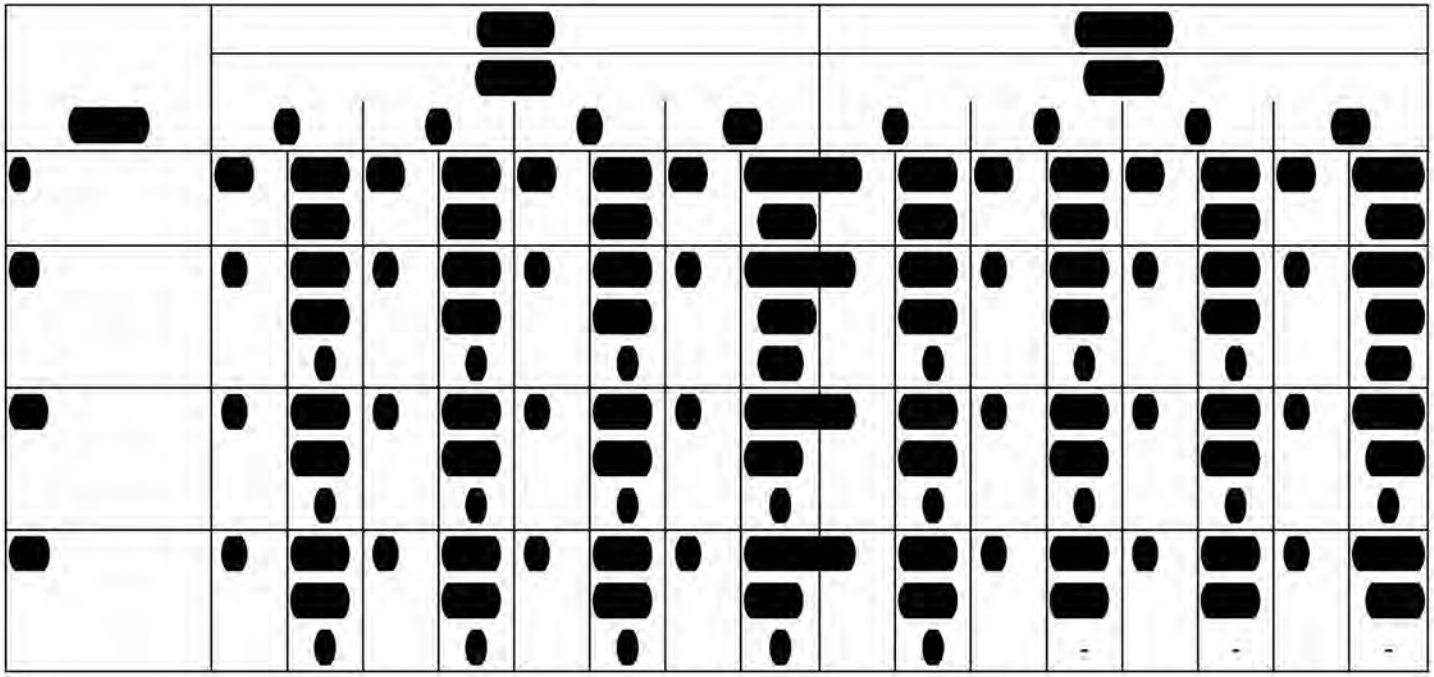

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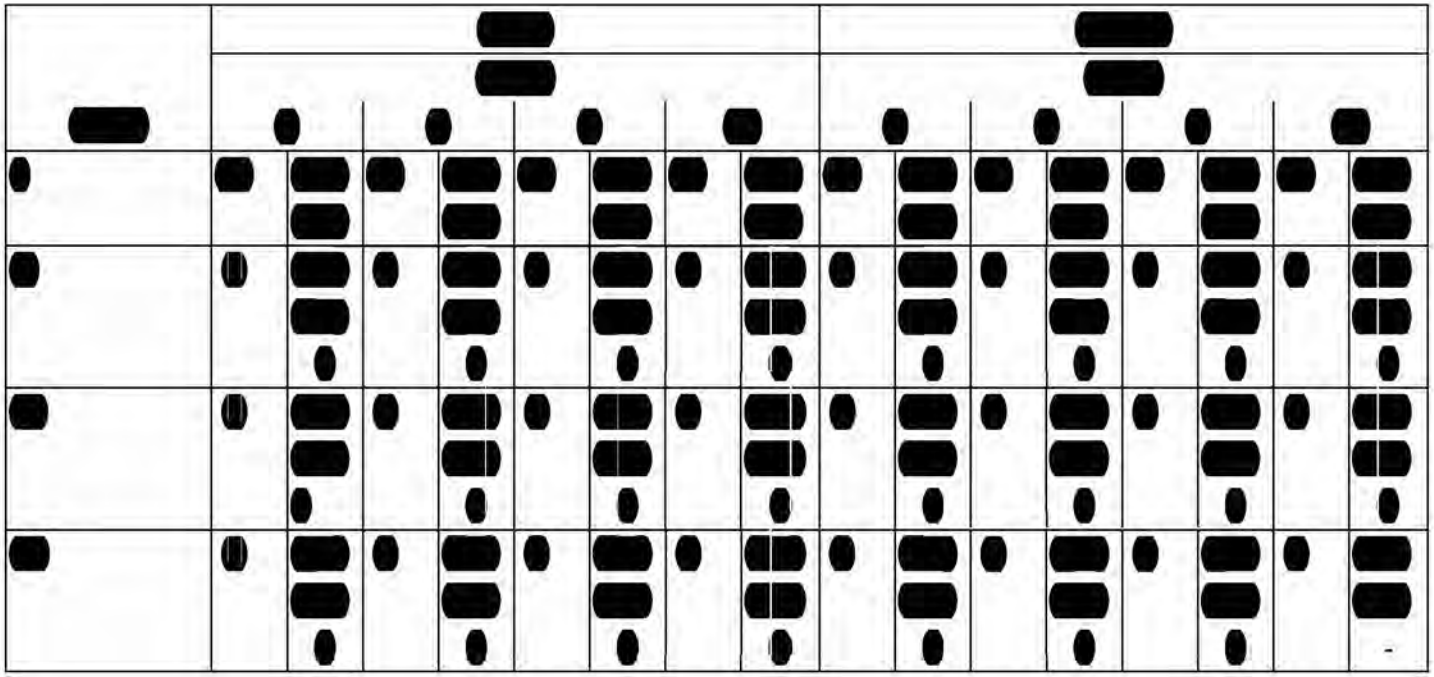

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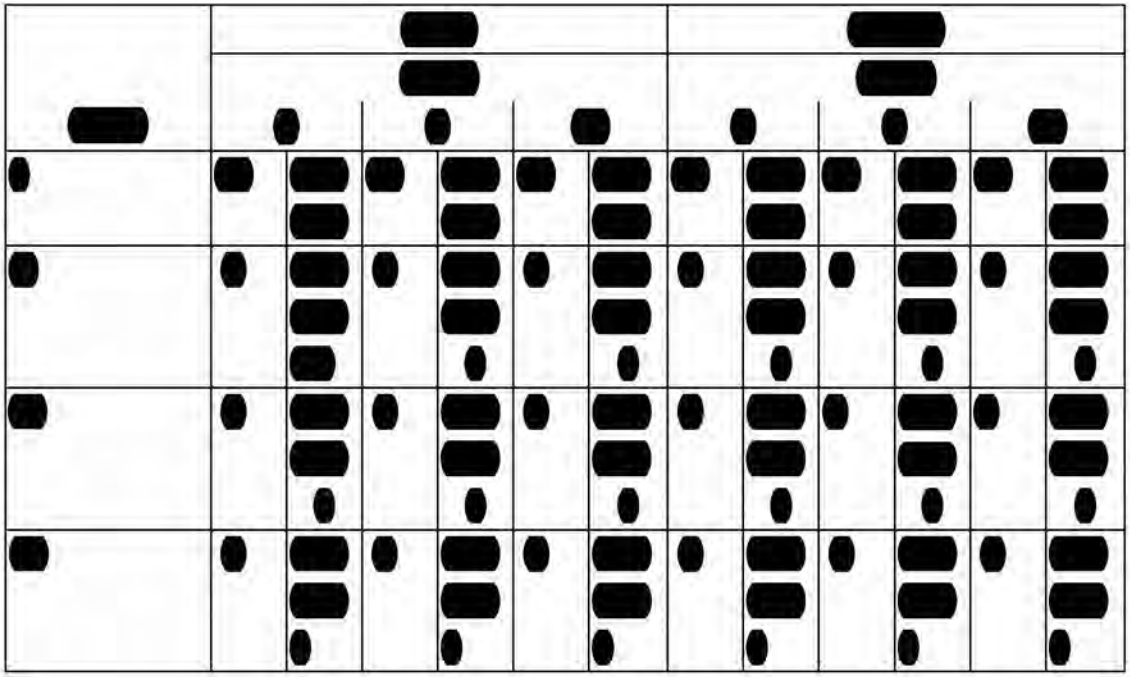

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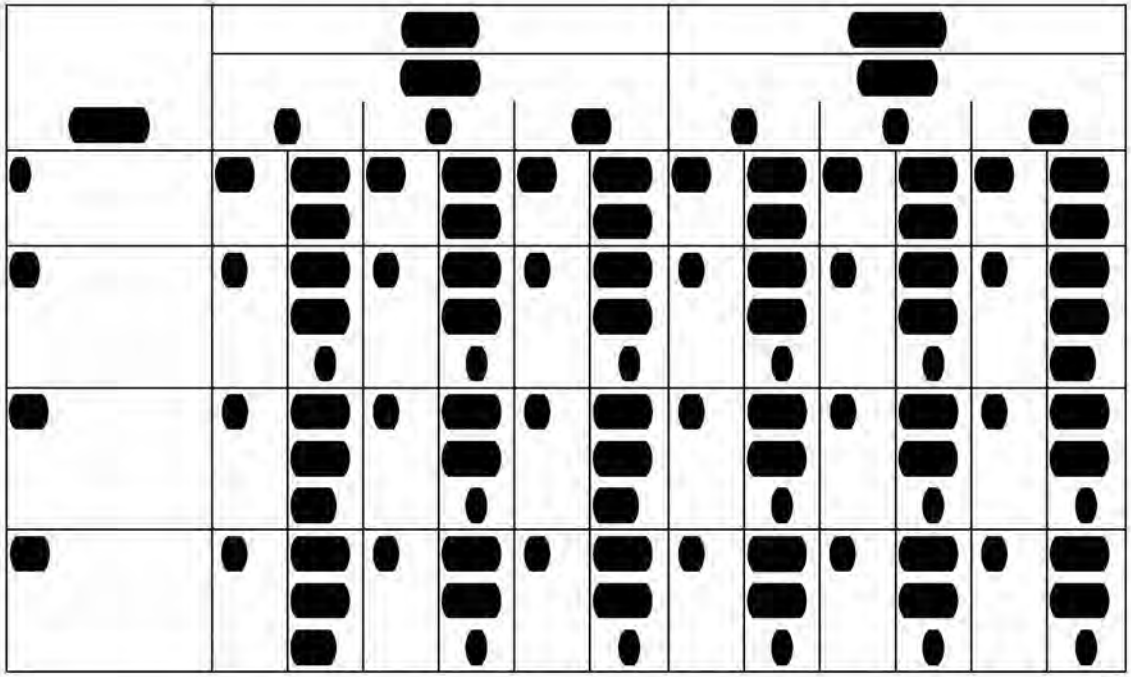

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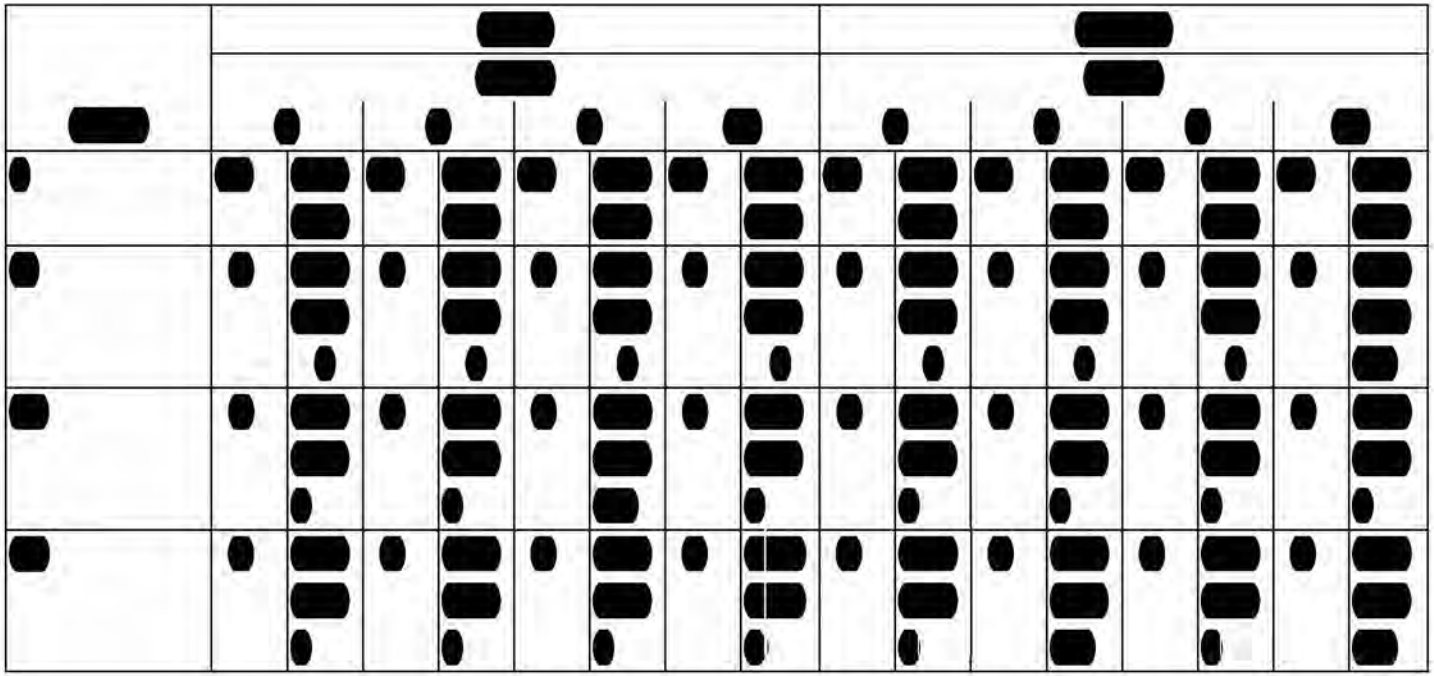

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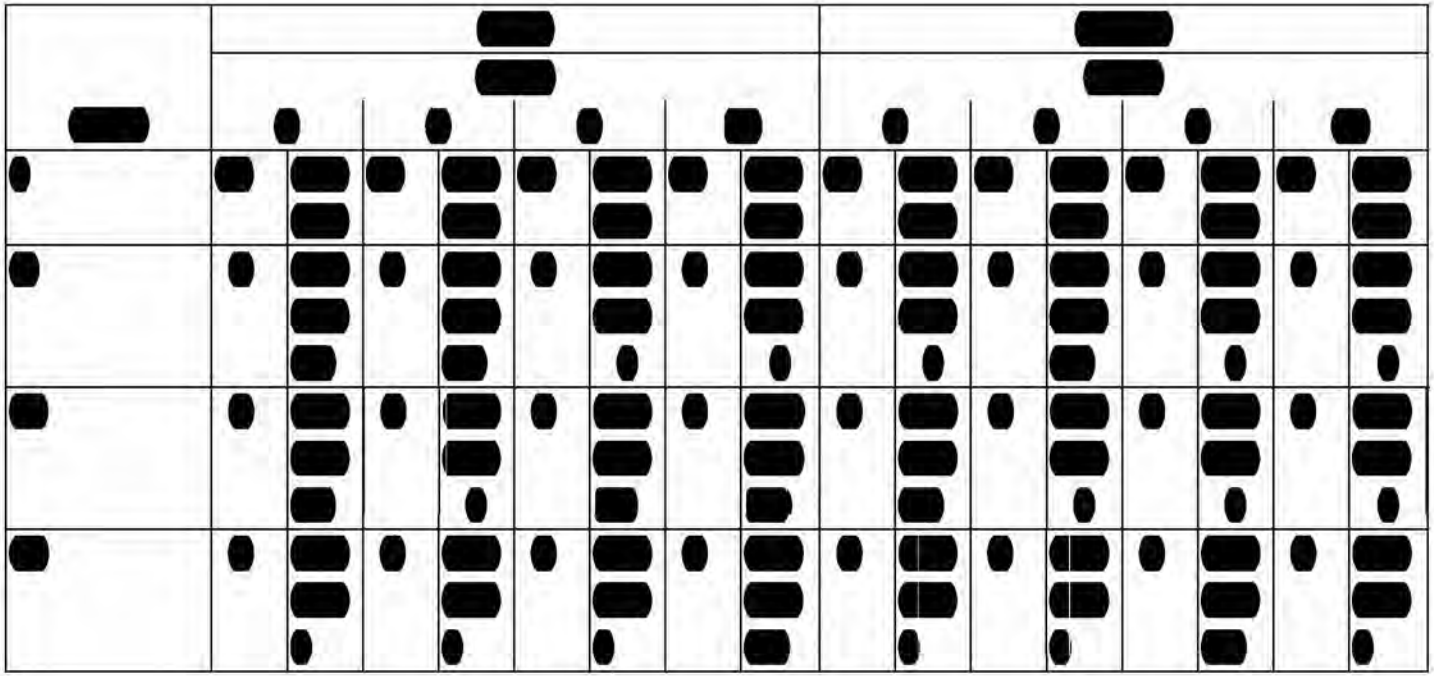

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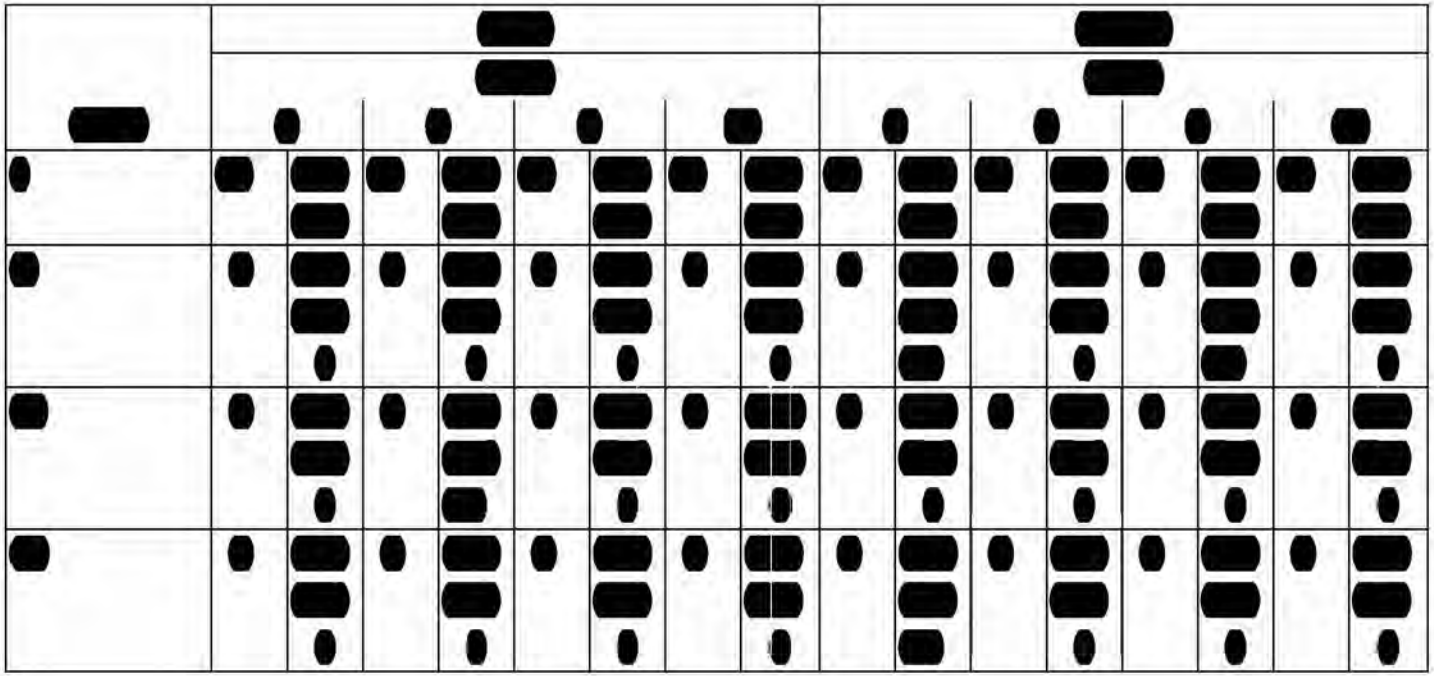

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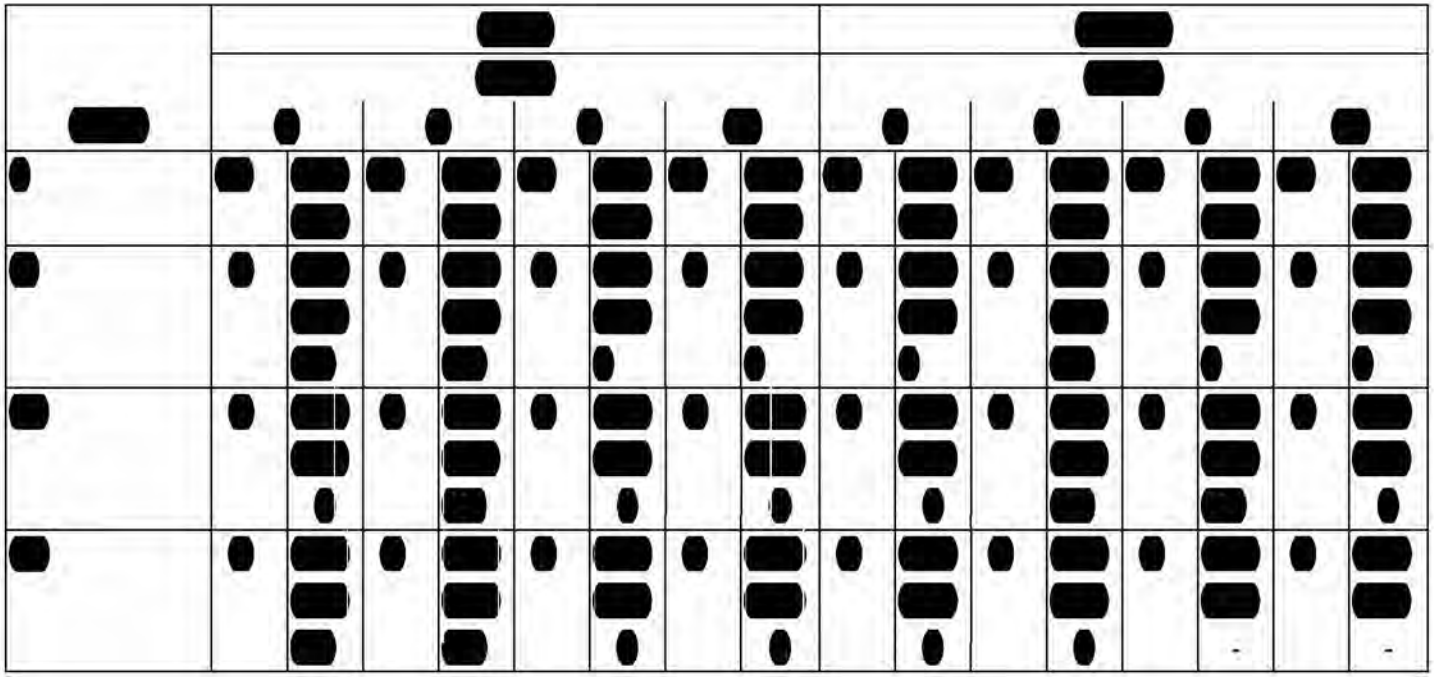


Section A6.4.1 Annex Point IIA VI 6.4	Subchronic oral toxicity test, non-rodent	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data [X]	**Technically not feasible [ ]**	**Scientifically unjustified [X]**
Limited exposure [ ]	**Other justification [ ]**	

Detailed justification:

[redacted]

Section A6.4.1 Annex Point IIA VI 6.4	Subchronic oral toxicity test, non-rodent
Undertaking of intended data submission [ ]	
	Evaluation by Competent Authorities
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Evaluation of applicant's justification	[redacted]
Conclusion	[redacted]
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A6.4.2 Annex Point IIA6.4	Subchronic toxicity (dermal)	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data [X]	**Technically not feasible [ ]** **Scientifically unjustified [X]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification: [redacted]		
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	
Conclusion	[redacted]	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA6.4.3 *(Subchronic inhalation toxicity test)*

Official use only

1 REFERENCE

1.1 Reference

[redacted] A THIRTEEN WEEK INHALATION TOXICITY STUDY OF PHOSPHINE (PH_3) IN THE RAT. [redacted]

1.2 Data protection

1.2.1 Data owner: Detia Freyberg GmbH

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: [redacted]

3. MATERIALS AND METHODS

3.1 Test material: [redacted]

3.1.1 Lot/Batch number: [redacted]

3.1.2 Specification: [redacted]

3.1.2.2 Purity: [redacted]

3.2 – 3.5 Test Animals/Administration/Exposure/Examinations/Sacrifice and pathology

[redacted]

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA6.4.3 *(Subchronic inhalation toxicity test)*

4 RESULTS AND DISCUSSION

Three 6-hour exposures to 10 ppm phosphine were fatal to female rats. All other haematology, clinical chemistry, body weight and food consumption effects seen at this and lower exposure levels were completely reversible either during the exposure period or after a four week recovery period.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	[redacted]
5.2	**Results and discussion**	[redacted]
5.3	**Conclusion**	
5.3.1	LO(A)EL	[redacted]
5.3.2	NO(A)EL	[redacted]
5.3.3	Reliability	[redacted]
5.3.4	Deficiencies	[redacted]

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA6.4.3 *(Subchronic inhalation toxicity test)*

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

Section A6.4.3 Annex Point IIA VI 6.4	Subchronic inhalation toxicity test, non-rodent	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data [X]	**Technically not feasible [ ]**	**Scientifically unjustified [X]**
Limited exposure [ ]	**Other justification [ ]**	

Detailed justification:

[redacted]

Section A6.4.3 Annex Point IIA VI 6.4	Subchronic inhalation toxicity test, non-rodent
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*
	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Evaluation of applicant's justification	[redacted]

Section A6.4.3 Annex Point IIA VI 6.4	Subchronic inhalation toxicity test, non-rodent
	[redacted]
Conclusion	[redacted]
Remarks	

	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA6.5/01 *Chronic toxicity (inhalation)*

Official use only

	1 REFERENCE	
1.1	**Reference**	[redacted]2-YEAR COMBINED INHALATION CHRONIC TOXICITY AND ONCOGENICITY STUDY OF PHOSPHINE IN RATS.[redacted]
1.2	**Data protection**	Yes
1.2.1	Data owner	Detia Freyberg GmbH
1.2.2		
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**	[redacted]
	3 MATERIALS AND METHODS	
3.1	**Test material**	[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]
3.1.2.3	Stability	[redacted]
3.2	**Test Animals**	
3.2.1	Species	[redacted]
3.2.2	Strain	[redacted]
3.2.3	Source	[redacted]
3.2.4	Sex	[redacted]
3.2.5	Age/weight at study initiation	[redacted]
3.2.6	Number of animals per group	[redacted]
3.2.7	Control animals	[redacted]

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA6.5/01 *Chronic toxicity (inhalation)*

3.3	**Administration/ Exposure**	[redacted]
3.3.1	Duration of treatment	[redacted]
3.3.2	Frequency of exposure	[redacted]
3.3.3	Postexposure period	[redacted]
3.3.4	**Oral**	
3.3.4.1	Type	[redacted]
3.3.4.2	Concentration	[redacted]
3.3.4.3	Vehicle	[redacted]
3.3.4.4	Concentration in vehicle	[redacted]
3.3.4.5	Total volume applied	[redacted]
3.3.4.6	Controls	[redacted]
3.3.5	**Inhalation**	
3.3.5.1	Concentrations	[redacted]
3.3.5.2	Particle size	[redacted]
3.3.5.3	Type or preparation of particles	[redacted]
3.3.5.4	Type of exposure	[redacted]
3.3.5.5	Vehicle	[redacted]
3.3.5.6	Concentration in vehicle	[redacted]
3.3.5.7	Duration of exposure	[redacted]
3.3.5.8	Controls	[redacted]

3.3.6 Dermal

3.3.6.1 Area covered

3.3.6.2 Occlusion

3.3.6.3 Vehicle

3.3.6.4 Concentration in vehicle

3.3.6.5 Total volume applied

3.3.6.6 Duration of exposure

3.3.6.7 Removal of test substance

3.3.6.8 Controls

3.3.7 Intraperitoneal/ Intravenous/ Intratracheal instillation

3.3.7.1 Vehicle

3.3.7.2 Concentration in vehicle

3.3.7.3 Total volume applied

3.3.7.4 Controls

3.4 Examinations

3.4.1 Observations

3.4.1.1 Clinical signs

3.4.1.2 Mortality

3.4.2 Body weight

3.4.3 Food consumption

3.4.4 Water consumption

3.4.5 Ophthalmoscopic examination

3.4.6 Haematology

[redacted]

3.4.7 Clinical Chemisty yes,

[redacted]

3.4.8 Urinalysis

[redacted]

3.5 Sacrifice and pathology

3.5.1 Organ Weights yes

[redacted]

3.5.2 Gross and histopathology

[redacted]

[redacted]

3.5.3 Other examinations

3.5.4 Statistics

[redacted]

3.6 Further remarks

4 RESULTS AND DISCUSSION

4.1 Observations

4.1.1 Clinical signs

Individual clinical signs and masses are presented in the original study report.

There was no apparent test article-related effect seen in the detailed clinical observations. The findings recorded occurred with a low incidence and were sporadic.

4.1.2 Mortality

A summary of mortality is presented in a table. A record of animal fate and disposition is presented in the original study report.

[redacted]

4.2 Body weight gain

[redacted]

4.3 Food consumption and compound intake

[redacted]

4.4 Ophtalmoscopic examination

[redacted]

4.5 Blood analysis

4.5.1 Haematology

[redacted]

4.5.2 Clinical chemistry

[redacted]

control males had an increase in mean cholesterol at this interval, these

4.5.3 Urinalysis

4.6 Sacrifice and pathology

4.6.1 Organ weights

4.6.2 Gross and histopathology

[redacted]

[redacted]

4.7 Other

[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted]

5.2 Results and discussion

[redacted]

5.3 Conclusion

5.3.1 LO(A)EL [redacted]

5.3.2 NO(A)EL [redacted]

5.3.3 Other

5.3.4 Reliability [redacted]

5.3.5 Deficiencies [redacted]

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

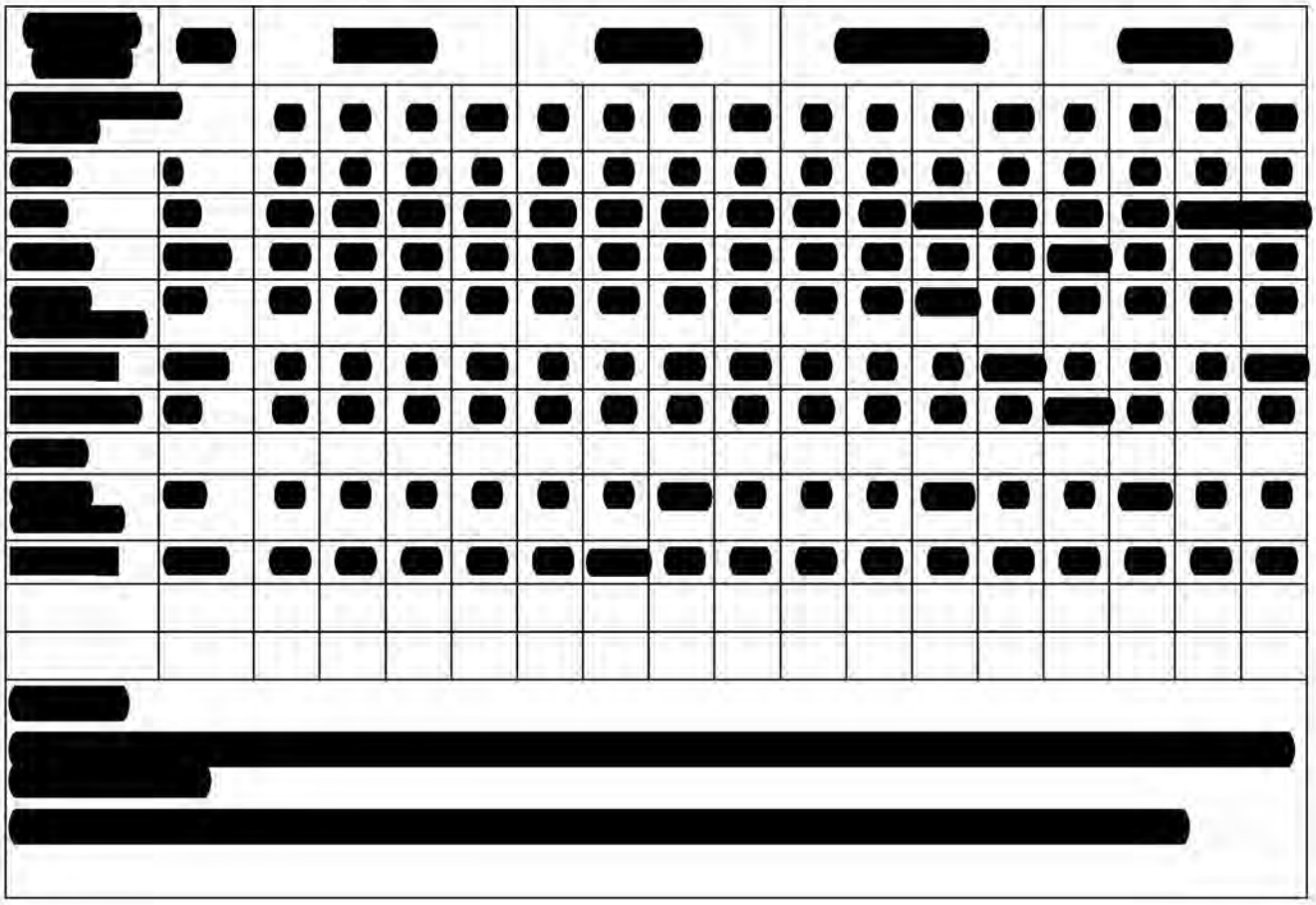
Date	[redacted]
Materials and Methods	
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	

COMMENTS FROM ... *(specify)*

Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*

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

[redacted]



[redacted]

[redacted]

[redacted]

[redacted]

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA VI.6.5/02 *Chronic toxicity*

Official use only

		1 REFERENCE
1.1	**Reference**	A.-M. Cabrol Telle et al (1985): NUTRITIONAL AND TOXICOLOGICAL EFFECTS OF LONG-TERM INGESTION OF PHOSPHINE-FUMIGATED DIET BY THE RAT, Fd. Chem. Toxic., Vol 23, No. 11, pp. 1001 – 1009, 1985
1.2	**Data protection**	No
1.2.1	Data owner	published
1.2.2		
1.2.3	Criteria for data protection	No data protection claimed
		2 GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	No. (no guidelines available)
2.2	**GLP**	not stated
2.3	**Deviations**	n.a.
		3 MATERIALS AND METHODS
3.1	**Test material**	Phosphine released from aluminium phosphide. The study was conducted with Aluminium phosphide, not with Magnesium phosphide. Since both Metal phosphides react with moisture to evolve Phosphine gas which is the substance responsible for the toxicity of the product, tests with Aluminium phosphide can be used to assess the toxicity of Magnesium phosphide.
3.1.1	Lot/Batch number	not stated
3.1.2	Specification	Deviating from specification given in section 2 as follows:
3.1.2.1	Description	The test diet was subjected to long-term fumigation with phosphine. The pellets were stored in bulk in sealed containers in which the level of fumigant was maintained at 2000 ppm. Sufficient quantities of diet were stored for periods of 6 months, so that over the 2-yr experiment the food received by the test animals had been fumigated for at least 6 months and had been maintained under phosphine until just before consumption, when it was aerated for 48 hr.
3.1.2.2	Purity	not stated
3.1.2.3	Stability	not stated
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain	Sprague-Dawley
3.2.3	Source	not stated
3.2.4	Sex	60 males, 60 females
3.2.5	Age/weight at study initiation	Approximately 50 g

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA VI.6.5/02 *Chronic toxicity*

3.2.6	Number of animals per group	30 males and 30 females per group
3.2.7	Control animals	Yes
3.3	**Administration/ Exposure**	Oral
3.3.1	Duration of treatment	2 years
3.3.2	Frequency of exposure	daily (fumigated diet)
3.3.3	Postexposure period	not stated
3.3.4	**Oral**	
3.3.4.1	Type	in food
3.3.4.2	Concentration	The average residual level of phosphine was 5 ppb.
3.3.4.3	Vehicle	diet
3.3.4.4	Concentration in vehicle	5 ppb (see 3.3.4.2)
3.3.4.5	Total volume applied	not stated
3.3.4.6	Controls	plain diet, kept under identical conditions but without fumigation.
3.4	**Examinations**	
3.4.1	Observations	
3.4.1.1	Clinical signs	yes, daily
3.4.1.2	Mortality	yes, daily
3.4.2	Body weight	yes, each week during the first 3 months and than at longer intervals (every 2 or 3 week)
3.4.3	Food consumption	yes, each week during the first 3 months and than at longer intervals (every 2 or 3 week)
3.4.4	Water consumption	not stated
3.4.5	Ophthalmoscopic examination	not stated
3.4.6	Haematology	yes, number of animals: ten males, ten females time points: every three months Parameters: Haematocrit, erythrocyte count, total and differential leukocyte count
3.4.7	Clinical Chemisty	yes, number of animals: ten males, ten females time points: every three months Parameters: sodium, potassium, glucose, total cholesterol, urea, total bilirubin, creatinine, total protein, alkaline phosphatase, calcium chloride, carbonate phosphate, iron, uric acid, glutamic-pyruvic and glutamic-oxalacetic transaminase
3.4.8	Urinalysis	yes,

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA VI.6.5/02 *Chronic toxicity*

		number of animals: ten males, ten females time points: every three months Parameters: diuresis, pH, sodium, potassium, phosphorus, urea, creatinine, glutamic-oxalacetic transaminase, glucose ketones, urobilinogen, proteins, nitrite and blood.
3.5	**Sacrifice and pathology**	
3.5.1	Organ Weights	yes After 1 year of feeding, 19 male and 20 female controls and 20 male and 19 female treated rats were killed (one control and one treated rat having already died). The survivors of the remaining 40 animals were killed after 2 yr. At each time, the organs were weighed and examined macroscopically. Histology was carried out on the tissues in each group at 1 yr. Tumour frequency was recorded of all animals following the method of determination used by Fischer, Hutchinson, Berry et al. (1983). organs: parotid glands, stomach, caecum, liver, adrenals, gonads, thymus, lung, heart, spleen, kidney, brain
3.5.2	Gross and histopathology	yes After 1 year of feeding, 19 male and 20 female controls and 20 male and 19 female treated rats were killed (one control and one treated rat having already died). The survivors of the remaining 40 animals were killed after 2 yr. At each time, the organs were weighed and examined macroscopically. Histology was carried out on the tissues in each group at 1 yr. Tumour frequency was recorded of all animals following the method of determination used by Fischer, Hutchinson, Berry et al. (1983). organs: parotid glands, stomach, small intestine, colon, liver, adrenals, gonads, thyroid, thymus, lung, heart, carotid artery, spleen, kidney, muscle samples
3.5.3	Other examinations	no
3.5.4	Statistics	Student's-t-test
3.6	**Further remarks**	
		4 RESULTS AND DISCUSSION
4.1	**Observations**	
4.1.1	Clinical signs	No particular behavioural problems compared with those on the untreated diet.
4.1.2	Mortality	Apart from the one control and one treated rat that died in the first year, three control males, two treated males and one control female died by month and a further three male and two female controls, two treated males and two treated females by month 24.
4.2	**Body weight gain**	The growth curves show a very similar pattern of body-weight gain in the rats on the fumigated diet and the controls. For both sexes, the curves are superimposable up to about wk 8 of the study, when the body weights were slightly greater in the male controls than in the treated males. The reverse being true for the control and treated females. No significant differences persisted in the body weights.
4.3	**Food consumption**	not stated

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA VI.6.5/02 *Chronic toxicity*

	and compound intake	
4.4	**Ophtalmoscopic examination**	no examination
4.5	**Blood analysis**	
4.5.1	Haematology	see table A6_5/02-1
4.5.2	Clinical chemistry	see table A6_5/02-2
4.5.3	Urinalysis	see table A6_5/02-3
4.6	**Sacrifice and pathology**	
4.6.1	Organ weights	The fresh weight of the organs taken from 20 rats of each group after 12 months on the diet did not show any significant differences between the control and treated groups when expressed relative to body weight, except in the case of the thymus, which was slightly heavier in the treated females than in the control group. (see table A6_5/02-4)
4.6.2	Gross and histopathology	Macroscopic examination on the various organs showed no anomalies either in the treated animals or in the controls. However, certain histopathological changes, notably congestion of the duodenum, ulcerous and necrotic zones in the colon and pigmentation indicating degeneration, were found more frequently in the treated animals. In all the other organs, changes of varying severity were observed in both control and treated animals. After 2 yrs in some organs histopathological changes were observed the colon of some treated animals showed ulceration or necrosis and a greater development of lymphoid tissue than in the controls, while zones of necrosis were seen to be more numerous in the duodenum of treated animals . All the organs, in both treated and control animals, showed signs of ageing, but these were particularly apparent in the spleen, kidneys, thymus, liver and adrenals. (see table A6_5/02-5)
4.7	**Other**	A certain number of tumours appeared in the rats killed at 2 yr, but the evaluation of tumour incidences did not show differences between treated and untreated rats.
		5 APPLICANT'S SUMMARY AND CONCLUSION
5.1	**Materials and methods**	Dietary toxicity study carried out over a period of 2 years.
5.2	**Results and discussion**	The results show that ingestion of a phosphine-fumigated diet by the rat for 2 years does not cause any marked modification of growth, food intake, nitrogen balance, body composition, functional behaviour or the incidence or type of tumours.
5.3	**Conclusion**	
5.3.1	LO(A)EL	not calculated
5.3.2	NO(A)EL	not calculated
5.3.3	Reliability	1
5.3.4	Deficiencies	No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ... *(specify)*
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A6_5/02-1. Results of clinical chemistry haematology and urinalysis

Haematological data for rats fed a phosphine-fumigated diet for up to 2 yr

Group		Erythrocytes (10^6/mm³)	Haematocrit (%)	Leucocytes: Total (10^3/mm³)	Differential* (%): N	E	L	M
Month 6								
Male								
	Control	9.33 ± 0.19	49 ± 1.6	7.88 ± 0.50	19 ± 0.8	1 ± 0.3	74 ± 1.2	6 ± 0.3
	Treated	9.69 ± 0.21	52 ± 0.8	8.98 ± 0.99	19 ± 0.8	3 ± 0.6	74 ± 1.4	5 ± 0.3
Female								
	Control	8.23 ± 0.12	49 ± 0.9	5.42 ± 0.36	22 ± 1.3	2 ± 0.5	70 ± 1.6	5 ± 0.5
	Treated	8.25 ± 0.20	48 ± 1.1	6.74 ± 0.57	18± 0.9	2± 0.6	74 ± 1.3	6 ± 0.3*
Month 12								
Male								
	Control	8.75 ± 0.35	49 ± 1.0	13.55 ± 1.38	21 ± 0.6	0 ± 0.3	76 ± 0.4	3 ± 0.7
	Treated	7.64 ± 0.23	45 ± 0.9	9.80 ± 1.22	22 ± 0.8	0 ± 0.2	72 ± 1.7	3 ± 0.7
Female								
	Control	8.82 ± 0.25	47 ± 0.7	10.49 ± 2.0	24 ± 2.6	1 ± 0.4	76 ± 1.0	3 ± 0.4
	Treated	8.00 ± 0.24	46 ± 0.6	11.27 ± 1.77	23 ± 1.1	1 ± 0.3	73 ± 2.7*	4 ± 0.4
Month 20								
Male								
	Control	8.01 ± 0.55	49 ± 1.3	13.3 ± 0.64				
	Treated	8.97 ± 0.91	48 ± 1.7	9.3 ± 0.32				
Female								
	Control	7.45 ± 0.77	47 ± 1.6	3.6 ± 0.35				
	Treated	8.97 ± 0.90	47 ± 0.8	3.5 ± 0.73				
Month 24								
Male								
	Control	5.79 ± 0.65	44 ± 1.6	6.0 ± 0.18	30 ± 1.2	0 ± 0.2	66 ± 1.3	4 ± 0.4
	Treated	6.70 ± 0.49	45 ± 1.3	10.7 ± 0.41	30 ± 1.2	1 ± 0.3	65 ± 1.1	4 ± 0.4
Female								
	Control	5.43 ± 0.56	45 ± 0.8	5.7 ± 0.24	26 ± 1.4	1 ± 0.2	68 ± 1.5	5 ± 0.4
	Treated	6.33 ± 0.60	45 ± 1.2	10.8 ± 0.32	30 ± 1.7**	1 ± 0.3	62 ± 1.8**	4 ± 0.5

N = Neutrophils, E = Eosinophils, L = Lymphocytes, M = Monocyte

*No basophils were found in any of these differential counts.

Values are means ± SEM for groups of ten rats. Those marked with asterisks differ significantly (by student's t test) from the corresponding control value: * $p < 0,05$; ** $p < 0.01$

Table A6_5/02-2. Results of repeated dose toxicity study

Plasma analysis data for rats fed a phosphine fumigated diet for up to 2 yr.

Plasma component	Values for samples taken at month:							
	3		6		12		24	
	Control group	Treated group	Control group	Treated group	Control group	Treated group	Control group	Treated group
	male							
Urea (mM)	6.01 ± 0.13	6.05 ± 0.31	5.87 ± 0.28	5.47 ± 0.28	6.35 ± 0.26	6.37 ± 0.21	5.71 ± 0.31	5.98 ± 0.75
Creatinine (µM)	46 ± 2.1	45 ± 1.5	39 ± 2.4	45 ± 2.2	53 ± 1.6	45 ± 1.1***	49 ± 3.2	57 ± 6.6
Calcium (mM)	2.67 ± 0.03	2.07 ± 0.32	2.62 ± 0.02	2.66 ± 0.04	2.57 ± 0.03	2.56 ± 0.03	2.61 ± 0.06	2.62 ± 0.06
Phosphate (mM)	2.20 ± 0.06	2.10 ± 0.06	1.65 ± 0.06	1.66 ± 0.09	1.41 ± 0.05	1.53 ± 0.10	1.85 ± 0.13	1.84 ± 0.31
Alk. Pase (U/litre)	255 ± 26.9	293 ± 27.6	182 ± 24.0	181 ± 15.0	141 ± 22.9	129 ± 14.3	97 ± 12.0	105 ± 19.8
Total bilirubin (µM)	2.0 ± 0.00	2.0 ± 0.20	2.0 ± 0.10	2.0 ± 0.10	2.0 ± 0.20	1.0 ± 0.20	2.0 ± 0.20	2.0 ± 0.20
GPT (U/litre)	92 ± 8.2	88 ± 9.2	143 ± 4.5	136 ± 1.7	198 ± 51.8	182 ± 52.8	172 ± 40.6	128 ± 49.4
GOT (U/litre)	52 ± 3.2	49 ± 3.3	70 ± 2.0	65 ± 1.7	245 ± 52.6	218 ± 70.7	284 ± 100	196 ± 124
Uric acid (µM)	28 ± 2.9	28 ± 2.7	21 ± 2.5	20 ± 2.5	13 ± 1.7	19 ± 3.0	23 ± 6.9	37 ± 16.4
Cholesterol (mM)	2.71 ± 0.18	2.87 ± 0.13	3.15 ± 0.13	3.22 ± 0.12	3.33 ± 0.11	3.56 ± 0.16	4.66 ± 0.57	4.01 ± 0.27
Glucose (mM)	7.83 ± 0.28	7.93 ± 0.24	6.32 ± 0.20	6.67 ± 0.18	9.98 ± 0.31	10.55 ± 1.06	9.59 ± 0.78	12.42 ± 2.61

Alk. Pase = Alkaline phosphatase; GPT = Glutamic-pyruvic transaminase; GOT = Glutamic-oxalacetic transaminase

Values are means ± SEM for groups of ten rats. Those marked with asterisks differ significantly (by student's t test) from the corresponding control value: * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Plasma component	Values for samples taken at month:							
	3		6		12		24	
	Control	Treated	Control	Treated	Control	Treated	Control	Treated
	female							
Urea (mM)	5.8 ± 0.17	5.92 ± 0.18	6.18 ± 0.32	5.88 ± 0.18	5.41 ± 0.44	5.57 ± 0.50	6.11 ± 0.65	8.20 ± 2.73
Creatinine (µM)	47 ± 1.3	51 ± 2.3	40 ± 3.8	43 ± 1.9	56 ± 2.4	46 ± 1.7**	67 ± 8.5	70 ± 15.4
Calcium (mM)	2.69 ± 0.05	2.78 ± 0.02	2.72 ± 0.03	2.73 ± 0.03	2.67 ± 0.06	2.57 ± 0.04	2.69 ± 0.10	2.66 ± 0.07
Phosphate (mM)	2.47 ± 0.10	2.41 ± 0.11	1.76 ± 0.03	1.74 ± 0.07	1.69 ± 0.03	1.67 ± 0.08	1.84 ± 0.45	2.09 ± 0.28
Alk. Pase (U/litre)	265 ± 32.7	329 ± 29.4	188 ± 16.6	232 ± 23.5	122 ± 24.8	114 ± 10.7	116 ± 12.2	124 ± 24.7
Total bilirubin (µM)	2.0 ± 0.00	2.0 ± 0.00	2.0 ± 0.30	2.0 ± 0.20	1.0 ± 0.30	1.0 ± 0.20	1.0 ± 0.20	1.0 ± 0.20
GPT (U/litre)	83 ± 5.7	89 ± 9.2	55 ± 3.4	52 ± 3.0	63 ± 5.0	71 ± 13.0	87 ± 7.6	86 ± 17.7
GOT (U/litre)	55 ± 2.4	59 ± 8.5	58 ± 3.2	78 ± 10.1	79 ± 16.0	95 ± 16.0	123 ± 17.3	74 ± 18.5
Uric acid (µM)	37 ± 17.2	35 ± 4.2	18 ± 2.6	14 ± 2.2	16 ± 2.2	15 ± 3.3	56 ± 18.9	65 ± 22.4
Cholesterol (mM)	2.43 ± 0.04	2.63 ± 0.05**	3.12 ± 0.08	3.74 ± 0.16*	3.79 ± 0.24	4.03 ± 0.32	6.11 ± 0.65	5.81 ± 0.44
Glucose (mM)	7.96 ± 0.17	7.95 ± 0.30	7.52 ± 0.17	6.99 ± 0.29	9.11 ± 0.32	9.76 ± 0.52	11.55 ± 1.00	11.52 ± 0.86

Alk. Pase = Alkaline phosphatase; GPT = Glutamic-pyruvic transaminase; GOT = Glutamic-oxalacetic transaminase

Values are means ± SEM for groups of ten rats. Those marked with asterisks differ significantly (by student's t test) from the corresponding control value: * $p < 0,05$; ** $p < 0,01$; *** $p<0.001$.

Table A6_5/02-3. Analysis of urine samples from rats fed a phosphine-fumigated diet for up to 2 yr

Group	Phosphorus (g 24 hr)	Urea (g 24 hr)	Creatinine (mg 24 hr)	GOT (U/litre)	Diuresis (ml 24 hr)	pH
Month 3						
Male						
Control	0.026 ± 0.034	0.67 ± 0.19	28.60 ± 10.5	7 ± 2.0	17.8 ± 5.28	7.3 ± 0.4
Treated	0.032 ± 0.0038	0.71 ± 0.19	21.62 ± 7.70	8 ± 1.2	12.3 ± 3.37	7 ± 0.3
Female						
Control	0.027 ± 0.0038	0.61 ± 0.15	16.08 ± 3.56	8 ± 4.1	15 ± 1.8	7 ± 0.2
Treated	0.034 ± 0.0048	0.52 ± 0.2	14.65 ± 4.71	7 ± 2.3	14 ± 2.8	7.3 ± 0.4
Month 6						
Male						
Control	0.016 ± 0.0022	0.45 ± 0.075	9.51 ± 1.44	7 ± 0.9	14 ± 3.4	7.8 ± 0.46
Treated	0.017 ± 0.0026	0.49 ± 0.052	8.96 ± 1.94	6 ± 1.0	11 ± 2.8	6.9 ± 0.45
Female						
Control	0.019 ± 0.0033	0.51 ± 0.061	14.63 ± 1.56	8 ± 1.5	10 ± 1.1	8 ± 0.5
Treated	0.016 ± 0.0024	0.45 ± 0.066	14.89 ± 2.52	9 ± 1.2	9 ± 2.1	6.9 ± 0.45
Month 10						
Male						
Control	0.017 ± 0.0033	0.42 ± 0.031	9.5 ± 1.15	4.8 ± 0.87	9 ± 1.2	5.8 ± 0.48
Treated	0.019 ± 0.0037	0.45 ± 0.049	7.1 ± 1.89	3.7 ± 1.25	10 ± 1.1	6.4 ± 0.20
Female						
Control	0.024 ± 0.00	0.52 ± 0.067	16.3 ± 2.0	6.92 ± 1.29	14 ± 2.2	6.9 ± 0.08
Treated	0.028 ± 0.002	0.52 ± 0.057	20.2 ± 2.45	5.13 ± 1.49	11 ± 1.4	6.9 ± 0.17
Month 12						
Male						
Control	0.018 ± 0.003	0.55 ± 0.18	14 ± 3.8		15 ± 2.7	7 ± 0.2
Treated	0.015 ± 0.0025	0.76 ± 0.15	15 ± 2.4		14 ± 2.4	7 ± 0.2
Female						
Control	0.025± 0.0031	0.70 ± 0.14	16 ± 3.7		20 ± 2.9	7 ± 0.3
Treated	0.029 ± 0.0053	0.89 ± 0.13	18.2 ± 2.93		17 ± 2.3	7 ± 0.2
Month 18						
Male						
Control	0.031 ± 0.005	0.66 ± 0.084	2.04 ± 0.2	3 ± 0.4	15 ± 2.3	7 ± 0.4
Treated	0.025 ± 0.004	0.56 ± 0.069	1.64 ± 0.14	5 ± 0.6	19 ± 1.8	7 ± 0.3
Female						
Control	0.039 ± 0.008	0.79 ± 0.053	17.72 ± 1.86	8 ± 1.4	20 ± 2.0	7 ± 0.2
Treated	0.033 ± 0.006	0.81 ± 0.19	20.33 ± 2.04	3 ± 0.5**	21 ± 2.8	8 ± 0.4

Month 21							
Male							
	Control	0.031 ± 0.0053	0.57 ± 0.144	13.2 ± 1.39	5 ± 0.5	22 ± 3.1	7 ± 0.2
	Treated	0.030 ± 0.0079	0.69 ± 0.049	15.49 ± 0.82	3 ± 0.7	26 ± 2.2	7 ± 0
Female							
	Control	0.038 ± 0.0043	0.64 ± 0.102	19.65 ± 2.64	1 ± 0	31 ± 8.3	7 ± 0.2
	Treated	0.037 ± 0.0049	1.31 ± 0.54	21.89 ± 3.69	3 ± 0.8	28 ± 6.4	7 ± 0.2
Month 24							
Male							
	Control	0.030 ± 0.0057	0.87 ± 0.1487	14.8 ± 1.45	4 ± 0.5	20 ± 3.8	7 ± 0.2
	Treated	0.031 ± 0.0045	0.73 ± 0.060	16.72 ± 0.76	3 ± 0.5	27 ± 3.7	6 ± 0.2
Female							
	Control	0.035 ± 0.0069	0.84 ± 0.143	22.7 ± 2.36	2 ± 0.4	18 ± 2.5	7 ± 0
	Treated	0.040 ± 0.0057	1.19 ± 0.30	23.99 ± 2.06	4 ± 0.9	20 ± 4.7	6.7 ± 0.15

GOT = Glutamic-oxalacetic transaminase

Values are means ± SEM for groups of ten rats. Those marked with asterisks differ significantly (by student`s t test) from the corresponding control value: * $p < 0,05$; ** $p < 0,01$

Table A6_5/02-4. Fresh (relative) weight of organs from rats fed a phosphine-fumigated diet for up to 2 yr

	Organ weights (g/100g body weight) after treatment for 2yr			
	Males		females	
Organ	Control	Treated	Control	Treated
Parotid gland	0.16 ± 0.06	0.18 ± 0.008	0.28 ± 0.091	0.19 ± 0.013
Stomach	0.53 ± 0.020	0.58 ± 0.055	0.60 ± 0.012	0.57 ± 0.032
Liver	3.74 ± 0.36	3.34 ± 0.26	3.27 ± 0.106	2.97 ± 0.201
Adrenals	0.012 ± 0.001	0.016 ± 0.001	0.018 ± 0.001	0.021 ± 0.001
Gonad	0.82 ± 0.081	0.85 ± 0.06	0.09 ± 0.008	0.09 ± 0.010
Thymus	0.11 ± 0.06	0.20 ± 0.081	0.10 ± 0.010	0.13 ± 0.010*
Lung	0.43 ± 0.08	0.44 ± 0.017	0.48 ± 0.015	0.41 ± 0.016**
Heart	0.37 ± 0.024	0.39 ± 0.054	0.38 ± 0.018	0.36 ± 0.020
Spleen	0.19 ± 0.027	0.20 ± 0.012	0.20 ± 0.022	0.16 ± 0.006
Kidney	0.80 ± 0.089	0.84 ± 0.075	1.37 ± 0.038	1.16 ± 0.010

Values are means ± SEM for groups of approximately 10 rats after 2 yr. Those marked with asterisks differ significantly (by student's t test) from the corresponding control value: * $p < 0,05$; ** $p < 0,01$

Table A6_5/02-5.

Tissue and lesion	No. of rats with lesion after 2 yr.			
	Males		females	
	Control	Treated	Control	Treated
Duodenum *No. examined...*	6	10	9	10
Ulcerous zones	0	0	0	0
Increased lymphoid tissue	5	10	9	9
Congestion	0	0	0	0
Necrotic zones	1	3	0	2
Colon *No. examined...*	7	10	10	9
Ulcerous or necrotic zones	0	2	0	0
Inflamed zones	0	0	0	0
Epithelial desquamation	0	0	0	0
Increased lymphoid tissue	0	2	0	1

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA VI.6.5/03 *Chronic toxicity*

Official use only

	1 REFERENCE	
1.1	**Reference**	[redacted] 2 years toxicity studies with PHOSTOXIN-treated food on rats. [redacted]
1.2	**Data protection**	[redacted]
1.2.1	Data owner	Detia Freyberg GmbH
1.2.2		
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**	[redacted]
	3 MATERIALS AND METHODS	
3.1	**Test material**	[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]
3.1.2.3	Stability	[redacted]
3.2	**Test Animals**	
3.2.1	Species	[redacted]
3.2.2	Strain	[redacted]
3.2.3	Source	[redacted]
3.2.4	Sex	[redacted]
3.2.5	Age/weight at study initiation	[redacted]
3.2.6	Number of animals per group	[redacted]
3.2.7	Control animals	[redacted]

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA VI.6.5/03 *Chronic toxicity*

3.3	**Administration/ Exposure**	[redacted]
3.3.1	Duration of treatment	[redacted]
3.3.2	Frequency of exposure	[redacted]
3.3.3	Postexposure period	[redacted]
3.3.4	**Oral**	
3.3.4.1	Type	[redacted]
3.3.4.2	Concentration	[redacted]
3.3.4.3	Vehicle	[redacted]
3.3.4.4	Concentration in vehicle	[redacted]
3.3.4.5	Total volume applied	[redacted]
3.3.4.6	Controls	[redacted]
3.4	**Examinations**	
3.4.1	Observations	
3.4.1.1	Clinical signs	[redacted]
3.4.1.2	Mortality	[redacted]
3.4.2	Body weight	[redacted]
3.4.3	Food consumption	[redacted]
3.4.4	Water consumption	[redacted]
3.4.5	Ophthalmoscopic examination	[redacted]
3.4.6	Haematology	[redacted]
3.4.7	Clinical Chemisty	[redacted]
3.4.8	Urinalysis	[redacted]

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA VI.6.5/03 *Chronic toxicity*

[redacted]

3.5 Sacrifice and pathology

3.5.1 Organ Weights [redacted]

3.5.2 Gross and histopathology [redacted]

3.5.3 Other examinations [redacted]

3.5.4 Statistics [redacted]

3.6 Further remarks [redacted]

4 RESULTS AND DISCUSSION

4.1 Observations

4.1.1 Clinical signs [redacted]

4.1.2 Mortality [redacted]

4.2 Body weight gain [redacted]

4.3 Food consumption and compound intake [redacted]

4.4 Ophtalmoscopic examination

4.5 Blood analysis

4.5.1 Haematology [redacted]

4.5.2 Clinical chemistry [redacted]

4.5.3 Urinalysis [redacted]

4.6 Sacrifice and

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA VI.6.5/03 *Chronic toxicity*

pathology

4.6.1 Organ weights

4.6.2 Gross and histopathology

4.7 Other

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA VI.6.5/03 *Chronic toxicity*

[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods [redacted]

5.2 Results and discussion

Feeding of male and female Wistar rats with Phostoxin-fumigated diet (phosphine level: 0.167 – 0.377 mg/kg the first 16 weeks, 0.996 mg/kg week 17 – 104) did not reveal any toxic effects in this 2 year dietary feeding study.

5.3 Conclusion

5.3.1 LO(A)EL [redacted]

5.3.2 NO(A)EL [redacted]

5.3.3 Other [redacted]

5.3.4 Reliability [redacted]

5.3.5 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]

COMMENTS FROM ... *(specify)*

Date *Give date of comments submitted*

Materials and Methods *Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.*
Discuss if deviating from view of rapporteur member state

Results and discussion *Discuss if deviating from view of rapporteur member state*

Section A6.3 / 6.4 / 6.5 Repeated dose toxicity

Annex Point IIA VI.6.5/03 *Chronic toxicity*

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_3-1. Results of clinical chemistry haematology and urinalysis

(Use this or similar table, if relevant effects occur and if time sequence is important.Give either symbols for increases or decreases (↑↓) or abbreviations inc., dec. Only if more information is needed, give figures or percentages.)

parameter changed	Unit	Controls			low dose			medium dose			high dose		
weeks after start of treatment													
males													
females													

* $p < 0,05$

Give only those parameters which are changed in at least one dose group compared to control. Usually only statistically significant effects

Depending on number of parameters changed one table each for Haematology, Clinical Chemistry, Urinalysis

Table A6_3-2. Results *(specify)* of repeated dose toxicity study

Parameter	Control		low dose		medium dose		high dose		dose-response +/-	
	m[a]	f[a]	m[a]	f[a]	m[a]	f[a]	m[a]	f[a]	m	f
number of animals examined										
Mortality										
clinical signs*										
body weight										
food consumption										
clinical chemistry*										
haematology*										
urinalysis*										
Organ x organ weight*										
gross pathology*										
microscopic pathology*										
Organ y										

** specify effects; for different organs give special findings in the order organ weight, gross pathology and microscopic pathology if there are effects*

[a] *give number of animals affected/total number of animals, percentage, or just ↑ or ↓ for increased or decreased*

Section A6.5/6.7 Annex Point IIA VI 6.5/6.7	Chronic toxicity/Carcinogenicity study, other mammalian	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data [X] **Limited exposure [X]**	**Technically not feasible [ ]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification: [redacted]		
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	

Section A6.5/6.7 Annex Point IIA VI 6.5/6.7	Chronic toxicity/Carcinogenicity study, other mammalian
	Evaluation by Competent Authorities
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Evaluation of applicant's justification	[redacted]
Conclusion	[redacted]
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A6.6.1 Genotoxicity in vitro

Annex Pt IIA VI.6.6.1/01 *In-vitro gene mutation study in bacteria*

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1 REFERENCE

1.1 Reference [redacted] IN VITRO MICROBIAL MUTAGENICITY TESTING OF HYDROGEN PHOSHIDE. [redacted]

1.2 Data protection [redacted]

1.2.1 Data owner: Detia Freyberg GmbH

1.2.2

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 [redacted]

3 MATERIALS AND METHODS

3.1 Test material [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]

3.1.2.3 Stability: [redacted]

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]

Section A6.6.1 Genotoxicity in vitro

Annex Pt IIA VI.6.6.1/01 *In-vitro gene mutation study in bacteria*

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	Pre-incubation time	[redacted]
3.3.4	Other modifications	[redacted]
3.4	**Examinations**	[redacted]
3.4.1	Number of cells evaluated	[redacted]

4 RESULTS AND DISCUSSION

4.1	**Genotoxicity**	
4.1.1	without metabolic activation	No
4.1.2	with metabolic activation	No
4.2	**Cytotoxicity**	n. a.
4.3	**Further examinations**	In the toxicity test of hydrogen phosphide with Salmonella typhimurium TA 98, approximately 20% growth inhibition was observed at the highest concentration, but no toxic effect was observed at lower concentrations.

Section A6.6.1 Genotoxicity in vitro

Annex Pt IIA VI.6.6.1/01 *In-vitro gene mutation study in bacteria*

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	[redacted]
5.2	**Results and discussion**	[redacted]
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	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	

Section A6.6.1 Genotoxicity in vitro

Annex Pt IIA VI.6.6.1/01 *In-vitro gene mutation study in bacteria*

	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_6_1-1. Table for Gene Mutation Assay (modify if necessary)

Concentration [µg/ml or other]	Number of mutant cells		Comments *give information on cytotoxicity or other*
	— S9	+ S9	
0			
x			
xx			

Table A6_6_1-2. Table for Cytogenetic In-Vitro-Test: Chromosomal Analysis (modify if necessary)

		control	low dose	mid dose	high dose
cytotoxicity *specify measure of cytotoxicity*		yes/no	yes/no	yes/no	yes/no
state mean and standard deviations below					
chromatid aberrations	gaps				
	breaks				
	interchanges				
Isochromatid aberrations	gaps				
	breaks				
	interchanges				
mitotic index					
polyploidy					
endo reduplication					

Section A6.6.1/6.6.2/ 6.6.3 Genotoxicity in vitro

Bacterial reverse mutation test

Annex Pt IIA VI.6.6.1/02

Official use only

1 REFERENCE

1.1	**Reference**	[redacted] Ames/Salmonella Plate Incorporation Assay on Hydrogen Phosphide (PH_3). [redacted]
1.1	**Data protection**	[redacted]
1.1.1	Data owner	Detia Freyberg GmbH
1.1.2		
1.1.3	Criteria for data protection	[redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	[redacted]
2.2	**GLP**	[redacted]
2.3	**Deviations**	[redacted]

3 MATERIALS AND METHODS

3.1	**Test material**	[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]
3.1.2.3	Stability	[redacted]
3.2	**Study Type**	[redacted]
3.2.1	Organism/cell type	[redacted]

Section A6.6.1/6.6.2/ 6.6.3

Genotoxicity in vitro

Bacterial reverse mutation test

Annex Pt IIA VI.6.6.1/02

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**	[redacted]
3.3.1	Concentrations	[redacted]

Section A6.6.1/6.6.2/ 6.6.3 **Genotoxicity in vitro**

Bacterial reverse mutation test

Annex Pt IIA VI.6.6.1/02

3.3.2 Way of application [redacted]

3.3.3 Pre-incubation time [redacted]

3.3.4 Other modifications [redacted]

3.4 Examinations [redacted]

3.4.1 Number of cells evaluated [redacted]

4 RESULTS AND DISCUSSION

4.1 Genotoxicity

Section A6.6.1/6.6.2/ 6.6.3 **Genotoxicity in vitro**

Bacterial reverse mutation test

Annex Pt IIA VI.6.6.1/02

4.1.1	without metabolic activation	[redacted]
4.1.2	with metabolic activation	see 4.1.1
4.2	**Cytotoxicity**	[redacted]

Section A6.6.1/6.6.2/ 6.6.3 **Genotoxicity in vitro**

Bacterial reverse mutation test

Annex Pt IIA VI.6.6.1/02

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods [redacted]

5.2 Results and discussion [redacted]

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 [redacted]

Materials and Methods [redacted]

Results and discussion

Conclusion [redacted]

Reliability [redacted]

Acceptability [redacted]

Remarks

Section A6.6.1/6.6.2/ 6.6.3 Genotoxicity in vitro

Bacterial reverse mutation test

Annex Pt IIA VI.6.6.1/02

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

[redacted]

[redacted]			
	[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 A6.6.1/6.6.2/ 6.6.3 — Genotoxicity in vitro

In-vitro cytogenicity study in mammalian cells

Annex Pt IIA VI.6.6.1/03

Official use only

1 REFERENCE

1.1	**Reference**	[redacted]Structural Chromosome Abberation Chinese Hamster Ovary (CHO) Cell induced by Hydrogen Phsophide (PH_3). [redacted]
1.2	**Data protection**	[redacted]
1.2.1	Data owner	Detia Freyberg GmbH
1.2.2		
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**	[redacted]

3 MATERIALS AND METHODS

3.1	**Test material**	[redacted]
3.1.1	Lot/Batch number	[redacted]
3.1.2	Specification	[redacted]

Section A6.6.1/6.6.2/ 6.6.3 Genotoxicity in vitro

In-vitro cytogenicity study in mammalian cells

Annex Pt IIA VI.6.6.1/03

3.1.2.1	Description	[redacted]
3.1.2.2	Purity	[redacted]
3.1.2.3	Stability	[redacted]
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	Pre-incubation time	[redacted]
3.3.4	Other modifications	[redacted]
3.4	**Examinations**	Slide Analysis: A total of 300 well spread, metaphases with minimum [redacted]
3.4.1	Number of cells evaluated	[redacted]

Section A6.6.1/6.6.2/ 6.6.3 **Genotoxicity in vitro**

In-vitro cytogenicity study in mammalian cells

Annex Pt IIA VI.6.6.1/03

4 RESULTS AND DISCUSSION

4.1 Genotoxicity

4.1.1 without metabolic activation [redacted]

4.1.2 with metabolic activation [redacted]

4.2 Cytotoxicity [redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods [redacted]

5.2 Results and discussion [redacted]

5.3 Conclusion

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]

Section A6.6.1/6.6.2/ 6.6.3 Genotoxicity in vitro

In-vitro cytogenicity study in mammalian cells

Annex Pt IIA VI.6.6.1/03

Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

[redacted]

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

Section A6.6.1/6.6.2/ [redacted]

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

Section A 6.6.5 Genotoxicity in vivo

Annex Point IIA VI.6.6.5 *Unscheduled DNA Synthesis in primary hepatocytes in-vivo / in-vitro*

Official use only

1 REFERENCE

1.1	**Reference**	[redacted]GENOTOXICITY TEST ON PHOSPHINE IN THE IN VIVO /IN VITRO ASSAY FOR UNSCHEDULED DNA SYNTHESIS IN RAT PRIMARY HEPATOCYTE CULTURES AT TWO TIMEPOINTS.[redacted]
1.2	**Data protection**	[redacted]
1.2.1	Data owner	Detia Freyberg GmbH
1.2.2		
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**	[redacted]

3 MATERIALS AND METHODS

3.1	**Test material**	[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]
3.1.2.3	Stability	[redacted]
3.1.2.4	Maximum tolerable dose	[redacted]

3.2 Test Animals

3.2.1 Species

3.2.2 Strain

3.2.3 Source

3.2.4 Sex

3.2.5 Age/weight at study initiation

3.2.6 Number of animals per group

3.2.7 Control animals

3.3 Administration/ Exposure

3.3.1 Number of applications

3.3.2 Interval between applications

3.3.3 Postexposure period

Inhalation

3.3.4 Type

3.3.5 Concentration

3.3.6 Vehicle

3.3.7 Concentration in vehicle

3.3.8 Total volume applied

3.3.9 Controls

3.4 Examinations

3.4.1 Clinical signs

3.4.2 Tissue

3.5 Further remarks

4 RESULTS AND DISCUSSION

4.1	**Clinical signs**	Labored breathing was seen in the animals exposed to 18 and 23 ppm of phosphine. A 5 to 7 percent weight loss was seen in the animals exposed to 13, 18 and 23 ppm.
4.2	**Haematology / Tissue examination**	n. a.
4.3	**Genotoxicity**	No
4.4	**Other**	see 4.1

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	[redacted]
5.2	**Results and discussion**	[redacted]
5.3	**Conclusion**	
5.3.1	Reliability	[redacted]
5.3.2	Deficiencies	[redacted]

Evaluation by Competent Authorities

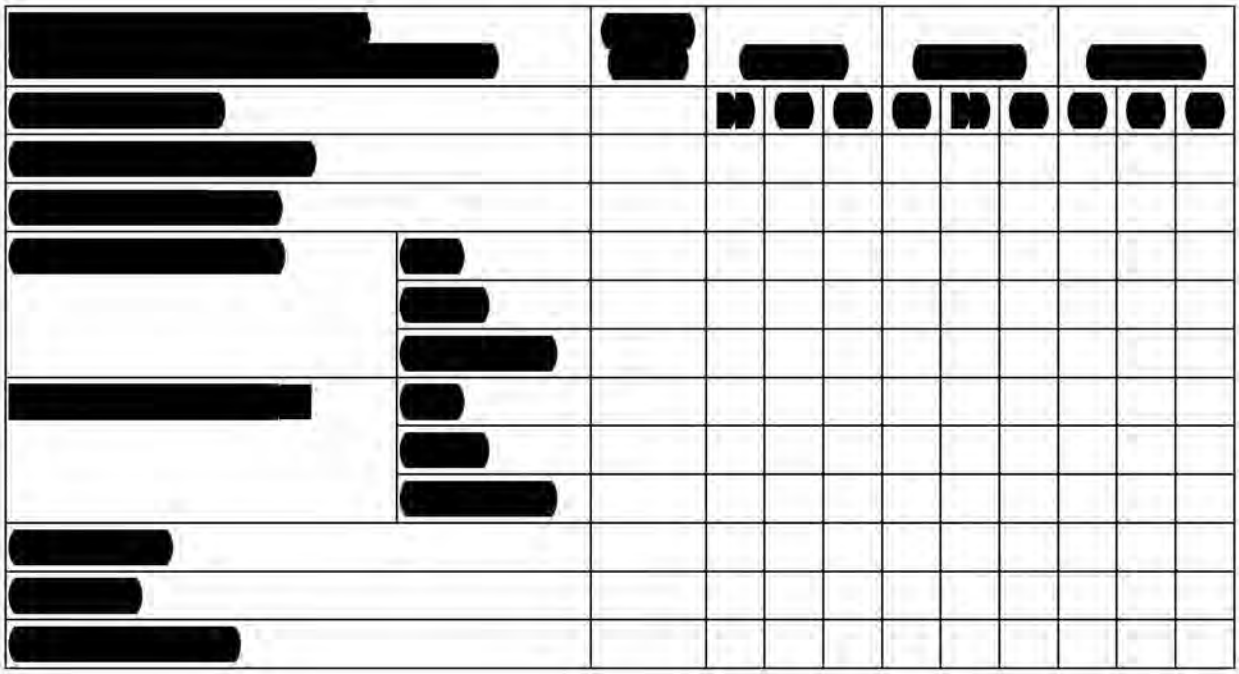
EVALUATION BY RAPPORTEUR MEMBER STATE

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

	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

[redacted]

[redacted]



Section A6.6.4/6.6.5/ 6.6.6 — Genotoxicity in vivo

Cytogenetic in-vivo-test

Annex Point IIA6.6.4 / 01

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1 REFERENCE

1.1	**Reference**	Kligerman, A.D.; et al. (1994): Cytogenetic effects of phosphine inhalation by rodents. I: Acute 6-hour exposure of mice; Environ. Mol. Mutagen. 23, 186 - 189
1.2	**Data protection**	No
1.2.1	Data owner	published
1.2.2		
1.2.3	Criteria for data protection	No data protection claimed

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes. Approved by the "Animal Care Committee of the Health Effects Research Laboratory of the U.S. EPA " and set by "The National Institute of Health".
2.2	**GLP**	not stated (It is not stated in this publication, if the original study was conducted according GLP, but since the investigations were carried out in 1994, it can be presumed that the study was conducted in compliance with the GLP regulations.)
2.3	**Deviations**	not applicated

3 MATERIALS AND METHODS

3.1	**Test material**	Phosphine
3.1.1	Lot/Batch number	not stated
3.1.2	Specification	Deviating from specification given in section 2 as follows
3.1.2.1	Description	gaseous
3.1.2.2	Purity	750 ppm Phosphine in nitrogen, purity: 99.99 %
3.1.2.3	Stability	not indicated
3.1.2.4	Maximum tolerable dose	not indicated
3.2	**Test Animals**	
3.2.1	Species	mouse
3.2.2	Strain	CD-1
3.2.3	Source	Charles River Breeding Laboratories, Raleigh, NC, USA
3.2.4	Sex	male
3.2.5	Age/weight at study initiation	12 weeks approximately
3.2.6	Number of animals	5m per dose

Section A6.6.4/6.6.5/ 6.6.6 **Genotoxicity in vivo**
Cytogenetic in-vivo-test

Annex Point IIA6.6.4 / 01

	per group	
3.2.7	Control animals	Yes
3.3	**Administration/ Exposure**	inhalation
3.3.1	Number of applications	1
3.3.2	Interval between applications	6 h
3.3.3	Postexposure period	20 h after treatment
		Inhalation
3.3.4	Type	Whole-body inhalation
3.3.5	Concentration	0, 5, 10 and 15 ppm PH_3 (norminal)
		0, 5.24 ± 0.69, 9.94 ± 0.69 and 16.00 ± 1.15 (actual)
3.3.6	Vehicle	Nitrogen
3.3.7	Concentration in vehicle	750 ppm PH_3 in Nitrogen
3.3.8	Total volume applied	n. a.
3.3.9	Controls	Vehicle
3.4	**Examinations**	
3.4.1	Clinical signs	Yes
3.4.2	Tissue	bone marrow
		Number of animals: all animals
		Number of cells: not indicated
		Time points: 20 h after treatment
		Type of cells bone marrow smears
		Parameters: chromosomal aberrations (CA)
		sister chromatid exchanges (SCE)
		micronuleus (MN) formation
3.5	**Further remarks**	

4 RESULTS AND DISCUSSION

4.1	**Clinical signs**	After exposure to 15 ppm, the animals appeared lethargic and their breathing was shallow, but all survived. The controls and other exposed animals showed no outward signs of toxicity.

Section A6.6.4/6.6.5/ 6.6.6 — Genotoxicity in vivo

Cytogenetic in-vivo-test

Annex Point IIA6.6.4 / 01

4.2	**Haematology / Tissue examination**	See table A6_6_4-1
4.3	**Genotoxicity**	No
4.4	**Other**	no other significant effects

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	In-vivo mutagenicity study as described in 3.
5.2	**Results and discussion**	After exposure to 15 ppm, the animals appeared lethargic and their breathing was shallow, but all survived. The controls and other exposed animals showed no outward signs of toxicity. All measures of cytogenetic damage analyzed were negative. No evidence was found of SCE, CA, or MN induction. There was also no indication of rare highly damaged cells in any of the treated animals, with the vast majority of aberrations being simple chromatid deletions. The only statistically significant effect observed was a concentration-related slowing of the cell cycle (P =0.009) in the cultured splenocytes at all exposure levels. Thus in this study, there is no evidence that PH_3 is clastogenic, aneuploidogenic, or capable of inducing SCEs at or near toxic concentrations in male mice exposed by inhalation.
5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Evaluation by Competent Authorities

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

EVALUATION BY RAPPORTEUR MEMBER STATE

Date [redacted]

Materials and Methods [redacted]

Results and discussion [redacted]

Conclusion [redacted]

Reliability [redacted]

Section A6.6.4/6.6.5/ 6.6.6 — Genotoxicity in vivo

Cytogenetic in-vivo-test

Annex Point IIA6.6.4 / 01

Acceptability	Acceptable
Remarks	
	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 A6.6.4/6.6.5/ 6.6.6 **Genotoxicity in vivo**

Cytogenetic in-vivo-test

Annex Point IIA6.6.4 / 01

Table A6_6_4-1. Results Table

[redacted]							
[redacted]	[redacted]	% [redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

Section A6.6.4/6.6.5/ 6.6.6 — Genotoxicity in vivo

Cytogenetic in-vivo test

Annex Point IIA6.6.4 / 02

Official use only

1 REFERENCE

1.1	**Reference**	Kligerman, A.D.; et al. (1994): Cytogenetic and germ cell effects of phosphine inhalation by rodents: II. Sub-acute exposure to rats and mice; Environ. Mol. Mutagen. 24, 301 - 306
1.2	**Data protection**	No
1.2.1	Data owner	published
1.2.2		
1.2.3	Criteria for data protection	No data protection claimed

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes. Approved by the "Animal Care Committee of the Health Effects Research Laboratory of the U.S. EPA " and set by "The National Institute of Health".
2.2	**GLP**	not stated (It is not stated in this publication, if the original study was conducted according GLP, but since the investigations were carried out in 1994, it can be presumed that the study was conducted in compliance with the GLP regulations.)
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Test material**	Phosphine
3.1.1	Lot/Batch number	not stated
3.1.2	Specification	Deviating from specification given in section 2 as follows
3.1.2.1	Description	gaseous
3.1.2.2	Purity	21500 ppm Phosphine in nitrogen.
3.1.2.3	Stability	not indicated
3.1.2.4	Maximum tolerable dose	not indicated
3.2	**Test Animals**	
3.2.1	Species	mouse and rat
3.2.2	Strain	B6C3F1 mice and F344/N rats
3.2.3	Source	Mice: Charles River Breeding Laboratories, Raleigh , NC, USA Rat: Charles River Breeding Laboratories, Portage, MI, USA
3.2.4	Sex	male
3.2.5	Age/weight at study	Approximately 8 weeks

Section A6.6.4/6.6.5/ 6.6.6 Genotoxicity in vivo

Cytogenetic in-vivo test

Annex Point IIA6.6.4 / 02

	initiation	
3.2.6	Number of animals per group	5m per dose
3.2.7	Control animals	Yes
3.3	**Administration/ Exposure**	Inhalation
3.3.1	Number of applications	6 hr/day for 9 days over an 11-day period
3.3.2	Interval between applications	5 days exposed, 2 days off, 4 days exposed
3.3.3	Postexposure period	18 to 20 h after treatment
		Inhalation
3.3.4	Type	whole-body inhalation
3.3.5	Concentration	0, 1.25, 2.5 and 5 ppm PH_3
3.3.6	Vehicle	Nitrogen
3.3.7	Concentration in vehicle	21,500 ppm PH_3 in nitrogen
3.3.8	Total volume applied	not indicated
3.3.9	Controls	Vehicle
3.4	**Examinations**	
3.4.1	Clinical signs	not indicated
3.4.2	Tissue	bone marrow, peripheral blood
		Number of animals: all
		Number of cells: not indicated
		Time points: 18 to 20 h after treatment
		Type of cells bone marrow smears (rat)
		peripheral blood (rat and mice)
		In mice, isolated mononuclear leucocytes were analysed for sister chromatid exchange (SCE); chromosomal aberrations (CA) were determined in peripheral blood cells (PBL), and micronucleus (MN) formation in binucleated (BN) lymphocytes and polychromatic erythrocytes (PCE). Bone marrow smears of rats were analysed for micronucleated PCEs, and peripheral blood was investigated for SCE and CA.
3.5	**Further remarks**	

Section A6.6.4/6.6.5/ 6.6.6 **Genotoxicity in vivo**

Cytogenetic in-vivo test

Annex Point IIA6.6.4 / 02

4 RESULTS AND DISCUSSION

4.1	**Clinical signs**	not indicated
4.2	**Haematology / Tissue examination**	See tables A6_6_4-1 and A6_6_4-2
4.3	**Genotoxicity**	No
4.4	**Other**	no other significant effect

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	In vivo cytogenetic study as described in 3
5.2	**Results and discussion**	Mouse (table A6_6_4-1): PH3 inhalation caused no statistically significant increases in SCE or CAs in PBLs. Or MN in peripheral blood PCEs or BN lymphocytes. In addition, all of the CAs observed were either simple chromatid or chromosome deletions and no highly damaged cells or complex exchanges were seen. As an additional verification of the MN data the mouse peripheral blood normochromatic erythrocytes (NCEs) were scored for MN induction. No statistically significant increases were found (data not shown). Rat (table A6_6_4-2): Cytogenetic results for the rat were similar to those observed with the mouse. There were no statistically significant increases in SCEs or CAs in PBLs or MN data, the rat bone marrow NCEs were scored for MN induction. No statistically increases were found (data not shown). Therefore, there is no evidence that PH3 causes cytogenetic damage in mice or rats under the conditions of this test.
5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Evaluation by Competent Authorities

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

EVALUATION BY RAPPORTEUR MEMBER STATE

Date [redacted]

Materials and Methods [redacted]

Section A6.6.4/6.6.5/ 6.6.6 **Genotoxicity in vivo**

Cytogenetic in-vivo test

Annex Point IIA6.6.4 / 02

Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
[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_6_4-1. **Cytogenetic Effects of Phosphine inhalation in the Peripheral Blood of Mice**

[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]

Table A6_6_4-2. Cytogenetic Effects of Phosphine inhalation in the Peripheral Blood and Bone Marrow of Rats

					(%)

Section A6.7 Carcinogenicity

Annex Point IIA6.7

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1 REFERENCE

1.1	**Reference**	[redacted]2-YEAR COMBINED INHALATION CHRONIC TOXICITY AND ONCOGENICITY STUDY OF PHOSPHINE IN RATS. [redacted]
1.2	**Data protection**	Yes
1.2.1	Data owner	Detia Freyberg GmbH
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**	[redacted]

[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 A6.7 Carcinogenicity

Annex Point IIA6.7

	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 A6.5/6.7 Annex Point IIA VI 6.5/6.7	Chronic toxicity/Carcinogenicity study, other mammalian	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data [X]	**Technically not feasible [ ]** **Scientifically unjustified [X]**	
Limited exposure [X]	**Other justification [ ]**	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	