Doc IIIA Section A1 Applicant

BPD Data Set IIA/ Annex Point I

1.1 Applicant

Name: Reckitt Benckiser Healthcare (UK) Ltd.
Address: Dansom Lane
Hull
HU6 7RQ
United Kingdom
Telephone: 00 44 1482 582 511
Fax number: 00 44 1482 582 491
E-mail address: tina.parker@reckittbenckiser.com
Contact Name: Tina Parker

1.2 Manufacturer of Active Substance (if different)

[redacted]

1.3 Manufacturer of Product(s) (if different)

The representative product which is being submitted to support the application for the existing active substance, hydrochloric acid is:

Harpic Limescale Remover

Name: Waldemar Golebiewski (Operations Director)
Reckitt Benckiser (Poland) SA
Address: Ul Okunin
05-100 Nowy Dwor
Mazowiecki
Poland
Telephone: 00 48 22 765 9500
Fax number: 00 48 22 765 9984
Location of manufacturing plant: Poland

Name: Adam Youd (Site Director)
Reckitt Benckiser (UK) Ltd
Address: Sinfin Lane
Derby
Derbyshire
DE24 9GG
UK
Telephone: 00 44 1332 760212
Fax number: 00 44 1332 760226
Location of manufacturing plant: UK

Doc IIIA Section A2 Identity of Active Substance

BPD Data Set IIA/
Annex Point II

Subsection (Annex Point)		Official use only
2.6 **Method of manufacture of the active substance (IIA2.1)**	The active substance, hydrochloric acid (HCl) is an HPV chemical and is not exclusively manufactured for biocidal purposes within the EU. It is therefore considered that the manufacture of the active substance is assessed by other EU legislation. Available technical meeting guidance (TMI06GEN-item8-human-exposure-manufacture) states that in such cases, detailed manufacturing information is not required in order to address potential human or environmental risk. [redacted]	

Doc IIIA Section A2 Identity of Active Substance

BPD Data Set IIA/
Annex Point II

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*Give date of action*
Materials and methods	*State if the applicant's version is acceptable or indicate relevant discrepancies referring to the (sub) heading numbers and to applicant's summary and conclusion.*
Conclusion	*Adopt applicant's version or include revised version*
Reliability	*Based on the assessment of the method include appropriate reliability indicator*
Acceptability	acceptable / not acceptable *(give reasons if necessary, e.g. if a study is acceptable despite a poor reliability indicator). Discuss the relevance of deficiencies.*
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	

Doc IIIA/Section A2.8/01
BPD Data Set IIA/ Annex Point II

Identity of Impurities and Additives

CONFIDENTIAL

Subsection			Official use only
2.8.1.1	Common name	[redacted]	
2.8.1.2	Function	[redacted]	
2.8.2	IUPAC name	[redacted]	
2.8.3	CAS-No	[redacted]	
2.8.4	EC-No	[redacted]	
2.8.5	Other	[redacted]	
2.8.6	Molecular formula	[redacted]	
2.8.7	Structural formula	[redacted]	
2.8.8	Molecular mass	[redacted]	
2.8.9	Concentration of the impurity or additive *typical and range of concentrations*	[redacted]	

Doc IIIA/Section A2.8/01
BPD Data Set IIA/ Annex Point II

Identity of Impurities and Additives

CONFIDENTIAL

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*Give date of action*
Materials and methods	*State if the applicants version is acceptable or indicate relevant discrepancies referring to the (sub) heading numbers and to applicant's summary and conclusion.*
Conclusion	*Adopt applicant's version or include revised version*
Reliability	*Based on the assessment of the method include appropriate reliability indicator*
Acceptability	acceptable / not acceptable *(give reasons if necessary, e.g. if a study is acceptable despite a poor reliability indicator). Discuss the relevance of deficiencies.*
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	

Doc IIIA/Section A2.8/01	Identity of Impurities and Additives
BPD Data Set IIA/ Annex Point II	

Please refer to Confidential Section A2.8/01

Doc IIIA/Section A2.8/02
BPD Data Set IIA/ Annex Point II

Identity of Impurities

CONFIDENTIAL

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible [ ]** **Scientifically unjustified [√]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]	Not applicable.	

Doc IIIA/Section A2.8/02 Identity of Impurities

BPD Data Set IIA/ Annex Point II

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*Give date of action*
Evaluation of applicant's justification	*Discuss applicant's justification and, if applicable, deviating view*
Conclusion	*Indicate whether applicant's justification is acceptable or not. If unacceptable because of the reasons discussed above, indicate which action will be required, e.g. submission of specific test/study data*
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	

Table 2.8/02-1 [redacted] Hydrochloric acid specification

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

Table 2.8/02-2 [redacted] Hydrochloric acid specification

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

Doc IIIA Section A2.10 Exposure data in conformity with Annex VIIA to Council Directive 92/32/EEC (OJ No L, 05.06.1992, p. 1) amending Council Directive 67/548/EEC

BPD Data Set IIA/

Annex Point II.2.10

Subsection		Official use only
2.10.1 Human exposure towards active substance		
2.10.1.1 Production	Production of active substance The active substance, hydrochloric acid (HCl) is an HPV chemical and is not exclusively manufactured for biocidal purposes within the EU. It is therefore considered that the manufacture of the active substance is assessed by other EU legislation. Production of formulated product Harpic Limescale Remover is formulated at two sites within the EU (Derby, UK and Nowy Dwor, Poland) and both sites use the same process for formulation of the product. The formulation process is considered to be a closed system and entirely automated (and hence negligible opportunity for exposure). However, there is the possibility of workers having to enter the facility for either routine inspection/repair of the machinery or for the taking of quality control samples after the mixing phase, prior to transfer to storage tanks. Workers use standard PPE in the form of coveralls and gloves. However, if exposure to either the raw ingredients or formulated products is anticipated, full PPE is available.	
2.10.1.2 Intended use(s)	The intended use for the product Harpic Limescale Remover, is for the amateur, (home use) market only. There are no professional uses.	
1. Professional Users	The proposed use of the product is as a ready-to-use household product to be used indoors by non-professional users.	
2. Non-professional Users including the general public		
(i) *via* inhalational contact	During use of the product by non-professionals, potential exposure may occur *via* the inhalation route (through exposure to hydrogen chloride vapours). A laboratory headspace study gives values in the range of 0.2 – 3ppm. However, this scenario is not representative of true consumer use conditions, as any emissions would normally be diluted into the indoor room volume and concurrent indoor air exchange with the outdoor air. For non-professional users of Harpic, actual exposure durations will be much shorter and less frequent than the occupational standard for HCl of 8 mg/m^3 (8 hr/day, 250 day/yr exposure) and therefore, it is considered that there is no concern for inhalation exposures for consumers who use Harpic Limescale Remover in the home.	

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BPD Data Set IIA/
Annex Point II.2.10

Exposure data in conformity with Annex VIIA to Council Directive 92/32/EEC (OJ No L, 05.06.1992, p. 1) amending Council Directive 67/548/EEC

(ii) *via* skin contact	Dermal exposure to toilet cleaners primarily occurs during the brushing (cleaning) of the lavatory pan rather than during the application of the product to the toilet rim. The robust design of the product also adds an extra degree of reassurance, as it specifically includes a non-drip spout to eliminate any possible contact with the product. Low dermal exposures were predicted by Consexpo, with external dermal doses ranging from 0.183 – 0.917 mg/kg bw/day for acute exposure and 0.0065 – 0.0033 mg/kg bw/day for chronic exposure. Dermal exposures predicted by Consexpo do not take into consideration the use of PPE, specifically gloves, as for residential (non-professional) users it is usually assumed that they have limited access to PPE. The TNsG suggests that the use of gloves reduces the potential exposure by 90%. Although this reduction factor for the use of gloves has not been applied to the exposures predicted in Document IIB, it is reasonable to assume that the use of gloves would reduce the potential dermal exposure to a negligible level that would not cause localised skin reactions.
(iii) *via* drinking water	The proposed indoor use of Harpic Limescale Remover results in negligible concentrations in the environment. Therefore contamination of drinking water will not occur.
(iv) *via* food	Harpic Limescale Remover is not used in a manner that would cause it to come into contact with food or feedingstuffs so post application environmental exposure from dislodgeable residues will not occur.
(v) indirect *via* environment	The proposed indoor use of hydrochloric acid results in negligible concentrations in the environment (see PECS in 2.10.2 below).

2.10.2 Environmental exposure towards active substance

2.10.2.1 Production

Production of active substance

The active substance, hydrochloric acid (HCl) is an HPV chemical and is not exclusively manufactured for biocidal purposes within the EU. It is therefore considered that the manufacture of the active substance is assessed by other EU legislation. Available technical meeting guidance (TMI06GEN-item8-human-exposure-manufacture) states that in such cases, detailed manufacturing information is not required in order to address potential environmental risk.

Production of formulated product

Details of the formulating processes are given in Confidential Document IIIA, Section 2.6 and Document IIB Section 3. Harpic Limescale Remover is formulated at two sites within the EU (Derby, UK and Nowy Dwor, Poland) and both sites use the same process for formulation of the product. The formulation process involves primarily automated mixing of raw materials in a closed system.

(i) Releases into water

Production of active substance

See above.

Production of formulated product

There is no direct release to water (or soil). Potential release of HCl fumes to air is controlled through scrubbers, in which NaOH solution is used to absorb any HCl. The NaOH solution is periodically

	replaced and effluent is pH-adjusted in an on-site treatment plant, or is collected and treated at another waste water treatment plant. The pH and chloride concentration are monitored at the output of the waste-water treatment plants. The effluent is pH-adjusted on site and is released at pH 7. Chloride is below the maximum allowable limit of 4700 mg Cl⁻/L.
(ii) Releases into air	Production of active substance See above. Production of formulated product Potential release of HCl fumes to air is controlled through scrubbers, in which NaOH solution is used to absorb any HCl. There is no monitoring of HCl fumes residual as quantities are not detectable.
(iii) Waste disposal	Production of active substance See above. Production of formulated product Liquid waste is directed *via* on-site treatment plants and effluent is pH-adjusted and the chloride monitored and controlled. A portion of liquid waste is subsequently condensed through evaporation and incinerated. Sludge from the treatment plant is collected by outside contractors who are registered waste disposers There is no exposure to any environmental compartment.

2.10.2.2 Intended use(s)

Affected compartment(s):	As a consequence of the use of Harpic Limescale Remover, there are no direct releases to soil. The environmental exposure assessment for Harpic Limescale Remover concludes that no significant perturbation of pH will occur in either the sewage treatment plant or receiving surface waters following the proposed formulation and use of the product as a toilet cleaner. Emission of hydrochloric acid to air as a result of the proposed use is predicted to be insignificant use (see PECs below). Finally, no significant perturbation of soil pH is expected from the proposed use.
water	Hydrochloric acid released from liquid lavatory disinfectant cleaners, when used as a non-professional cleaning product, enters the sewage system in its dissociated form and will not cause significant change to the pH levels in a standard sewage treatment plant due to the high level of dilution and the well buffered environment of the STP. As a result of the low concentrations entering the STP, buffering capacity of wastewater and also of EU water quality legislation governing quality of discharges, predicted emissions of chloride and hydronium ions are expected to have negligible impact on the receiving aquatic environment (freshwater and marine).
sediment	As a result of the low concentrations entering the STP, buffering capacity of natural water/sediment systems and also of EU water quality legislation governing quality of discharges, predicted emissions of chloride and hydronium ions as a result of the proposed use of Harpic Limescale Remover are expected to have negligible impact on the receiving aquatic environment (freshwater and marine).
air	The contribution of HCl to the atmosphere from the proposed use of

Doc IIIA Section A2.10 / BPD Data Set IIA/ Annex Point II.2.10 — Exposure data in conformity with Annex VIIA to Council Directive 92/32/EEC (OJ No L, 05.06.1992, p. 1) amending Council Directive 67/548/EEC

	Harpic Limescale Remover is considered to be insignificant compared to that from other natural and man-made sources.
soil	Hydrochloric acid is not directly released to the terrestrial compartment, under normal conditions of use. Potential indirect routes considered are application of sewage sludge and deposition from air immediately outside the dwelling where the product is used. Concentrations from both routes are predicted to be negligible. As a result of the buffering capacity of soils and also of EU legislation governing application of sewage sludge to land, any emissions of chloride and hydronium ions as a result of the proposed use of Harpic Limescale Remover are expected to have negligible impact on the terrestrial environment.
Predicted concentration in the affected compartment(s)	An estimation of the expected concentrations of a.s. in the affected compartments, using relevant algorithms in the TGD, are detailed in Document IIB, section 3.3 and summarised below.
water	Negligible exposure (see above).
sediment	No exposure
air	2.7×10^{-9} mg/m^3 (worst case). 1.83×10^{-10} mg/m^3 (realistic use) $Clocal_{air}$, as defined in TGD, 100m from source (Document IIB, section 3.3.3
soil	No exposure (see above)

Doc IIIA Section A2.10 Exposure data in conformity with Annex VIIA to Council Directive 92/32/EEC (OJ No L, 05.06.1992, p. 1) amending Council Directive 67/548/EEC

BPD Data Set IIA/

Annex Point II.2.10

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*20.05.2009*
Materials and methods	*Applicants version is acceptable*
Conclusion	*Adopt applicant´s version.*
Reliability	*2*
Acceptability	acceptable
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	

Table 2.10-1: Inhalation and dermal acute and chronic exposure as calculated using Consexpo 4.1

Exposure Assessment for Adults Associated with Application of Harpic Limescale Remover		
Exposure Scenario	**Acute Exposure**	**Chronic Exposure**
Non-professionals - Worst case scenario		
Inhalation	3.0 ppm (4.9 mg/m³)	NA
Dermal (external dose)	0.917 mg/kg/d	0.033 mg/kg/d
Non-professionals - Realistic scenario		
Inhalation	0.2 ppm (0.33 mg/m³)	NA
Dermal (external dose) – 1st application	0.183 mg/kg/d	0.0065 mg/kg/d

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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	EEC A1	Batch no.: X-1S/1 Concentration: 34.1%	Freezing temperature: < -20°C	Test material did not freeze down to and including -20°C	Y	1	Bell, A. (2007) Physical and Chemical Properties of Concentrated HCl. CEM Analytical Services Ltd (CEMAS), Report no.: CEMR-3305 Ref. IIIA3.1.1/01	
	Not specified	Not specified	Melting point: -40°C	-	N	2	[redacted]	
3.1.2 Boiling point	Not specified	Not specified	85°C	Considering the safety implications of heating a concentrated acid it is not considered practical or necessary to repeat this test and so *additional* data has not been submitted for the hydrochloric acid concentrate.	N	2	[redacted]	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
	-	-	No *additional* data are available for the 34.1% hydrochloric acid concentrate. However, values for the gas hydrogen chloride are cited in public literature: -85.05°C	-	N	2	The Merck Index, 13th Ed. (2001). Ref IIIA 3.1.2/03	
3.1.3 Bulk density/ relative density	CIPAC MT 3.2.1 (in accordance with EEC A3)	Batch no.: X-1S/1 Concentration: 34.1%	Density : 1.1782 g/mL	-	Y	1	Bell, A. (2007) Physical and Chemical Properties of Concentrated HCl. CEM Analytical Services Ltd (CEMAS), Report no.: CEMR-3305 Ref. IIIA3.1.3/01	
	Polish Standard PN-91/C-84046	Not specified	33% HCl: 1.167 g/cm^3 33.5% HCl: 1.170 g/cm^3 34% HCl: 1.172 g/cm^3	It can be seen that the density varies with the concentration of HCl. However results for density are also available for the reported concentration of the active substance as manufactured (34.1%) to address this variation (see Bell, A. (2007) above).	N	2	[redacted]	
3.2 Vapour pressure (IIA3.2)	Not specified	Not specified	c(%) Pressure (Pa) 30 6.2726 x 10^2 40 3.1064 x 10^4	-	N	2	[redacted]	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
	-	-	-	Data are available for the active substance at concentrations of 30 and 40%. As a justification for non-submission of *additional* data, it is considered technically difficult to perform this test. All laboratories that were approached to conduct this test according to EEC A4 indicated that they would be unable to carry out such a test due to the corrosive nature of concentrated hydrochloric acid.	-	-	-	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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)	-	-	No data are available for the 34.1% hydrochloric acid concentrate. However, a range of theoretical values for the gas hydrogen chloride are cited in public literature: 0.01 – 2 x 10^4 mol/m^3/Pa	It is not possible to calculate the Henry's Law Constant for this specific source of active material. The physico-chemical properties are dependent on the hydrochloric acid concentration and so the water solubility and vapour pressure data would have to relate specifically to a 34.1% HCl concentrate. The available literature data does not satisfy this requirement. Furthermore, as concentrated hydrochloric acid dissociates immediately in water this parameter is not considered relevant. However a range of theoretical values for the gas hydrogen chloride is available from the literature.	N	2	Sander, R.(1999) Compilation of Henry's Law Constants for Inorganic and Organic Species of Potential Importance in Environmental Chemistry (Version 3). http://www.mpch-mainz.mpg.de/~sander/res/henry.html Ref. IIIA3.2.1	
3.3 Appearance (IIA3.3)								
3.3.1 Physical state	None specified (SOP CEM-3249)	Batch no.: X-1S/1 Concentration: 34.1%	Liquid	-	Y	1	Bell, A. (2007) Physical and Chemical Properties of Concentrated HCl. CEM Analytical Services Ltd (CEMAS), Report no.: CEMR-3305 Ref. IIIA3.3.1/01	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
	Polish Standard PN-91/C-84046	Not specified	Smoky liquid	-	N	1	[redacted]	
3.3.2 Colour	None specified (SOP CEM-3249)	Batch no.: X-1S/1 Concentration: 34.1%	Clear, colourless, uniform	-	Y	1	Bell, A. (2007) Physical and Chemical Properties of Concentrated HCl. CEM Analytical Services Ltd (CEMAS), Report no.: CEMR-3305 Ref. IIIA3.3.2/01	
	Polish Standard PN-91/C-84046	Not specified	Colourless or slightly yellow	-	N	1	[redacted]	
3.3.3 Odour	Organoleptic	Not specified	Acute, pungent odour (hydrogen chloride smoking)	-	N	2	M[redacted] Ref. IIIA3.3.3/01	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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	-	-	-	Not applicable. The nature of the active substance means that it is not possible to obtain a UV/Vis spectrum. Hydrochloric acid is an aqueous solution of hydrogen chloride. As such the active substance is present in its completely ionised form (H_3O^+ + Cl^-, effectively H^+ and Cl^-) and it would not be possible to detect using a UV/Vis spectrophotometer. The primary use of a UV/Vis absorption spectrum is to provide an indication of the wavelengths at which the compound may be susceptible to photochemical degradation. This is not relevant to hydrochloric acid as it does not undergo photochemical degradation.	-	-	-	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
IR	-	-	-	Although it is technically possible to obtain an IR spectrum of hydrogen chloride gas no useful information can be gained from this. The active substance being supported is the aqueous solution of hydrogen chloride, for which is not possible to obtain an IR spectra. Infrared spectra are used to confirm the identity of the test substance by comparing the spectra obtained to tables of infrared data containing characteristic infrared absorptions due to stretching of bonds in organic molecules. Hydrochloric acid is not an organic molecule and as such will not exhibit any of these characteristic absorptions, therefore this is not a valid technique for confirming the identity of the test substance.	-	-	-	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
NMR	-	-	-	Not applicable. The nature of the active substance means that it is not possible to obtain a NMR spectrum. Hydrochloric acid is an aqueous solution of hydrogen chloride. As such the active substance is present in its completely ionised form ($H_3O^+ + Cl^-$, effectively H^+ and Cl^-). If it was possible to obtain an NMR spectra then a single peak would be obtained, as all protons are in the same environment.	-	-	-	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
MS	-	-	-	Although it is technically possible to obtain a MS spectrum of hydrogen chloride gas, no useful information can be gained from this. The active substance being supported is the aqueous solution of hydrogen chloride, for which it is not possible to obtain an MS spectra. Furthermore, if a MS spectrum is to be used for identification then it should ideally contain three fragment ions with m/z ratios >100. This is not possible for hydrochloric acid as its molecular weight is only 36.5 g/mol; the spectrum would not contain any ions with m/z ratios >100.	-	-	-	
3.5 Solubility in water (IIA3.5)	Not specified	Not specified	Unlimited with heat emission	-	N	3	[redacted]	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
	-	-	No data are available for the 34.1% hydrochloric acid concentrate. However, a value for the gas hydrogen chloride is cited in public literature: 823 g/L at 0°C	Although data are available for the gas hydrogen chloride, solubility in water is not considered a relevant parameter for hydrochloric acid. By definition hydrochloric acid is an aqueous solution of hydrogen chloride. Hence any addition of hydrochloric acid to water results in dilution of the acid rather than determining its solubility.	N	2	The Merck Index, 13th Ed. (2001). Ref. IIIA3.5/02	
3.6 Dissociation constant (-)	-	-	-	Dissociation constant is not considered a relevant parameter for hydrochloric acid. By definition hydrochloric acid is an aqueous solution of hydrogen chloride. As such the active substance is present in its completely dissociated form ($H_3O^+ + Cl^-$, effectively H^+ and Cl^-) and it is not possible to determine the dissociation constant.	-	-	-	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
3.7 Solubility in organic solvents, including the effect of temperature on solubility (IIIA3.1)	-	-	-	The solubility of hydrochloric acid in organic solvents is not considered a relevant parameter. The biocidal product does not contain any organic solvents, and it is highly unlikely that any subsequent products will contain organic solvents. Furthermore, as hydrochloric acid is an aqueous solution it will be immiscible with many organic solvents.	-	-	-	
	Not specified	Not specified	Soluble in ethyl alcohol	-	N	3	[redacted]	
3.8 Stability in organic solvents used in b.p. and identity of relevant breakdown products (IIIA3.2)	-	-	-	Not applicable. The biocidal product does not include any organic solvents therefore it is not necessary to assess the stability of hydrochloric acid in such solvents.	-	-	-	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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)	-	-	-	It is not considered technically possible to perform this test. The test method (EEC A8) states that measurements should be made on ionisable substances only in their non-ionised forms. By definition hydrochloric acid is an aqueous solution of hydrogen chloride. As such the active substance is present in its completely ionised form ($H_3O^+ + Cl^-$, effectively H^+ and Cl^-). It is not possible to obtain a non-ionised form of hydrochloric acid and hence not possible to conduct this test.	-	-	-	
3.10 Thermal stability, identity of relevant breakdown products (IIA3.7)	-	-	-	Considering the safety implications of heating a concentrated acid, it is not considered practical or necessary to conduct this test.	-	-	-	
3.11 Flammability, including auto-flammability and identity of combustion products (IIA3.8)	-	-	-	Test Guidelines EEC A10, A11 and A16 are not applicable as they are suitable for solid and/or gaseous substances only. The technical material is supplied as an aqueous concentrate. Test guideline EEC A13 determines the pyrophoric	-	-	-	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
				properties of solids and liquids and EEC A12 the flammability of substances in contact with water. However it is stated in the TNsG that these tests can be omitted if experience indicates that negative results would be obtained. Hydrochloric acid is not classified as R17 (Spontaneously flammable in air) or R14/15 (Reacts violently with water, liberating extremely flammable gases) and hence it is not considered necessary to carry out these tests. Considering the safety implications of heating a concentrated acid it is not considered practical or necessary to conduct the auto-ignition temperature test as outlined in EEC A15. Hydrochloric acid is an aqueous solution of hydrogen chloride and as such is not considered to have any flammable properties. A minimum of 64% of the technical material is water.				

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
	Not specified	Not specified	Non-flammable liquid		N	3	[redacted]	
3.12 Flash-point (IIA3.9)	-	-	-	It is not considered technically possible to perform this test. All laboratories that were approached to conduct this test according to EEC A9 indicated that they would be unable to carry out such a test due to the corrosive nature of concentrated hydrochloric acid towards the metal apparatus used. In addition, considering the safety implications of heating a concentrated acid it is not considered practical or necessary to conduct this test. Hydrochloric acid is an aqueous solution of hydrogen chloride and as such is not considered to have any flammable properties. A minimum of 64% of the technical material is water.	-	-	-	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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)	-	-	-	It is not considered technically possible to conduct this study. The harmonised ring method described in OECD 115, uses a ring made of platinum-iridium wire of specific dimensions to measure the surface tension of the system. Hydrochloric acid is a corrosive substance and would corrode the surface of the ring thus making it impossible to obtain an accurate reading of the surface tension. Furthermore, hydrochloric acid on contact with metals has the potential to release hydrogen gas which poses a risk of explosion and hence makes the test unsafe to perform.	-	-	-	
3.14 Viscosity (-)	CIPAC MT 22	Batch no.: X-1S/1 Concentration: 34.1%	1.70 x 10^{-6} m^2/s at 20°C 1.33 x 10^{-6} m^2/s at 40°C	-	Y	1	Bell, A. (2007) Physical and Chemical Properties of Concentrated HCl. CEM Analytical Services Ltd (CEMAS), Report no.: CEMR-3305 Ref. IIIA3.14/01	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
3.15 Explosive properties (IIA3.11)	-	-	-	It is not technically possible to conduct the test specified due to the corrosive nature of hydrochloric acid. The flame (thermal sensitivity) and shock (sensitivity to mechanical stimuli) tests given in guideline EEC A14 involve the use of steel containers which would not be compatible with the test substance. Hydrochloric acid does not itself have any explosive properties. However, on contact with a majority of metals hydrogen is emitted and this can pose a risk of explosion. If instructions for safe use (e.g. the acid must not be stored in metal packaging), as stated on the MSDS, are followed then hydrochloric acid does not pose an explosion risk (see 3.17 below).	N/A	1	[redacted]	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
3.16 Oxidizing properties (IIA3.12)	-	-	-	Examination of the structure of hydrochloric acid indicates that the substance will not have any oxidising properties. Hydrochloric acid is an aqueous solution of hydrogen chloride, and as such the active substance is present in its completely dissociated form ($H_3O^+ + Cl^-$, effectively H^+ and Cl^-). Although chlorine is an electronegative atom, in this case it is present as chloride ion and will not facilitate the oxidation of other compounds. It is stated in the MSDS that "In reaction with oxidising compounds it (HCl) is oxidised to available chlorine."	N/A	2	[redacted]	
3.17 Reactivity towards container material (IIA3.13)	N/A	N/A	Hydrochloric acid should be stored in ceramic containers, metal containers lined with acid-proof material or plastic containers. The acid must not be stored in metal packaging due to the risk of formation of hydrogen.	-	N/A	1	[redacted] Ref. IIIA3.17/01	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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	EEC A1	Batch no.: CER_HCL_T220B Concentration: 36.2%	Freezing temperature: < -20°C	Test material did not freeze down to and including -20°C	Y	1	Bell, A. (2007) Physical and Chemical Properties of Concentrated HCl. CEM Analytical Services Ltd (CEMAS), Report no.: CEMR-3305 Ref. IIIA3.1.1/01	
	Not specified	Not specified	Freezing point: -63°C (28%) -27°C (36%)	It can be seen that the freezing temperature varies with the concentration of HCl. This test has been conducted on the active substance as manufactured to address this variation (see above).	N	2	[redacted]	
3.1.2 Boiling point	Not specified	Not specified	97.7°C (28%) 56.1°C (36%)	Considering the safety implications of heating a concentrated acid it is not considered practical or necessary to repeat this test and so *additional* data has not been submitted for the hydrochloric acid concentrate.	N	2	[redacted]	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
			No *additional* data are available for the 36.2% hydrochloric acid concentrate. However, values for the gas hydrogen chloride are cited in public literature: -85.05°C		N	2	The Merck Index, 13th Ed. (2001). Ref IIIA 3.1.2/03	
3.1.3 Bulk density/ relative density	CIPAC MT 3.2.1 (in accordance with EEC A3)	Batch no.: CER_HCL_T220B Concentration: 36.2%	Density : 1.1716 g/mL	-	Y	1	Bell, A. (2007) Physical and Chemical Properties of Concentrated HCl. CEM Analytical Services Ltd (CEMAS), Report no.: CEMR-3305 Ref. IIIA3.1.3/01	
	Not specified	Not specified	Specific gravity (relative density): 1.14 (28%) at 15°C 1.18 (36%) at 15°C	It can be seen that the density varies with the concentration of HCl. However results for density are also available for the reported concentration of the active substance as manufactured (36.2%) to address this variation (see 3.1.3/01 above).	N	2	[redacted]	

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Source: [redacted]

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 Vapour pressure (IIA3.2)	Not specified	Not specified	11 mmHg (28%) at 20°C [1.47 x 10^3 Pa] 115 mmHg (36%) at 20°C [1.53 x 10^4 Pa]	-	N	2	[redacted]	
	-	-	-	Data are available for the active substance at concentrations of 28 and 36%. As a justification for non-submission of *additional* data, it is considered technically difficult to perform this test. All laboratories that were approached to conduct this test according to EEC A4 indicated that they would be unable to carry out such a test due to the corrosive nature of concentrated hydrochloric acid.	-	-	-	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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)	-	-	No data are available for the 36.2% hydrochloric acid concentrate. However, a range of theoretical values for the gas hydrogen chloride are cited in public literature: 0.01 – 2 x 10^4 mol/m3/Pa	It is not possible to calculate the Henry's Law Constant for this specific source of active material. The physico-chemical properties are dependent on the hydrochloric acid concentration and so the water solubility and vapour pressure data would have to relate specifically to a 36.2% HCl concentrate. The available literature data does not satisfy this requirement. Furthermore, as concentrated hydrochloric acid dissociates immediately in water this parameter is not considered relevant. However a range of theoretical values for the gas hydrogen chloride is available from the literature.	N	2	Sander, R. (1999) Compilation of Henry's Law Constants for Inorganic and Organic Species of Potential Importance in Environmental Chemistry (Version 3). http://www.mpch-mainz.mpg.de/~sander/res/henry.html Ref. IIIA3.2.1	
3.3 Appearance (IIA3.3)								
3.3.1 Physical state	None specified (SOP CEM-3249)	Batch no.: CER_HCL_T220B Concentration: 36.2%	Liquid	-	Y	1	Bell, A. (2007) Physical and Chemical Properties of Concentrated HCl. CEM Analytical Services Ltd (CEMAS), Report no.: CEMR-3305 Ref. IIIA3.3.1/01	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
	Not specified	Not specified	Fuming liquid	-	N	1	[redacted]	
3.3.2 Colour	None specified (SOP CEM-3249)	Batch no.: CER_HCL_T220B Concentration: 36.2%	Clear, colourless, uniform	-	Y	1	Bell, A. (2007) Physical and Chemical Properties of Concentrated HCl. CEM Analytical Services Ltd (CEMAS), Report no.: CEMR-3305 Ref. IIIA3.3.2/01	
	Not specified	Not specified	Almost colourless to pale yellow	-	N	1	[redacted]	

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Source: [redacted]

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
3.3.3 Odour	Organoleptic	Not specified	Characteristically pungent	-	N	2	[redacted] Ref. IIIA3.3.2/02	
3.4 Absorption spectra (IIA3.4)								

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Source: [redacted]

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
UV/VIS	-	-	-	Not applicable. The nature of the active substance means that it is not possible to obtain a UV/Vis spectrum. Hydrochloric acid is an aqueous solution of hydrogen chloride. As such the active substance is present in its completely ionised form (H_3O^+ + Cl^-, effectively H^+ and Cl^-) and it would not be possible to detect using a UV/Vis spectrophotometer. The primary use of a UV/Vis absorption spectrum is to provide an indication of the wavelengths at which the compound may be susceptible to photochemical degradation. This is not relevant to hydrochloric acid as it does not undergo photochemical degradation.	-	-	-	

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Source: [redacted]

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
IR	-	-	-	Although it is technically possible to obtain an IR spectrum of hydrogen choride gas no useful information can be gained from this. The active substance being supported is the aqueous solution of hydrogen chloride, for which is not possible to obtain an IR spectra. Infrared spectra are used to confirm the identity of the test substance by comparing the spectra obtained to tables of infrared data containing characteristic infrared absorptions due to stretching of bonds in organic molecules. Hydrochloric acid is not an organic molecule and as such will not exhibit any of these characteristic absorptions, therefore this is not a valid technique for confirming the identity of the test substance.	-	-	-	

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Source: [redacted]

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
NMR	-	-	-	Not applicable. The nature of the active substance means that it is not possible to obtain a NMR spectrum. Hydrochloric acid is an aqueous solution of hydrogen chloride. As such the active substance is present in its completely ionised form ($H_3O^+ + Cl^-$, effectively H^+ and Cl^-). If it was possible to obtain an NMR spectra then a single peak would be obtained as all protons are in the same environment.	-	-	-	

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Source: [redacted]

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
MS	-	-	-	Although it is technically possible to obtain a MS spectrum of hydrogen chloride gas, no useful information can be gained from this. The active substance being supported is the aqueous solution of hydrogen chloride, for which it is not possible to obtain an MS spectra. Furthermore, if a MS spectrum is to be used for identification then it should ideally contain three fragment ions with m/z ratios >100. This is not possible for hydrochloric acid as its molecular weight is only 36.5 g/mol; the spectrum would not contain any ions with m/z ratios >100.	-	-	-	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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)	Not specified	Not specified	Soluble	-	N	3	[redacted]	
	-	-	No data are available for the 36.2% hydrochloric acid concentrate. However, a value for the gas hydrogen chloride is cited in public literature: 823 g/L at 0°C	Although data are available for the gas hydrogen chloride, solubility in water is not considered a relevant parameter for hydrochloric acid. By definition hydrochloric acid is an aqueous solution of hydrogen chloride. Hence any addition of hydrochloric acid to water results in dilution of the acid rather than determining its solubility.	N	2	The Merck Index, 13th Ed. (2001). Ref. IIIA3.5/02	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
3.6 Dissociation constant (-)	-	-	-	Dissociation constant is not considered a relevant parameter for hydrochloric acid. By definition hydrochloric acid is an aqueous solution of hydrogen chloride. As such the active substance is present in its completely dissociated form ($H_3O^+ + Cl^-$, effectively H^+ and Cl^-) and it is not possible to determine the dissociation constant.	-	-	-	
3.7 Solubility in organic solvents, including the effect of temperature on solubility (IIIA3.1)	-	-	-	The solubility of hydrochloric acid in organic solvents is not considered a relevant parameter. The biocidal product does not contain any organic solvents, and it is highly unlikely that any subsequent products will contain organic solvents. Furthermore, as hydrochloric acid is an aqueous solution it will be immiscible with many organic solvents.	-	-	-	

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Source: [redacted]

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
3.8 Stability in organic solvents used in b.p. and identity of relevant breakdown products (IIIA3.2)	-	-	-	Not applicable. The biocidal product does not include any organic solvents therefore it is not necessary to assess the stability of hydrochloric acid in such solvents.	-	-	-	
3.9 Partition coefficient n-octanol/water (IIA3.6)	-	-	-	It is not considered technically possible to perform this test. The test method (EEC A8) states that measurements should be made on ionisable substances only in their non-ionised forms. By definition hydrochloric acid is an aqueous solution of hydrogen chloride. As such the active substance is present in its completely ionised form ($H_3O^+ + Cl^-$, effectively. H^+ and Cl^-). It is not possible to obtain a non-ionised form of hydrochloric acid and hence not possible to conduct this test.	-	-	-	
3.10 Thermal stability, identity of relevant breakdown products (IIA3.7)	-	-	-	Considering the safety implications of heating a concentrated acid it is not considered practical or necessary to conduct this test.	-	-	-	

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Source: [redacted]

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
3.11 Flammability, including auto-flammability and identity of combustion products (IIA3.8)	-	-	-	Test Guidelines EEC A10, A11 and A16 are not applicable as they are suitable for solid and/or gaseous substances only. The technical material is supplied as an aqueous concentrate. Test guideline EEC A13 determines the pyrophoric properties of solids and liquids and EEC A12 the flammability of substances in contact with water. However it is stated in the TNsG that these tests can be omitted if experience indicates that negative results would be obtained. Hydrochloric acid is not classified as R17 (Spontaneously flammable in air) or R14/15 (Reacts violently with water, liberating extremely flammable gases) and hence it is not considered necessary to carry out these tests. Considering the safety implications of heating a concentrated acid it is not considered practical or necessary to conduct the auto-ignition temperature test as	-	-	-	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
				outlined in EEC A15. Hydrochloric acid is an aqueous solution of hydrogen chloride and as such is not considered to have any flammable properties. A minimum of 64% of the technical material is water.				
3.12 Flash-point (IIA3.9)	-	-	-	It is not considered technically possible to perform this test. All laboratories that were approached to conduct this test according to EEC A9 indicated that they would be unable to carry out such a test due to the corrosive nature of concentrated hydrochloric acid towards the metal apparatus used. In addition, considering the safety implications of heating a concentrated acid it is not considered practical or necessary to conduct this test. Hydrochloric acid is an aqueous solution of hydrogen chloride and as such is not considered to have any flammable properties. A minimum of 64% of the technical material is water.	-	-	-	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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)	-	-	-	It is not considered technically possible to conduct this study. The harmonised ring method described in OECD 115, uses a ring made of platinum-iridium wire of specific dimensions to measure the surface tension of the system. Hydrochloric acid is a corrosive substance and would corrode the surface of the ring thus making it impossible to obtain an accurate reading of the surface tension. Furthermore, hydrochloric acid on contact with metals has the potential to release hydrogen gas which poses a risk of explosion and hence makes the test unsafe to perform.	-	-	-	
3.14 Viscosity (-)	CIPAC MT 22	Batch no.: CER_HCL_T220B Concentration: 36.2%	1.66 x 10^{-6} m^2/s at 20°C 1.31 x 10^{-6} m^2/s at 40°C	-	Y	1	Bell, A. (2007) Physical and Chemical Properties of Concentrated HCl. CEM Analytical Services Ltd (CEMAS), Report no.: CEMR-3305 Ref. IIIA3.14/01	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
3.15 Explosive properties (IIA3.11)	-	-	-	It is not technically possible to conduct the test specified due to the corrosive nature of hydrochloric acid. The flame (thermal sensitivity) and shock (sensitivity to mechanical stimuli) tests given in guideline EEC A14 involve the use of steel containers which would not be compatible with the test substance. Hydrochloric acid does not itself have any explosive properties. However, on contact with a majority of metals hydrogen is emitted and this can pose a risk of explosion. If instructions for safe use (e.g. the acid must not be stored in metal packaging) as stated on the MSDS are followed then hydrochloric acid does not pose an explosion risk (see 3.17 below).	N/A	1	[redacted]	

Doc IIIA Section A3 Physical and Chemical Properties of Active Substance

Source: [redacted]

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
3.16 Oxidizing properties (IIA3.12)	-	-	-	Examination of the structure of hydrochloric acid indicates that the substance will not have any oxidising properties. Hydrochloric acid is an aqueous solution of hydrogen chloride, and as such the active substance is present in its completely dissociated form ($H_3O^+ + Cl^-$, effectively H^+ and Cl^-). Although chlorine is an electronegative atom, in this case it is present as chloride ion and will not facilitate the oxidation of other compounds. It is stated in the MSDS that the substance "Can react violently if in contact with oxidising agents, liberating chlorine."	N/A	2	[redacted]	
3.17 Reactivity towards container material (IIA3.13)	N/A	N/A	Bulk quantities should be stored in rubber lined steel or suitable plastic equipment. Smaller quantities should be stored in suitable plastic or glass containers.	-	N/A	1	[redacted]	

Evaluation by Competent Authorities	
Date	Evaluation by Rapporteur Member State *17.06.2008.*

Materials and methods

The all physical/chemical information mostly is based on information from [redacted]
However, appearance, density, viscosity and freezing point are tested in GLP laboratories.

Justifications:

The all justifications are acceptable.

[redacted]

3.2. *Vapour pressure.*

Test is not carried out taking into consideration the corrosive nature of HCl. The equipment used for vapour pressure determination has metallic part which can be damaged by HCl.

3.2.1. Henry`s Law Constant.

Henry`s Law can be applied only for substances which diluting and do not dissociating. Therefore, this parameter can not be used for HCl (quickly disscociating).

3.4. Absorption spectra

Agree with applicant`s version of justification.

3.5. Solubility in water

Agree with applicant`s version of justification.

3.6. Dissociation constant

Agree with applicant`s version of justification.

3.7. Solubility in organic solvents, including the effect of temperature on solubility

Agree with applicant`s version of justification.

3.8. Stability in organic solvents used in biocidal product and identity of relevant breakdown products

The justification is acceptable according to TNsG on data requirements, chapter 3, point 3.8.

3.9. Partition coefficient n-octanol/water

Agree with applicant`s version of justification. In accordance with EC method A.8 the test can be conducted only in substance non-ionized form. However, the HCl can not be obtained in non-ionized form.

3.10. Thermal stability, identity of relevant breakdown products

Agree with applicant`s version of justification.

3.11. Flammability, including auto-flammability and identity of combustion products

Agree with applicant`s version of justification.
The justification (EC method A12/A13) is acceptable according to TNsG on data requirements, chapter 2, point 3.11.
The HCl is not classified as flammable therefore the justification of generation of auto-ignition test is acceptable.

3.12. Flash point

Agree with applicant`s version of justification.

Test is not carried out taking into consideration that the substance is not classified as flammable and the corrosive nature of HCl. The equipment used for vapour pressure determination has metallic part which can be damaged by HCl.

3.13. *Surface tension*

Agree with applicant`s version of justification.

Test is not carried out taking into consideration the corrosive nature of HCl. The equipment used for surface tension determination has metallic part which can be damaged by HCl.

3.15. Explosive properties

Agree with applicant`s version of justification.

3.16. Oxidizing properties

Agree with applicant`s version of justification.

Conclusion *Agree with the applicant`s version*

Reliability *1*

Acceptability *Acceptable*

Remarks [redacted]

Comments from ...

Date

Results and discussion

Conclusion

Reliability

Acceptability

Remarks

Doc IIIA/Section A4.1/01
BPD Data Set IIA/
Annex Point IV.4.1

Analytical Methods for Detection and Identification

Analytical methods for the determination of pure active substance

			Official use only
		1 REFERENCE	
1.1	**Reference**	Anon (1991) Polish Standard. Industrial hydrochloric acid. Polish Committee for Standardization, Measures and Quality. Standard No.: PN-91/C-84046 Established: 20/08/1991 Published	
1.2	**Data protection**	No	
1.2.1	Data owner	Not applicable	
1.2.2	Companies with letters of access	None	
1.2.3	Criteria for data protection	No data protection claimed	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Not applicable – Polish standard method.	
2.2	**GLP**	Not applicable – Polish standard method.	
2.3	**Deviations**	None	
		3 MATERIALS AND METHODS	
3.1	**Preliminary treatment**		
3.1.1	Enrichment	None – titrimetric or density measurement	
3.1.2	Cleanup	None – titrimetric or density measurement	
3.2	**Detection**		
3.2.1	Separation method	None – titrimetric or density measurement	
3.2.2	Detector	None – titrimetric or density measurement	
3.2.3	Standard(s)	None – titrimetric or density measurement	
3.2.4	Interfering substance(s)	Titration method – sulphuric acid is a potentially interfering substance and hence a correction factor is applied.	
3.3	**Linearity**		
3.3.1	Calibration range	Not applicable – Polish standard method.	
3.3.2	Number of measurements	Not applicable – Polish standard method.	
3.3.3	Linearity	Not applicable – Polish standard method.	

Doc IIIA/Section A4.1/01 BPD Data Set IIA/ Annex Point IV.4.1		Analytical Methods for Detection and Identification Analytical methods for the determination of pure active substance
3.4	**Specificity; interfering substances**	Titration method – sulphuric acid is a potentially interfering substance and hence a correction factor is applied.
3.5	**Recovery rates at different levels**	Not applicable – Polish standard method.
3.5.1	Relative standard deviation	Not applicable – Polish standard method.
3.6	**Limit of determination**	Not applicable – Polish standard method.
3.7	**Precision**	Not applicable – Polish standard method.
3.7.1	Repeatability	Not applicable – Polish standard method.
3.7.2	Independent laboratory validation	Not applicable – Polish standard method.

Doc IIIA/Section A4.1/01

BPD Data Set IIA/ Annex Point IV.4.1

Analytical Methods for Detection and Identification

Analytical methods for the determination of pure active substance

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods

Within the Polish standard PN-91/C-84046 two methods are presented for the determination of the hydrogen chloride content of hydrochloric acid. These are the determination of hydrogen chloride content by density measurement and the determination of hydrogen chloride content by titration. As stated under the Additional Information section, point 5 of this standard, these methods are considered consistent with the ISO standards 905-1976 and 904-1976 respectively. As these are internationally adopted standards it is not considered scientifically justified to provide any additional validation data. An outline of both the methods is presented below.

Determination of hydrogen chloride content by density measurement

The density of a 500mL sample of industrial hydrochloric acid is measured at 20±0.5°C using a hydrometer. The concentration (%w/w) of hydrogen chloride corresponding to the measured density is then established by comparison to tabulated values (Table 4.1-01). Intermediate values are determined by interpolation of the data.

Determination of hydrogen chloride content by titration

The total acidity of a sample of industrial hydrochloric acid is determined by titration with a sodium hydroxide solution in the presence of an indicator (bromocresol green). To use this method a correction has to be made for sulphuric acid content (a method for determination of sulphuric acid content is given in the standard).

4.2 Conclusion

Two methods are presented within the Polish standard PN-91/C-84046 for the determination of hydrogen chloride in hydrochloric acid. These methods are considered consistent with the ISO standards 905-1976 and 904-1976, and hence it is not necessary to provide any additional validation data as these are internationally accepted methods.

4.2.1 Reliability 1

4.2.2 Deficiencies None.

Doc IIIA/Section A4.1/01

BPD Data Set IIA/ Annex Point IV.4.1

Analytical Methods for Detection and Identification

Analytical methods for the determination of pure active substance

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	30 July 2008
Materials and methods	Applicant's version is acceptable.
Conclusion	Adopt applicant's version.
Reliability	1
Acceptability	Acceptable.
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	

Table 4.1-01 Density related concentration tables for determining hydrogen chloride content of hydrochloric acid

Density at 20°C	HCl concentration	Density at 20°C	HCl concentration
g/ml	%(w/w)	g/ml	%(w/w)
1	2	3	4
1.000	0.4	1.105	21.4
1.005	1.4	1.110	22.3
1.010	2.4	1.115	23.3
1.015	3.4	1.120	24.2
1.020	4.4	1.125	25.2
1.025	5.4	1.130	26.2
1.030	6.4	1.135	27.2
1.035	7.5	1.140	28.2
1.040	8.5	1.145	29.2
1.045	9.5	1.150	30.2
1.050	10.5	1.155	31.2
1.055	11.5	1.160	32.2
1.060	12.5	1.165	33.2
1.065	13.5	1.170	34.2
1.070	14.5	1.175	35.2
1.075	15.5	1.180	36.2
1.080	16.5	1.185	37.3
1.085	17.4	1.190	38.3
1.090	18.4	1.195	39.4
1.095	19.4	1.198	40.0[1)]
1.100	20.4		

[1)] Concentration of a saturated solution at a temperature of 20°C.

Doc. IIIA/ Section 4.1/02 **BPD Data set IIA/ Annex Point IV.4.2**	**Analytical Methods for the determination of pure active substance and, where appropriate, for relevant degradation products, isomers and impurities of active substances and their additives (e.g. stabilisers)** **CONFIDENTIAL**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [√]** **Other justification [ ]**	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]	Not applicable.	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	*Give date of action*	
Evaluation of applicant's justification	*Discuss applicant's justification and, if applicable, deviating view*	
Conclusion	*Indicate whether applicant's justification is acceptable or not. If unacceptable because of the reasons discussed above, indicate which action will be required, e.g. submission of specific test/study data*	
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		

Doc. IIIA/ Section 4.2/01 **BPD Data set IIA/ Annex Point IV.4.2**	**Analytical Methods for the active substance in Soil**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible [ ]** **Scientifically unjustified [√]**	
Limited exposure [√]	**Other justification [ ]**	
Detailed justification:	Environmental fate and exposure assessments have been carried out and are presented in Document IIA section 4.1 and Document IIB section 3.3. As a consequence of Harpic Limescale Remover formulation and use there is no direct release into the soil compartment. Potential indirect routes of exposure are application of sewage sludge and deposition from air immediately outside the dwelling where the product is used. However, as a result of the buffering capacity of soils and EU legislation governing application of sewage sludge to land, any emissions of chloride or hydronium ions (hydrochloric acid would be completely dissociated) are expected to have a minimal effect on the terrestrial environment. Furthermore, both hydrogen and chlorine are ubiquitous in the environment from natural and man-made sources making it impossible to determine the exact source. Analytical methods to monitor residues of hydrochloric acid in soil are therefore considered to be scientifically unjustified.	
Undertaking of intended data submission [ ]	Not applicable.	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	*28.09.2009*	
Evaluation of applicant's justification	*Applicant's justification is acceptable.*	
Conclusion	*Applicant's justification is acceptable.*	
Remarks	*None.*	
	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		

Doc. IIIA/ Section 4.2/02 BPD Data set IIA/ Annex Point IV.4.2	Analytical Methods for the active substance in air	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible [ ]** **Scientifically unjustified [√]**	
Limited exposure [√]	**Other justification [ ]**	
Detailed justification:	Environmental fate and exposure assessments have been carried out and are presented in Document IIA section 4.1 and Document IIB section 3.3. As a consequence of Harpic Limescale Remover formulation and use concentrations in air are predicted to be insignificant 1.83 x 10^{-10} mg/m^3 (normal use) and 2.7 x 10^{-9} mg/m^3 (worst case). In the presence of moisture in air, hydrogen chloride is dissolved into the moisture and exists in the dissociated form. Furthermore, both hydrogen and chlorine are ubiquitous in the environment from natural and man-made sources making it impossible to determine the exact source. The contribution of HCl to the atmosphere from the proposed use of Harpic Limescale Remover is considered to be insignificant compared to that from other natural and man-made sources. Analytical methods to monitor residues of hydrochloric acid in air are therefore considered to be scientifically unjustified.	
Undertaking of intended data submission [ ]	Not applicable.	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	*28.09.2009*	
Evaluation of applicant's justification	*Applicant's justification is acceptable.*	
Conclusion	*Applicant's justification is acceptable.*	
Remarks	*None.*	
	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		

Doc. IIIA/ Section 4.2/03 BPD Data set IIA/ Annex Point IV.4.2	Analytical Methods for the active substance in water	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible** [ ] **Scientifically unjustified** [√]	
Limited exposure [√]	**Other justification** [ ]	
Detailed justification:	Environmental fate and exposure assessments have been carried out and are presented in Document IIA section 4.1 and Document IIB section 3.3. Hydrochloric acid dissociates completely in water to form chloride ions and hydronium ions. Therefore any effects observed are due to the ion concentrations; the major effect being the resultant pH. Exposures in aqueous compartments have been assessed considering pH changes due to the addition of HCl to water. Predicted emissions of chloride and hydronium ions are expected to have minimal impact on the aquatic environment as hydrochloric acid enters the sewage system in a dissociated form and will not cause a significant change in the pH levels due to the high level of dilution and the well buffered environment of the STP. Furthermore, both hydrogen and chlorine are ubiquitous in the environment from natural and man-made sources making it impossible to determine the exact source. Analytical methods to monitor residues of hydrochloric acid in water are considered to be scientifically unjustified.	
Undertaking of intended data submission [ ]	Not applicable.	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	*11.04.2008.*	
Evaluation of applicant's justification	*Taking into consideration hydrochloric acid behaviour in the water completely dissociation, analytical method application is considered scientifically unjustified.*	
Conclusion	*Justification 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		

Doc. IIIA/ Section 4.2/04 BPD Data set IIA/ Annex Point IV.4.2	Analytical methods for the active substance in animal and human body fluids and tissues	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [√]** **Other justification [ ]**	
Detailed justification:	Analytical methods must be submitted for determination of residues in body fluids and tissues when an active substance is classified as toxic or highly toxic. Since hydrochloric acid is not classified as toxic nor highly toxic (Document IIIA, Section 9), analytical methods to monitor levels in body fluids and tissues are scientifically unjustified.	
Undertaking of intended data submission [ ]	Not applicable.	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	*11.04.2008.*	
Evaluation of applicant's justification	*Analytical methods for detection and identification are required only if an active substance is classified toxic or highly toxic, which isn't the case here.*	
Conclusion	*Justification is acceptable.*	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date		
Evaluation of applicant's justification		
Conclusion		
Remarks		

Doc. IIIA/ Section 4.3 BPD Data set IIA/ Annex Point IV.4.2	Analytical Methods for the active substance in/on food or feedstuffs	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [√]**	**Technically not feasible [ ]** **Scientifically unjustified [√]** **Other justification [ ]**	
Detailed justification:	Hydrochloric acid is formulated as a ready-to-use product intended to be applied indoors only, in toilets. Hydrochloric acid is not used in a manner that would cause it to come in to contact with food or feedstuffs (see Document IIIA, section 2.10). Therefore, the need to conduct studies on residues of the biocidal product in food and feedstuffs are unjustified. Consequently, analytical methods to monitor residues of hydrochloric acid in/on food and feedstuff are not scientifically justified.	
Undertaking of intended data submission [ ]	Not applicable.	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	*11.04.2008.*	
Evaluation of applicant's justification	*Analytical methods for detection and identification are required if the active substance or trated material can contact with food and feedstuffs. Hydrochlorid acid intended to be used in toilets.*	
Conclusion	*Justification is acceptable*	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date		
Evaluation of applicant's justification		
Conclusion		
Remarks		

Doc IIIA Section A5 Effectiveness against Target Organisms and Intended Uses

BPD Data Set IIA/ Annex Point V

Subsection (Annex Point)			Official use only
5.8	Likely tonnage to be placed on the market per year (IIA5.8)	[redacted]	

Doc. IIIA/ Section A5/01 — Effectiveness against target organisms and intended uses

BPD Data set IIA/ Annex Point V.5

		1 REFERENCE
1.1	**Reference**	Mazzola, P. G., Martins, A. M. S., Penna, T. C. V. (2006) Chemical resistance of the gram-negative bacteria to different sanitizers in a water purification system. Department of Biochemical and Pharmaceutical Technology, School of Pharmaceutical Sciences, University of Sao Paulo, Avda, Professor Lineu Prestes, 580, Bloco 16, 05508-900, Sao Paulo, Brazil. Published: 16 August 2006 BMC Infectious Diseases 2006, 6:131
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Criteria for data protection	*None*
1.2.3		No data protection claimed.
1.3	**Guideline study**	Basic Suspension Test (Phase 1) [ISO 14698-3].
1.4	**Deviations**	Not applicable
		2 METHOD
2.1	**Test Substance (active substance)**	
2.1.1	Active substance	Hydrochloric acid (HCl)
2.1.2	Composition of active substance tested	0.5% solution (pH 3.0)
2.1.3	Physical state and nature	Liquid
2.1.4	Monitoring of active substance concentration	Not required
2.1.5	Method of analysis	Not required
2.2	**Reference substance**	Not required
2.2.1	Method of analysis for reference substance	Not required
2.3	**Testing procedure**	
2.3.1	Test population / inoculum / test organism	See Table A5/01-2
2.3.2	Test system	See Table A5/01-2
2.3.3	Application of TS	See Table A5/01-2
2.3.4	Test conditions	See Table A5/01-2

2.3.5	Duration of the test / Exposure time	Contact time varied between test organisms, as samples were taken from the test mixture (organisms + HCl solution) at 1 minute intervals for vegetative forms and 5 minute intervals from spore forms. These were then plated for counting, and survivor counts were compared to the initial counts, until 1 $\log_{10}$ reduction was achieved.
2.3.6	Number of replicates performed	1 per bacterial species
2.3.7	Controls	No
2.4	**Examination**	
2.4.1	Effect investigated	Bactericidal activity ($\log_{10}$ Reduction in CFU)
2.4.2	Method for recording / scoring of the effect	Re-suspended treated inoculum serially diluted and plated onto tryptic soy agar
2.4.3	Intervals of examination	At 1 minute intervals for vegetative forms and 5 minute intervals from spore forms.
2.4.4	Statistics	Not required
2.4.5	Post monitoring of the test organism	Not required
		3 RESULTS
3.1	**Efficacy**	
3.1.1	Dose/Efficacy curve	Single dilution tested (0.5% HCl)
3.1.2	Begin and duration of effects	Effects determined at intervals (see section 2.4.3)
3.1.3	Observed effects in the post monitoring phase	Not applicable
3.2	**Effects against organisms or objects to be protected**	Highly effective reduction in number of colony forming units observed after contact with test substance. 4 $\log_{10}$ reduction times for the test organisms ranged from 11.24 – 43.52 minutes (calculated from D-values).
3.3	**Other effects**	None
3.4	**Efficacy of the reference substance**	No relevant reference substance
3.5	**Tabular and/or graphical presentation of the summarised results**	See Table A5/01-3
3.6	**Efficacy limiting factors**	

3.6.1	Occurrences of resistances	None observed
3.6.2	Other limiting factors	None recorded
		4 RELEVANCE OF THE RESULTS COMPARED TO FIELD CONDITIONS
4.1	**Reasons for laboratory testing**	Standard test protocol for evaluation of surface disinfectants
4.2	**Intended actual scale of biocide application**	Comparable
4.3	**Relevance compared to field conditions**	
4.3.1	Application method	Comparable (product will be applied undiluted)
4.3.2	Test organism	Representative, including species as required in standard test protocol
4.3.3	Observed effect	Representative
4.4	**Relevance for read-across**	The results from this test, although based on a simple preparation of 0.5% HCl, are highly relevant to the proposed biocide product 'Harpic Limescale Remover' (containing HCl).
		5 APPLICANT'S SUMMARY AND CONCLUSION
5.1	**Materials and methods**	In accordance with ISO 14698-3: 'Methodology for measuring the efficiency of processes of cleaning and/or disinfection of inert surfaces bearing bio-contaminated wet soiling or biofilms examines processes incorporating one or more of the following activities: rinsing, cleaning, disinfection, combined cleaning and disinfection, biochemical action, and mechanical action'. Part 3 defines the principles for measuring the efficiency of processes of rinsing and/or cleaning and/or disinfection and/or combined cleaning and disinfection of wet, soiled surfaces on which micro-organisms are developing (with or without formation of a biofilm), in cleanrooms and associated controlled environments. The bactericidal activity of a 0.5% HCl solution was evaluated against seven laboratory culture Gram negative bacterial species and seven 'wild strain' Gram negative bacterial species (collected from a typical water purification system) on a non-porous surface under dirty (organic soiling) conditions. Cultures of the 14 test organisms (listed in Table A5/01-1) were used to prepare stock solutions of 24 hr old inoculum, adjusted to approximately 1 x 10^5-10^6 colony forming units (CFU)/ml. 1 ml of 24hr bacterial suspension transferred to 100 ml of the test solution (0.5% HCl), and kept, with constant agitation at 25°C (± 1.0°C). At regular intervals (1 minute for vegetative forms and 5 minutes for spore forms) a 1ml sample of the mixture (HCl/microorganism suspension) was transferred to 9 ml of tryptic soy broth (TSB). Serial dilutions in saline were made of the TSB/HCl/microorganism mixture and samples were then taken for plating onto tryptic soy agar for assessment.

		The number of surviving CFU from each sampling were counted and a D-value (time for 1 $\log_{10}$ reduction from initial levels) was calculated. From the D-values the exposure times required for 6 $\log_{10}$ reductions (required for water purification in the USA) and 4 $\log_{10}$ reductions (required for PT02 disinfectants in the EU) in test organisms were calculated for each bacterial species.
5.2	**Reliability**	The study was considered to be very reliable. The methods and the use of a 0.5% HCl solution on a non-porous surface against a range of laboratory and 'wild strain' bacterial cultures is highly relevant to the proposed use of the biocide product 'Harpic Limescale Remover'. Reliability Factor: 1
5.3	**Assessment of efficacy, data analysis and interpretation**	The test substance reduced the numbers of CFU of the 14 bacterial species by a factor of at least 10^4 (i.e. 4 $\log_{10}$ units) within 45 minutes. The label use instructions for 'Harpic Limescale Remover' requires 30 minutes initial exposure followed by cleaning, flushing of the toilet and a repeat application with a further exposure time of 15 minutes. This gives a total exposure time of 45 minutes, within which time, according to these data, all 14 test species would have a reduction of 4 $\log_{10}$ CFU.
5.4	**Conclusion**	A 0.5% HCl solution was very effective in reducing populations of 14 representative Gram negative bacterial species on a smooth surface in the presence of organic soiling, given a 30-45 minute contact period.
5.5	**Proposed efficacy specification**	'Harpic Limescale Remover' is an effective surface bactericide in the presence of organic soiling, with a contact time of 30-45 minutes.

Doc. IIIA/ Section A5/01 — Effectiveness against target organisms and intended uses

BPD Data set IIA/ Annex Point V.5

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*17.06.2009.*
Materials and Methods	*Applicant's version is acceptable. The ISO 14698-3 method "Methodology for measuring the efficiency of processes of cleaning and/or disinfection of inert surfaces bearing bio-contaminated wet soiling or biofilms examines processes incorporating one or more of the following activities: rinsing, cleaning, disinfection, combined cleaning and disinfection, biochemical action, and mechanical action" has been applied. The bactericidal activity of a 0.5% HCl solution was evaluated against seven laboratory culture Gram negative bacterial species and seven 'wild strain' Gram negative bacterial species. The number of surviving CFU of bacteria were counted and a D-value (time for 1 log_{10} reduction from initial levels) was calculated.*
Results and discussion	*Applicant's version is adopted. The test substance reduced the numbers of CFU of the 14 bacterial species by a factor of at least 10^4 (i.e. 4 log_{10} units) within 45 minutes. The label use instructions for 'Harpic Limescale Remover' requires 30 minutes initial exposure followed by a repeat application with a further exposure time of 15 minutes. This gives a total exposure time of 45 minutes.*
Conclusion	*Applicant's version is adopted. A 0.5% HCl solution is very effective in reducing populations of 14 representative Gram negative bacterial species on a smooth surface in the presence of organic soiling, given a 30-45 minute contact period.*
Reliability	*1*
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 A5/01-1 Test organisms

Criteria	Details
Species	*Pseudomonas aeruginosa*
Strain	Wild strain
Source	Collected from a water purification system
Laboratory culture	No
Stage of life cycle and stage of stadia	Vegetative
Mixed age population	n/a
Other specification	n/a
Number of organisms tested	Stock culture adjusted to 10^6 CFU/ml
Method of cultivation	Incubation on tryptic soy agar
Pretreatment of test organisms before exposure	24 hr culture grown on TSA 30-35°C, harvested from tryptic soy broth, re-suspended in saline. These suspensions were then plated onto Cetrimide Agar Base and incubated at 30-35°C for 18-24 hrs.
Initial density/number of test organisms in the test system	Bacterial test suspension ~10^5-10^6 CFU/ml

Criteria	Details
Species	*Pseudomonas alcaligenes*
Strain	Wild strain
Source	Collected from a water purification system
Laboratory culture	No
Stage of life cycle and stage of stadia	Vegetative
Mixed age population	n/a
Other specification	n/a
Number of organisms tested	Stock culture adjusted to 10^6 CFU/ml
Method of cultivation	Incubation on tryptic soy agar
Pretreatment of test organisms before exposure	24 hr culture grown on TSA 30-35°C, harvested from tryptic soy broth, re-suspended in saline. These suspensions were then plated onto Cetrimide Agar Base and incubated at 30-35°C for 18-24 hrs.
Initial density/number of test organisms in the test system	Bacterial test suspension ~10^5-10^6 CFU/ml

Criteria	**Details**
Species	*Pseudomonas diminuta*
Strain	Wild strain
Source	Collected from a water purification system
Laboratory culture	No
Stage of life cycle and stage of stadia	Vegetative
Mixed age population	n/a
Other specification	n/a
Number of organisms tested	Stock culture adjusted to 10^6 CFU/ml
Method of cultivation	Incubation on tryptic soy agar
Pretreatment of test organisms before exposure	24 hr culture grown on TSA 30-35°C, harvested from tryptic soy broth, re-suspended in saline. These suspensions were then plated onto Cetrimide Agar Base and incubated at 30-35°C for 18-24 hrs.
Initial density/number of test organisms in the test system	Bacterial test suspension ~10^5-10^6 CFU/ml

Criteria	**Details**
Species	*Pseudomonas fluorescens*
Strain	Wild strain
Source	Collected from a water purification system
Laboratory culture	No
Stage of life cycle and stage of stadia	Vegetative
Mixed age population	n/a
Other specification	n/a
Number of organisms tested	Stock culture adjusted to 10^6 CFU/ml
Method of cultivation	Incubation on tryptic soy agar
Pretreatment of test organisms before exposure	24 hr culture grown on TSA 30-35°C, harvested from tryptic soy broth, re-suspended in saline. These suspensions were then plated onto Cetrimide Agar Base and incubated at 30-35°C for 18-24 hrs.
Initial density/number of test organisms in the test system	Bacterial test suspension ~10^5-10^6 CFU/ml

Criteria	Details
Species	*Pseudomonas picketti*
Strain	Wild strain
Source	Collected from a water purification system
Laboratory culture	No
Stage of life cycle and stage of stadia	Vegetative
Mixed age population	n/a
Other specification	n/a
Number of organisms tested	Stock culture adjusted to 10^6 CFU/ml
Method of cultivation	Incubation on tryptic soy agar
Pretreatment of test organisms before exposure	24 hr culture grown on TSA 30-35°C, harvested from tryptic soy broth, re-suspended in saline. These suspensions were then plated onto Cetrimide Agar Base and incubated at 30-35°C for 18-24 hrs.
Initial density/number of test organisms in the test system	Bacterial test suspension ~10^5-10^6 CFU/ml

Criteria	Details
Species	*Flavobacterium aureum*
Strain	Wild strain
Source	Collected from a water purification system
Laboratory culture	No
Stage of life cycle and stage of stadia	Vegetative
Mixed age population	n/a
Other specification	n/a
Number of organisms tested	Stock culture adjusted to 10^6 CFU/ml
Method of cultivation	Incubation on tryptic soy agar
Pretreatment of test organisms before exposure	24 hr culture grown on TSA 30-35°C, harvested from tryptic soy broth, re-suspended in saline. These suspensions were then plated onto Cetrimide Agar Base and incubated at 30-35°C for 18-24 hrs.
Initial density/number of test organisms in the test system	Bacterial test suspension ~10^5-10^6 CFU/ml

Criteria	Details
Species	*Acinetobacter lowffi*
Strain	Wild strain
Source	Collected from a water purification system
Laboratory culture	No
Stage of life cycle and stage of stadia	Vegetative
Mixed age population	n/a
Other specification	n/a
Number of organisms tested	Stock culture adjusted to 10^6 CFU/ml
Method of cultivation	Incubation on tryptic soy agar
Pretreatment of test organisms before exposure	24 hr culture grown on TSA 30-35°C, harvested from tryptic soy broth, re-suspended in saline. These suspensions were then plated onto Cetrimide Agar Base and incubated at 30-35°C for 18-24 hrs.
Initial density/number of test organisms in the test system	Bacterial test suspension ~10^5-10^6 CFU/ml

Criteria	Details
Species	*Eschericia coli*
Strain	ATCC 25922
Source	-
Laboratory culture	Yes
Stage of life cycle and stage of stadia	Vegetative
Mixed age population	n/a
Other specification	n/a
Number of organisms tested	Stock culture adjusted to 10^6 CFU/ml
Method of cultivation	Incubation on tryptic soy agar
Pretreatment of test organisms before exposure	24 hr culture grown on TSA 30-35°C, harvested from tryptic soy broth, re-suspended in saline. These suspensions were then plated onto Cetrimide Agar Base and incubated at 30-35°C for 18-24 hrs.
Initial density/number of test organisms in the test system	Bacterial test suspension ~10^5-10^6 CFU/ml

Criteria	Details
Species	*Pseudomonas aeruginosa*
Strain	ATCC 15442
Source	From stock
Laboratory culture	Yes
Stage of life cycle and stage of stadia	Vegetative
Mixed age population	n/a
Other specification	n/a
Number of organisms tested	Stock culture adjusted to 10^6 CFU/ml
Method of cultivation	Incubation on tryptic soy agar
Pretreatment of test organisms before exposure	24 hr culture grown on TSA 30-35°C, harvested from tryptic soy broth, re-suspended in saline. These suspensions were then plated onto Cetrimide Agar Base and incubated at 30-35°C for 18-24 hrs.
Initial density/number of test organisms in the test system	Bacterial test suspension ~10^5-10^6 CFU/ml

Criteria	Details
Species	*Pseudomonas alcaligenes*
Strain	INCQS
Source	From stock
Laboratory culture	Yes
Stage of life cycle and stage of stadia	Vegetative
Mixed age population	n/a
Other specification	n/a
Number of organisms tested	Stock culture adjusted to 10^6 CFU/ml
Method of cultivation	Incubation on tryptic soy agar
Pretreatment of test organisms before exposure	24 hr culture grown on TSA 30-35°C, harvested from tryptic soy broth, re-suspended in saline. These suspensions were then plated onto Cetrimide Agar Base and incubated at 30-35°C for 18-24 hrs.
Initial density/number of test organisms in the test system	Bacterial test suspension ~10^5-10^6 CFU/ml

Criteria	Details
Species	*Pseudomonas diminuta*
Strain	ATCC 11568
Source	Collected from a water purification system
Laboratory culture	No
Stage of life cycle and stage of stadia	Vegetative
Mixed age population	n/a
Other specification	n/a
Number of organisms tested	Stock culture adjusted to 10^6 CFU/ml
Method of cultivation	Incubation on tryptic soy agar
Pretreatment of test organisms before exposure	24 hr culture grown on TSA 30-35°C, harvested from tryptic soy broth, re-suspended in saline. These suspensions were then plated onto Cetrimide Agar Base and incubated at 30-35°C for 18-24 hrs.
Initial density/number of test organisms in the test system	Bacterial test suspension ~10^5-10^6 CFU/ml

Criteria	Details
Species	*Pseudomonas fluorescens*
Strain	ATCC 3178
Source	Collected from a water purification system
Laboratory culture	No
Stage of life cycle and stage of stadia	Vegetative
Mixed age population	n/a
Other specification	n/a
Number of organisms tested	Stock culture adjusted to 10^6 CFU/ml
Method of cultivation	Incubation on tryptic soy agar
Pretreatment of test organisms before exposure	24 hr culture grown on TSA 30-35°C, harvested from tryptic soy broth, re-suspended in saline. These suspensions were then plated onto Cetrimide Agar Base and incubated at 30-35°C for 18-24 hrs.
Initial density/number of test organisms in the test system	Bacterial test suspension ~10^5-10^6 CFU/ml

Criteria	Details
Species	*Pseudomonas picketti*
Strain	ATCC 5031
Source	From stock
Laboratory culture	Yes
Stage of life cycle and stage of stadia	Vegetative
Mixed age population	n/a
Other specification	n/a
Number of organisms tested	Stock culture adjusted to 10^6 CFU/ml
Method of cultivation	Incubation on tryptic soy agar
Pretreatment of test organisms before exposure	24 hr culture grown on TSA 30-35°C, harvested from tryptic soy broth, re-suspended in saline. These suspensions were then plated onto Cetrimide Agar Base and incubated at 30-35°C for 18-24 hrs.
Initial density/number of test organisms in the test system	Bacterial test suspension ~10^5-10^6 CFU/ml

Criteria	Details
Species	*Bacillus subtilis*
Strain	ATCC 9372
Source	From stock
Laboratory culture	Yes
Stage of life cycle and stage of stadia	Non-Vegetative (spore form)
Mixed age population	n/a
Other specification	n/a
Number of organisms tested	Stock culture adjusted to 10^5-10^6 CFU/ml
Method of cultivation	Maintained as a spore suspension
Pretreatment of test organisms before exposure	1 ml of spore suspension was sampled and transferred to 99 ml of sterile saline solution (0.9% NaCl) agitated for 15 minutes, and a repeat dilution made (1:100) into sterile saline solution. A 5ml sample was transferred to a small flask and subjected to thermal shock (80°C/10 min then immersion in a water/ice bath). Further serial dilutions were then made for counting purposes. 1 ml of each dilution was transferred to a sterile Petri dish and 8 ml of sterile plate count agar added. The plates were then incubated for 24 hrs at 35°C.
Initial density/number of test organisms in the test system	Bacterial test suspension ~10^5-10^6 CFU/ml

Table A5/01-2 Test system, Test Conditions, Application of Test Substance

Criteria	Details
Culturing apparatus / test chamber	Not stated.
Number of vessels / concentration	1
Test culture media and/or carrier material	1 ml of 24 hr bacterial suspension transferred to 100 ml of the test solution (0.5% HCl), and kept, with constant agitation at 25°C (± 1.0°C).
Nutrient supply	-
Measuring equipment	At regular intervals (1 minute for vegetative forms and 5 minutes for spore forms) a 1ml sample of the mixture (HCl/microorganism suspension) was transferred to 9 ml of tryptic soy broth (TSB). Serial dilutions in saline were made of the TSB/HCl/microorganism mixture and samples were then taken for plating onto tryptic soy agar for assessment.

Table A5/01-3 Tabulated results

Bactericidal activity of 0.5% HCl on a non-porous surface

Test organism	D-value (1 $\log_{10}$ reduction) [minutes]	6 $\log_{10}$ reduction [minutes]†	4 $\log_{10}$ reduction [minutes]†	Acceptability criteria ($\log_{10}$ units)
*Pseudomonas aeruginosa**	6.88	41.29	27.52	≥4
*Pseudomonas alcaligenes**	5.56	33.39	22.24	≥4
*Pseudomonas diminuta**	6.49	38.91	25.96	≥4
*Pseudomonas fluorescens**	9.12	54.74	36.48	≥4
*Pseudomonas picketti**	10.81	64.86	43.24	≥4
*Flavobacterium aureum**	5.67	34.03	22.68	≥4
*Acinetobacter lowffi**	7.26	43.57	29.04	≥4
Bacillus subtilis (ATCC 9372)	10.88	65.29	43.52	≥4
Eschericia coli (ATCC 25922)	3.70	22.19	14.80	≥4
Pseudomonas aeruginosa (ATCC 15442)	6.35	38.12	25.40	≥4
Pseudomonas alcaligenes (INCQS)	4.03	24.16	16.12	≥4
Pseudomonas diminuta (ATCC 11568)	2.81	16.87	11.24	≥4
Pseudomonas fluorescens (ATCC 3178)	4.22	25.34	16.88	≥4
Pseudomonas picketti (ATCC 5031)	4.78	28.71	19.12	≥4

*wild strains (isolated from a typical water purification system)
†Calculated value based on multiplication of D-value interval.

Doc. IIIA/ Section A5/02 — Effectiveness against target organisms and intended uses

BPD Data set IIA/ Annex Point V.5

		1 REFERENCE
1.1	**Reference**	Cavalleri, M. (2008a) Evaluation of disinfectant effectiveness [redacted]
1.2	**Data protection**	
1.2.1	Data owner	Reckitt Benckiser, Inc.
1.2.2	Companies with letter of access	Not applicable
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.
1.3	**Guideline study**	International Guideline Study (to GLP): EN 13697 (Aug 2001) 'Evaluation of bactericidal activity: Surface test'
1.4	**Deviations**	Plates containing 15-300 cfu were used for counts (as amended by CEN/TC216 – technical committee on disinfectants)
		2 METHOD
2.1	**Test Substance (active substance)**	
2.1.1	Active substance	Hydrochloric acid (HCl), Batch: XFA015 HH
2.1.2	Composition of active substance tested	[redacted]
2.1.3	Physical state and nature	Liquid
2.1.4	Monitoring of active substance concentration	Not required
2.1.5	Method of analysis	Not required
2.2	**Reference substance**	Not required
2.2.1	Method of analysis for reference substance	Not required
2.3	**Testing procedure**	EN 13697 (Aug 2001) 'Evaluation of bactericidal activity: Surface test'
2.3.1	Test population / inoculum / test organism	See Table A5/02-1
2.3.2	Test system	See Table A5/02-2
2.3.3	Application of TS	See Table A5/02-3

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BPD Data set IIA/ Annex Point V.5

2.3.4 Test conditions See Table A5/02-4

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BPD Data set IIA/ Annex Point V.5

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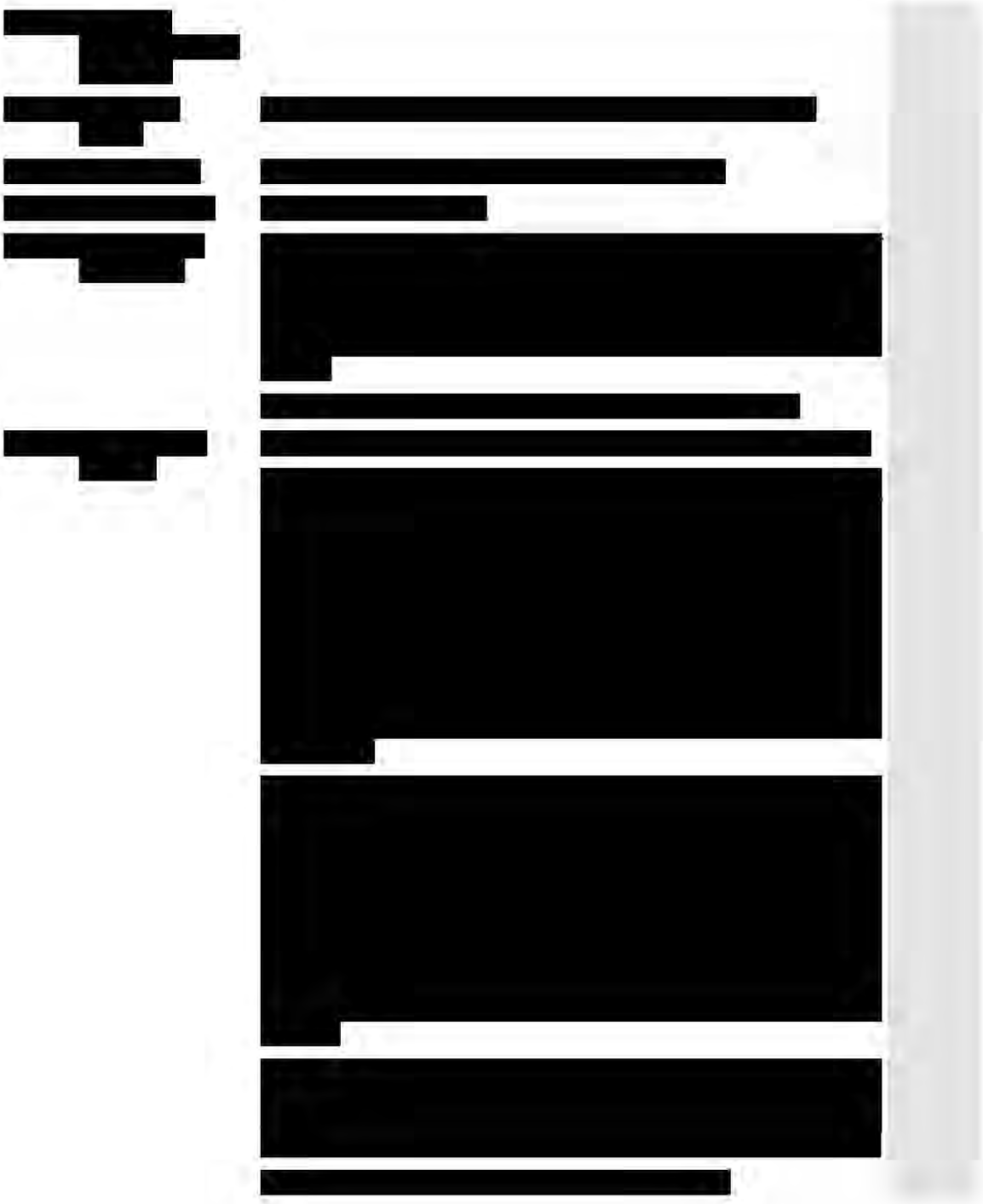
Doc. IIIA/ Section A5/02 **Effectiveness against target organisms and intended uses**

BPD Data set IIA/ Annex Point V.5



Doc. IIIA/ Section A5/02 **Effectiveness against target organisms and intended uses**

BPD Data set IIA/ Annex Point V.5

Doc. IIIA/ Section A5/02 — Effectiveness against target organisms and intended uses

BPD Data set IIA/ Annex Point V.5

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*17.06.2009.*
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	*1*
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	

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Doc. IIIA/ Section A5/03 — Effectiveness against target organisms and intended uses

BPD Data set IIA/ Annex Point V.5

		1 REFERENCE
1.1	**Reference**	Cavalleri, M. (2008a) Evaluation of disinfectant effectiveness [redacted]
1.2	**Data protection**	
1.2.1	Data owner	Reckitt Benckiser, Inc.
1.2.2	Companies with letter of access	Not applicable
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.
1.3	**Guideline study**	International Guideline Study (to GLP): EN 13697 (Aug 2001) 'Evaluation of fungicidal activity: Surface test'
1.4	**Deviations**	Plates containing 15-150 cfu were used for counts (as amended by CEN/TC216 – technical committee on disinfectants)
		2 METHOD
2.1	**Test Substance (active substance)**	
2.1.1	Active substance	Hydrochloric acid (HCl), Batch: XFA015 HH
2.1.2	Composition of active substance tested	[redacted]
2.1.3	Physical state and nature	Liquid
2.1.4	Monitoring of active substance concentration	Not required
2.1.5	Method of analysis	Not required
2.2	**Reference substance**	Not required
2.2.1	Method of analysis for reference substance	Not required
2.3	**Testing procedure**	EN 13697 (Aug 2001) 'Evaluation of fungicidal activity: Surface test'
2.3.1	Test population / inoculum / test organism	*Candida albicans* (ATCC 10231) *Aspergillus niger* (ATCC 16404) See Table A5/03-1
2.3.2	Test system	See Table A5/03-2

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2.3.3	Application of TS	See Table A5/03-3
2.3.4	Test conditions	See Table A5/03-4

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Doc. IIIA/ Section A5/03 **Effectiveness against target organisms and intended uses**

BPD Data set IIA/ Annex Point V.5

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BPD Data set IIA/ Annex Point V.5

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*17.06.2009.*
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	*1*
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 A5/03-1 Test organisms

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Doc. IIIA/ Section A5/04 — Effectiveness against target organisms and intended uses

BPD Data set IIA/ Annex Point V.5

		1 REFERENCE
1.1	**Reference**	Cavalleri, M. (2008a) Evaluation of disinfectant effectiveness [redacted]
1.2	**Data protection**	
1.2.1	Data owner	Reckitt Benckiser, Inc.
1.2.2	Companies with letter of access	Not applicable
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.
1.3	**Guideline study**	International Guideline Study (to GLP): EN 1276 (Jun 1997) 'Evaluation of bactericidal activity in suspension, filtration method'
1.4	**Deviations**	Plates containing 15-300 cfu were used for counts (as amended by CEN/TC216 – technical committee on disinfectants)
		2 METHOD
2.1	**Test Substance (active substance)**	
2.1.1	Active substance	Hydrochloric acid (HCl), Batch: XFA015 HH
2.1.2	Composition of active substance tested	[redacted]
2.1.3	Physical state and nature	Liquid
2.1.4	Monitoring of active substance concentration	Not required
2.1.5	Method of analysis	Not required
2.2	**Reference substance**	Not required
2.2.1	Method of analysis for reference substance	Not required
2.3	**Testing procedure**	EN 1276:1997 'Evaluation of bactericial activity in suspension: Filtration method'

Doc. IIIA/ Section A5/04 — Effectiveness against target organisms and intended uses

BPD Data set IIA/ Annex Point V.5

2.3.1	Test population / inoculum / test organism	*Staphylococcus aureus* (ATCC 6538) *Pseudomonas aeruginosa* (ATCC 15442) *Escherichia coli* (ATCC 10536) *Enterococcus hirae* (ATCC 10541) See Table A5/04-1
2.3.2	Test system	See Table A5/04-2
2.3.3	Application of TS	See Table A5/04-3
2.3.4	Test conditions	See Table A5/04-4

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Doc. IIIA/ Section A5/04 **Effectiveness against target organisms and intended uses**

BPD Data set IIA/ Annex Point V.5

Doc. IIIA/ Section A5/04 **Effectiveness against target organisms and intended uses**

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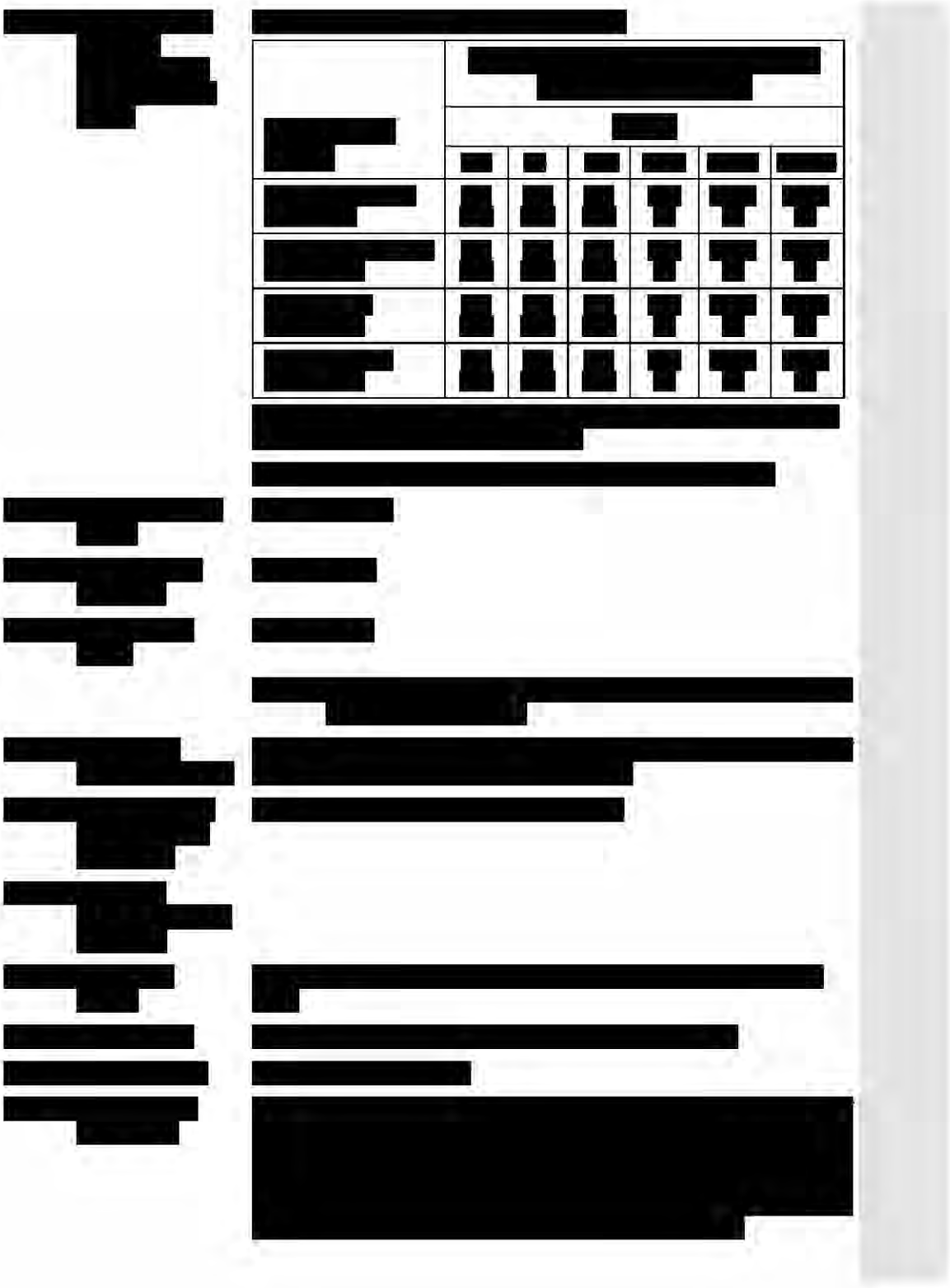
Effectiveness against target organisms and intended uses

BPD Data set IIA/ Annex Point V.5



Doc. IIIA/ Section A5/04 **Effectiveness against target organisms and intended uses**

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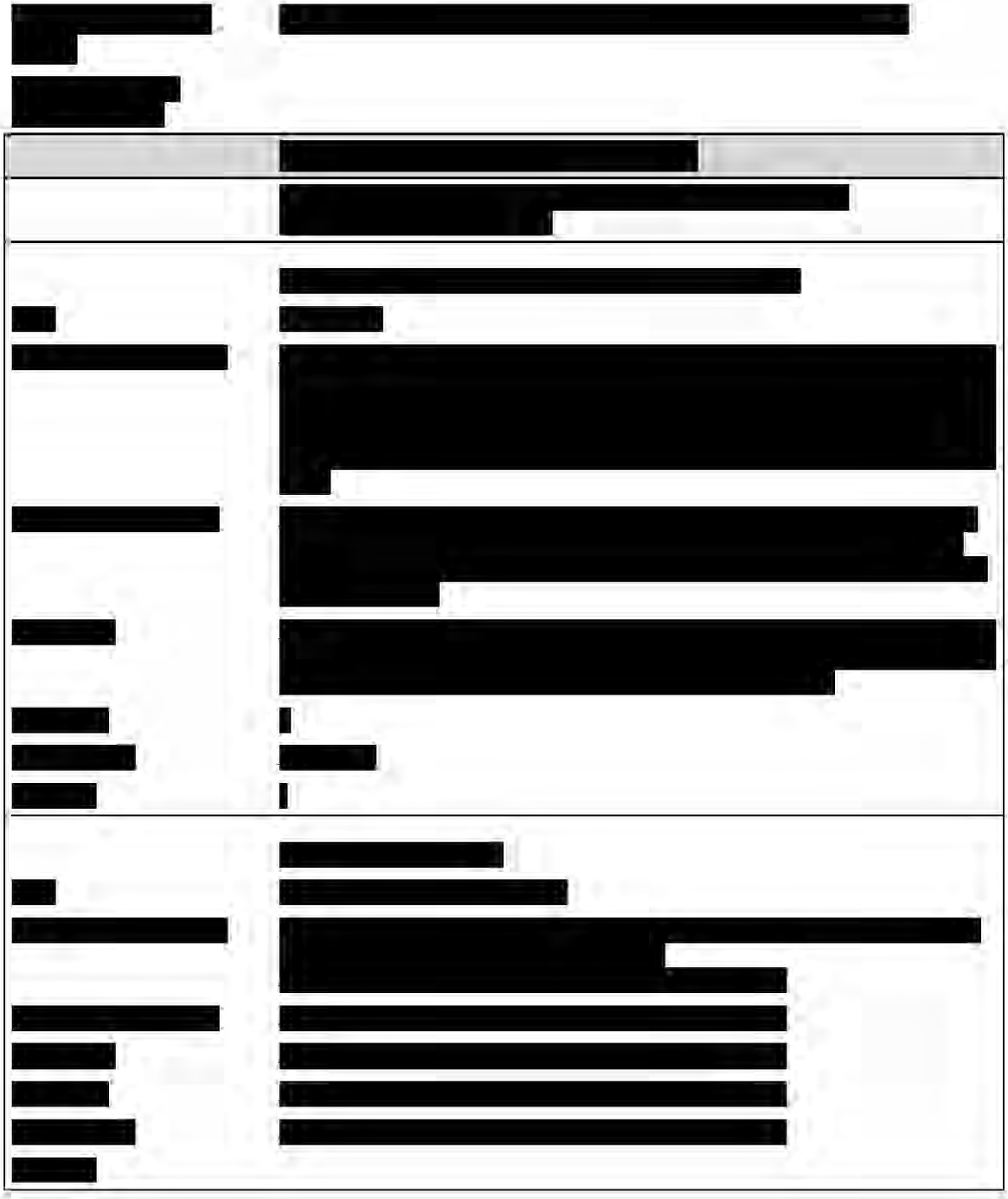

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Doc. IIIA/ Section A5/05 — Effectiveness against target organisms and intended uses

BPD Data set IIA/ Annex Point V.5

		1 REFERENCE
1.1	**Reference**	Cavalleri, M. (2008a) Evaluation of disinfectant effectiveness [redacted]
1.2	**Data protection**	
1.2.1	Data owner	Reckitt Benckiser, Inc.
1.2.2	Companies with letter of access	Not applicable
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.
1.3	**Guideline study**	International Guideline Study (to GLP): EN 1650 (Dec 1997) 'Evaluation of fungicidal activity in suspension, filtration method'
1.4	**Deviations**	Plates containing 15-150 cfu were used for counts (as amended by CEN/TC216 – technical committee on disinfectants)
		2 METHOD
2.1	**Test Substance (active substance)**	
2.1.1	Active substance	Hydrochloric acid (HCl), Batch: XFA015 HH
2.1.2	Composition of active substance tested	[redacted]
2.1.3	Physical state and nature	Liquid
2.1.4	Monitoring of active substance concentration	Not required
2.1.5	Method of analysis	Not required
2.2	**Reference substance**	Not required
2.2.1	Method of analysis for reference substance	Not required
2.3	**Testing procedure**	EN 1650:1997 'Evaluation of fungicidal activity in suspension, filtration method'.
2.3.1	Test population / inoculum / test organism	*Candida albicans* (ATCC 10231) *Aspergillus niger* (ATCC 16404) See Table A5/05-1

Doc. IIIA/ Section A5/05 Effectiveness against target organisms and intended uses

BPD Data set IIA/ Annex Point V.5

2.3.2	Test system	See Table A5/05-2
2.3.3	Application of TS	See Table A5/05-3
2.3.4	Test conditions	See Table A5/05-4

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Doc. IIIA/ Section A5/05 Effectiveness against target organisms and intended uses

BPD Data set IIA/ Annex Point V.5

Doc. IIIA/ Section A5/05 **Effectiveness against target organisms and intended uses**

BPD Data set IIA/ Annex Point V.5

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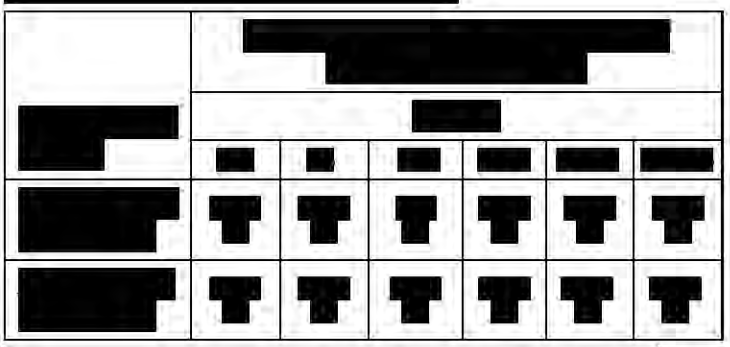

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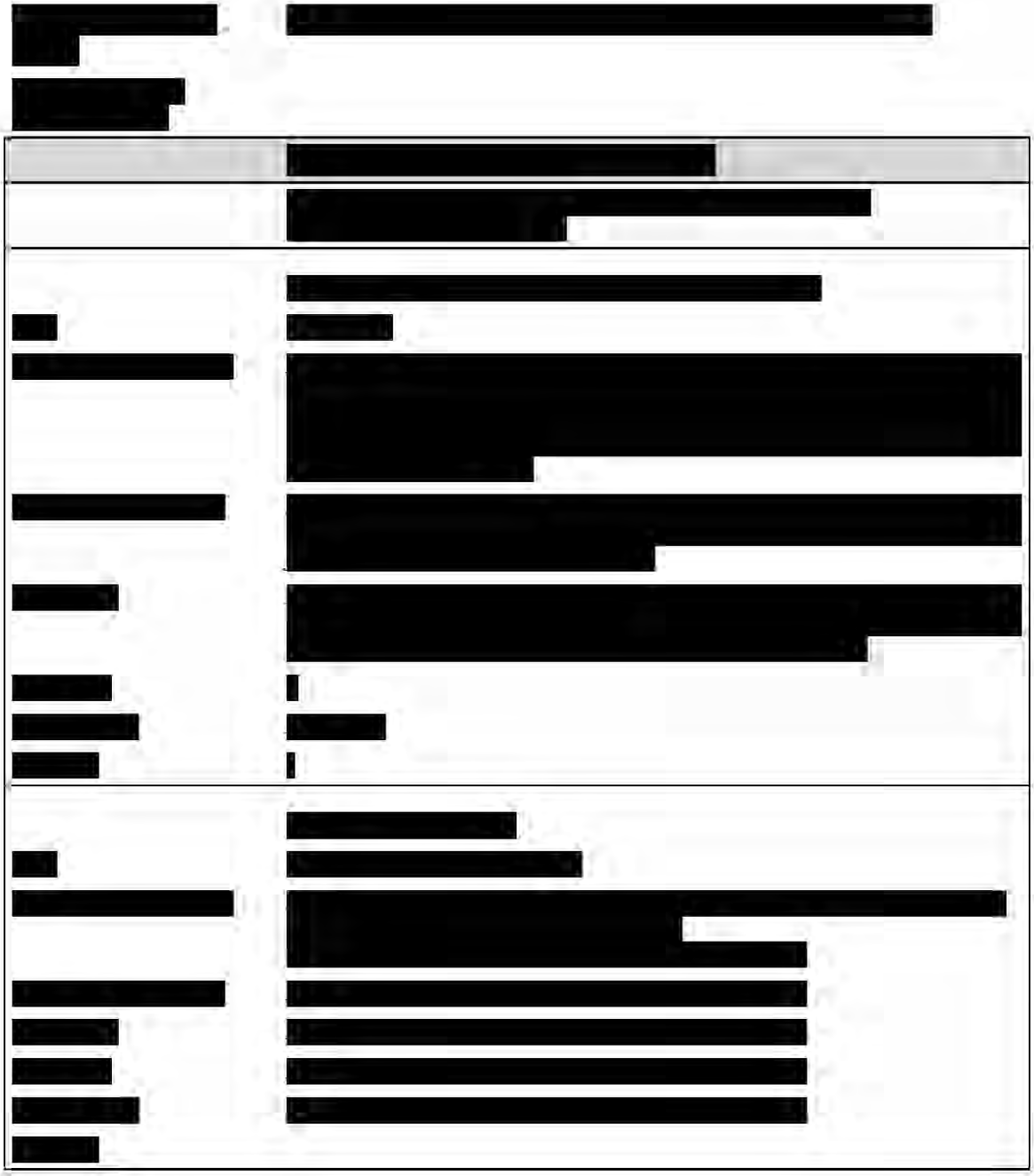
Doc. IIIA/ Section A5/05 **Effectiveness against target organisms and intended uses**

BPD Data set IIA/ Annex Point V.5



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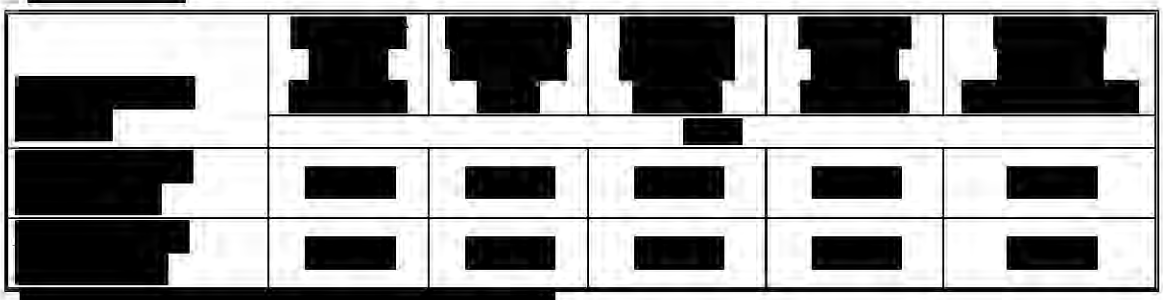

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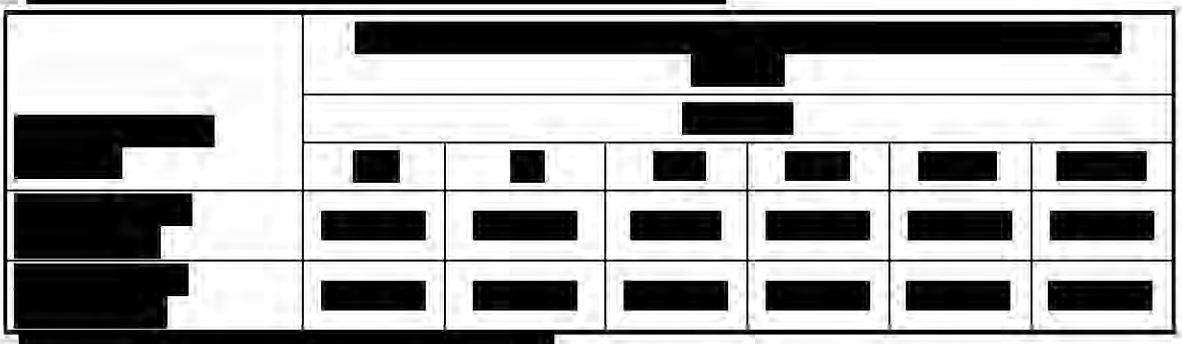

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Doc. IIIA/ Section A5/06 — Effectiveness against target organisms and intended uses

BPD Data set IIA/ Annex Point V.5

1 REFERENCE

1.1	**Reference**	Cavalleri, M. (2008b) Virucidal quantitative suspension test (EN 14476) Eurofins|Biolab, Biolab S.p.A., Via Bruno Buzzoni, 2, [redacted]
1.2	**Data protection**	
1.2.1	Data owner	Reckitt Benckiser, Inc.
1.2.2	Companies with letter of access	Not applicable
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.
1.3	**Guideline study**	International Guideline Study (to GLP): EN 14476 'Quantitative suspension test for the evaluation of virucidal activity' (April 2005 + A1, October 2006)
1.4	**Deviations**	None

2 METHOD

2.1	**Test Substance (active substance)**	
2.1.1	Active substance	Hydrochloric acid (HCl), Batch: XFA015 HH
2.1.2	Composition of active substance tested	[redacted]
2.1.3	Physical state and nature	Liquid
2.1.4	Monitoring of active substance concentration	Not required
2.1.5	Method of analysis	Not required
2.2	**Reference substance**	Not required
2.2.1	Method of analysis for reference substance	Not required
2.3	**Testing procedure**	EN 14476 'Quantitative suspension test for the evaluation of virucidal activity' (April 2005 + A1, October 2006)
2.3.1	Test population / inoculum / test organism	*Adenovirus* Type 5 (ATCC VR-5) *Poliovirus* Type 1 (Lsc2ab – Sabin strain) See Table A5/06-1
2.3.2	Test system	See Table A5/06-2

Doc. IIIA/ Section A5/06 — Effectiveness against target organisms and intended uses

BPD Data set IIA/ Annex Point V.5

2.3.3	Application of TS	See Table A5/06-3
2.3.4	Test conditions	See Table A5/06-4

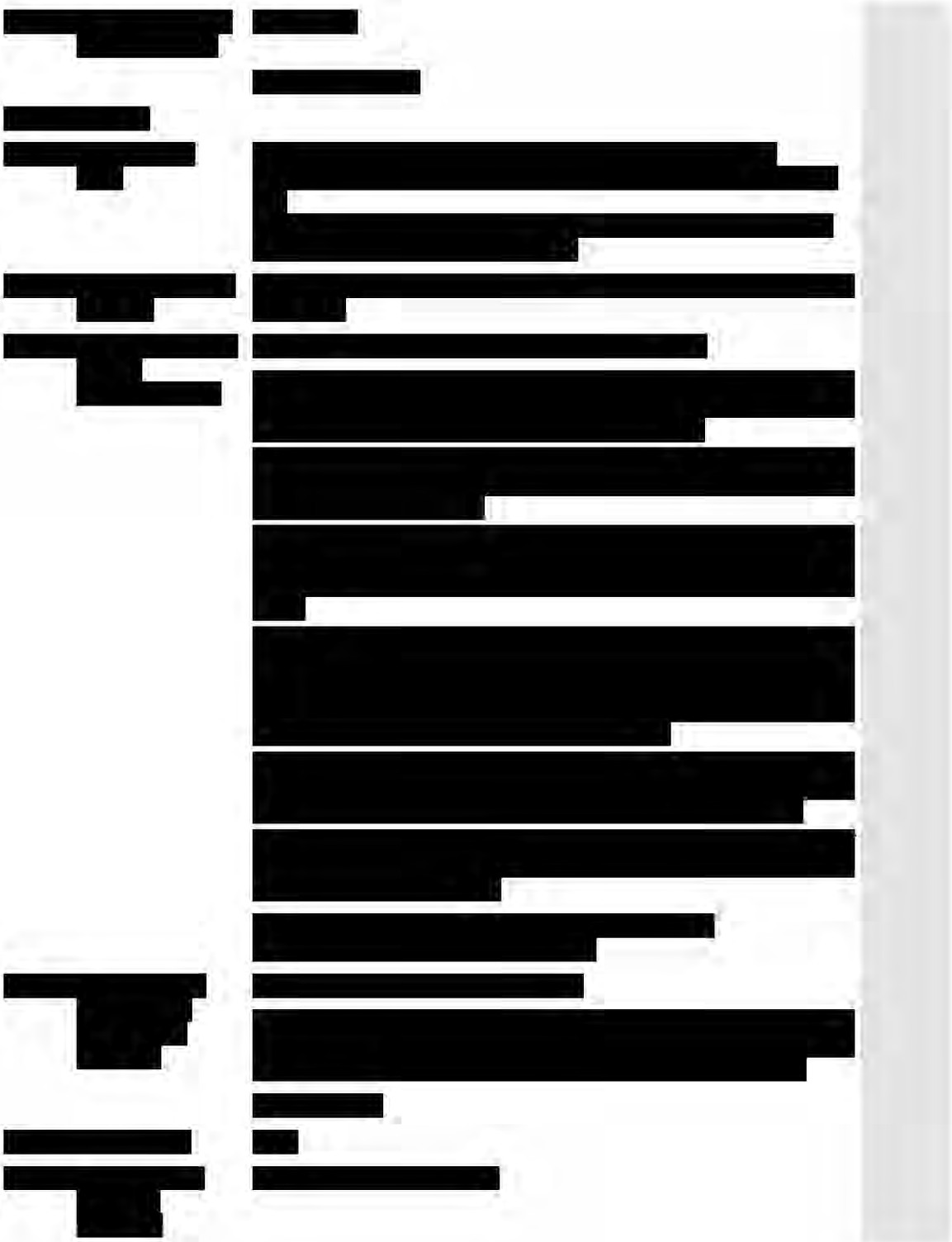
[redacted]

Doc. IIIA/ Section A5/06 **Effectiveness against target organisms and intended uses**

BPD Data set IIA/ Annex Point V.5

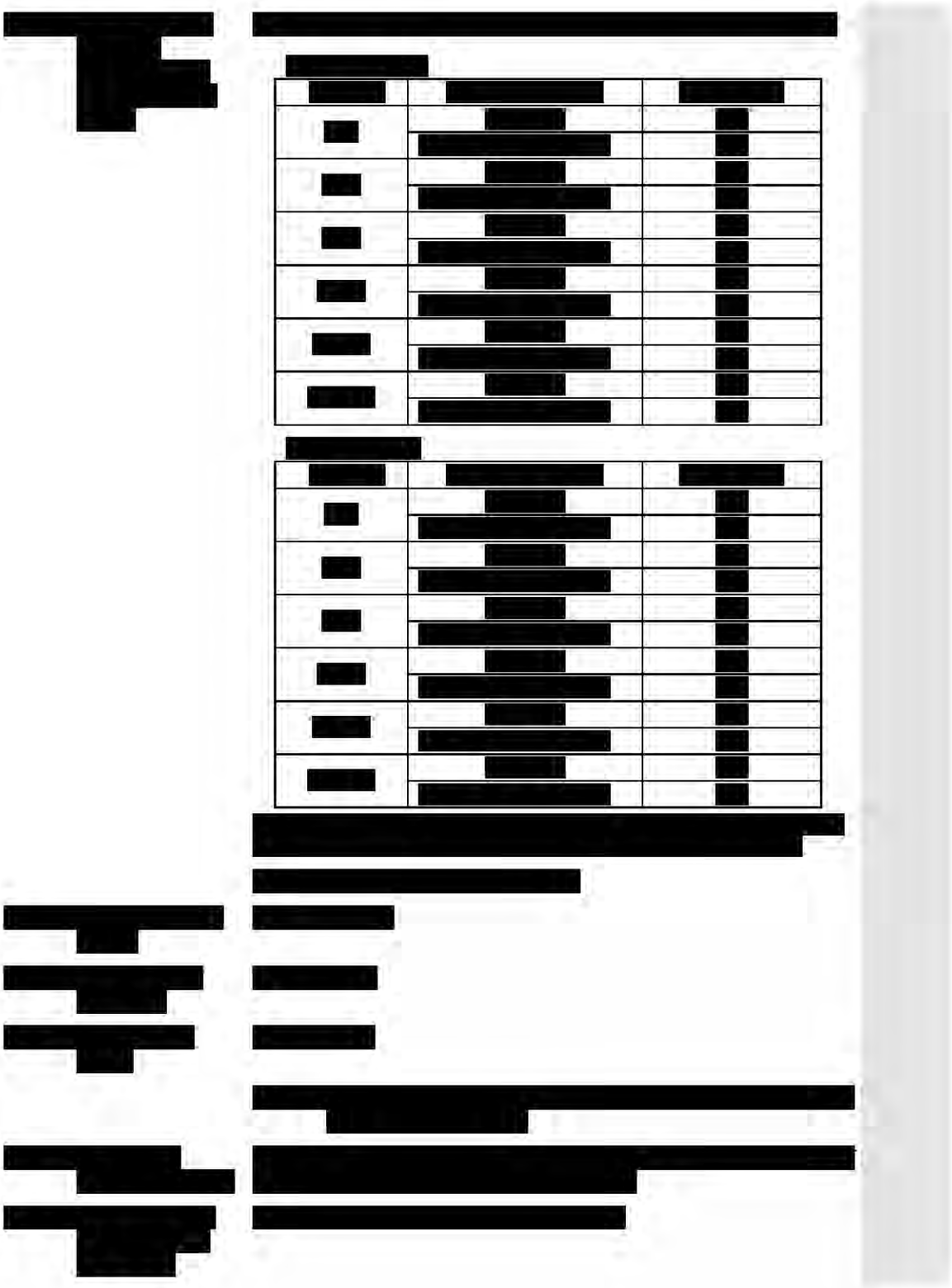
Doc. IIIA/ Section A5/06 **Effectiveness against target organisms and intended uses**

BPD Data set IIA/ Annex Point V.5



Doc. IIIA/ Section A5/06 **Effectiveness against target organisms and intended uses**

BPD Data set IIA/ Annex Point V.5



Doc. IIIA/ Section A5/06 **Effectiveness against target organisms and intended uses**

BPD Data set IIA/ Annex Point V.5

Doc. IIIA/ Section A5/06 **Effectiveness against target organisms and intended uses**

BPD Data set IIA/ Annex Point V.5

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Doc. IIIA/ Section A5/06 — Effectiveness against target organisms and intended uses

BPD Data set IIA/ Annex Point V.5

Evaluation by Competent Authorities
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Document IIIA/ Section 6.1.1 **BPD Data set IIA/ Annex Point VI.6.1.1**	**Acute Toxicity** Acute oral toxicity	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [✓] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [✓]** **Other justification [ ]**	
Detailed justification:	Hydrogen chloride is available commercially as an anhydrous gas or as aqueous solutions (hydrochloric acid), at the concentrations of 33 to 36%. Hydrochloric acid is a strong, highly corrosive acid and therefore, according to the principle of test method already stated in the now banned OECD guideline 401 (1987), "Dosing test substances in a way known to cause marked pain and distress due to corrosive or irritating properties need not to be carried out." The likely route of exposure is inhalation, and several studies are already provided to address the anticipated route of human exposure. A study is therefore not required, nor considered an appropriate use of animals because of the known corrosive properties.	
Undertaking of intended 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	*22.05.2009.*	
Evaluation of applicant's justification	*Agree with applicant` s justification. According to OECD guideline 401(1987) and Council Regulation (EC) no 440/2008 a study is not required if there is a knowledge that test substance cause marked pain and distress due to corrosive or irritating properties. The likely route of exposure is inhalation but not oral route. No additional testing is necessary because of the known corrosive properties of the substance.*	
Conclusion	*Agree with applicant's version*	
Remarks	*Council Regulation (EC) no 440/2008 of 30 May 2008 laying down test methods pursuant to Regulation 1907/2006 states that "Test substances at doses that are known to cause pain and distress, due to corrosive or severely irritant actions, need not be administered".*	
	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		

Document IIIA/ Section 6.1.2 **BPD Data set IIA/ Annex Point VI.6.1.2**	**Acute Toxicity** Acute dermal toxicity	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [✓] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [✓]** **Other justification [ ]**	
Detailed justification:	Hydrogen chloride is available commercially as an anhydrous gas or as aqueous solutions (hydrochloric acid), at the concentrations of 33 to 36%. Hydrochloric acid is a strong, highly corrosive acid and therefore, according to the principle of test method stated by OECD guideline 402, "Dosing test substances in a way known to cause marked pain and distress due to corrosive or irritating properties need not to be carried out." The likely route of exposure is inhalation, and several studies are already provided to address the anticipated route of human exposure. A study is therefore not required, nor considered an appropriate use of animals because of the known corrosive properties.	
Undertaking of intended 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	*22.05.2009.*	
Evaluation of applicant's justification	*Agree with applicant` s justification. As stated by OECD guideline 402 as well as by Council Regulation (EC) no 440/2008 of 30 May 2008, "Dosing test substances in a way known to cause marked pain and distress due to corrosive or irritating properties need not to be carried out". The likely route of exposure is inhalation but not dermal route. No additional testing is necessary because of the known corrosive properties of the substance.*	
Conclusion	*Agree with applicant's version*	
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		

Doc. IIIA/ Section A6.1.3/01

Acute Toxicity

Acute inhalation toxicity in the rat

BPD Data set IIA/ Annex Point VI.6.1.3

Official use only

		1 REFERENCE
1.1	**Reference**	Darmer K.I. Jr., Kinkead E.R. and DiPasquale L.C. (1974) Acute Toxicity in Rats and Mice Exposed to Hydrogen Chloride Gas and Aerosols. American Industrial Hygiene Association Journal **35**: 623-631 Published
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Companies with letters of access	None
1.2.3	Criteria for data protection	No data protection claimed.
		2 GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	No, but conducted according to the "Guide for Laboratory Animal Facilities and Care" (1965), prepared by the Committee on the Guide for Laboratory Animal Resources, Natl. Acad. Sci./Natl. Research Council: and Public Law 89-544, "Laboratory Animal Welfare Act," (1967)
2.2	**GLP**	No, GLP was not compulsory at the time the study was conducted
2.3	**Deviations**	Not applicable
		3 MATERIALS AND METHODS
3.1	**Test material**	HCl gas or HCl aerosol
3.1.1	Lot/Batch number	Not stated
3.1.2	Specification	HCl gas supplied in a cylinder obtained from Matheson Company. HCl aerosol was obtained by introducing HCl gas into an exposure chamber filled with saturated water droplet mist generated using a DeVilbiss modified ultrasonic nebulizer.
3.1.2.1	Description	Not stated
3.1.2.2	Purity	Not stated
3.1.2.3	Stability	Not stated
3.2	**Test Animals**	
3.2.1	Species	Rats
3.2.2	Strain	CFE (Sprague Dawley derived)
3.2.3	Source	Carworth Farms Inc.
3.2.4	Sex	Male
3.2.5	Age/weight at study initiation	Age not specified, bodyweight: 250 - 300 g
3.2.6	Number of animals per group	10 rats/group

Doc. IIIA/ Section A6.1.3/01

BPD Data set IIA/ Annex Point VI.6.1.3

Acute Toxicity

Acute inhalation toxicity in the rat

3.2.7	Control animals	No
3.3	**Administration/ Exposure**	Inhalation
3.3.1	Post exposure period	7 days
		Inhalation
3.3.2	Concentrations	Gas concentrations (5 min exposure): 30000, 32255, 39850, 45200 and 57290 ppm Gas concentrations (30 min exposure): 2078, 2678, 3071, 5180, 6068 and 6681 ppm Aerosol concentrations (5 min exposure): 9.7, 28.4, 37.3, 43.6, 57.0, 60.1 and 91.3 mg/litre (equivalent to 6571, 19312, 25324, 29648, 38746, 40810 and 62042 ppm) Aerosol concentrations (30 min exposure): 4.3, 6.6, 9.0 and 9.8 mg/litre (equivalent to 2910, 4481, 6078 and 6640 ppm) Concentrations were measured continuously during exposures using a chloride ion specific electrode with double distilled water as an absorber.
3.3.3	Particle size	The nebulizer was evaluated to confirm the production of droplets in the range specified by the manufacturer (i.e. 0.5 to 9 microns). Particle size distribution was determined by measuring 456 droplets which were rended visible in the filter by adding a 5% congo red solution. Results obtained were as follows:

Droplet size range (µm)	Number counted	Percentage of droplets	Cumulative percentage of droplets
≤ 1	292	64.0	64.0
1 – 2	134	29.4	93.4
2 – 5	30	6.5	99.9
> 5	0		

Doc. IIIA/ Section A6.1.3/01

BPD Data set IIA/ Annex Point VI.6.1.3

Acute Toxicity

Acute inhalation toxicity in the rat

3.3.4	Type or preparation of particles	HCl Gas was metered through a corrosion resistant gas regulator and a flow-meter and introduced into a modified Rochester chamber. The input air to the chamber was pre-dried and supplied at the constant rate of 10 cfm (ca. 283.169 L/min). HCl Aerosol was produced introducing HCl gas into a Longley chamber which was filled with a saturated water droplet mist. Water was supplied to the DeVilbiss ultrasonic nebulizer at the flow rate of 6.8 mL/min while predried air was maintained at the constant rate of 10 cfm (ca. 283.169 L/min). Animals were introduced into the chamber when the desired concentration was obtained by means of sliding cage "drawers" in the walls of the chamber. Concentrations were measured continuously during exposures using a chloride ion specific electrode with double distilled water as an absorber.
3.3.5	Type of exposure	Whole body
3.3.6	Vehicle	-
3.3.7	Concentration in vehicle	Not applicable
3.3.8	Duration of exposure	5 minutes or 30 minutes
3.3.9	Controls	No control animals were used
3.4	**Examinations**	Clinical signs and mortality were observed during exposure and up to 7 days post-exposure. Gross and histopathological examinations were made of representative samples of tissues from the animals.
3.5	**Method of determination of LC_{50}**	Not stated
3.6	**Further remarks**	It is considered that Table VII of the original paper (3rd column, 4th line) should contain a mistyping indicating a mortality ratio of 6/8 instead of 6/**10**.

4 RESULTS AND DISCUSSION

4.1 Clinical signs

See Tables A6.1.3/01-1 to A6.1.3/01-4. Mortalities were observed at all the doses, with the exception of the lowest ones. Toxic signs during exposure to HCl gas or aerosol were essentially identical. HCl was severely irritating to the eyes, mucous membranes and exposed areas of skin. Animals usually exhibited a rapid and shallow breathing pattern by the end of the exposure period. Corneal erosion and clouding were noted, as well as excessive grooming and ulceration of the scrotum. Animals which survived the exposure, especially at the higher concentrations of either HCl gas or aerosol, had bloody discharges from their nostrils and exhibited audible difficulty in breathing (producing a laboured 'clicking'). The fur had a 'singed' appearance and was discoloured to a greenish hue. Decrease in food consumption and weight loss following exposure was also noted.

4.2 Pathology

Gross examination of the animals which died during or at some time following exposure showed that the respiratory tract was the main target for the HCl damage. Moderate to severe alveolar emphysema, atelectasis and oedema of the lungs were observed, and occasional 'spotting' of the lung tissue was also noted. The upper respiratory tract was severely irritated with severe damage of the epithelia tissue of nose and trachea. Animals surviving up to terminal sacrifice (7 days after exposure) showed that recovery was not complete with abnormally coloured grey lungs failing to collapse upon opening the chest cavity. There was also evidence of consolidation of lung tissue.

Histopathological examination confirmed the damage of respiratory tract while no abnormality was detected in other tissues.

4.3 Other

None

4.4 LC_{50}

HCl gas (5 min exposure): 40989 ppm (34803-48272)

HCl gas (30 min exposure): 4701 ppm (4129-5352)

HCl aerosol (5 min exposure): 45.6 mg/L (39.5-52.8) equivalent to 31008 ppm (26824-35845)

HCl aerosol (30 min exposure): 8.3 mg/L (7.2-9.7) equivalent to 5666 ppm (4855-6614)

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

In an acute inhalation study, 10 male Sprague Dawley-derived rats/group were exposed for 5 or 30 minutes to different concentrations of either HCl gas or HCl aerosol in a whole-body exposure chamber. Particle size distribution indicated the aerosol to be entirely respirable. Animals were observed for 7 days for clinical signs and mortality. Gross and histopathological examinations were made of representative samples of tissues from the animals.

5.2 Results and discussion

Mortalities were observed at all the doses, with the exception of the lowest ones. HCl was severely irritating to the eyes, mucous membranes and exposed areas of skin. Animals usually exhibited a rapid and shallow breathing pattern by the end of the exposure period. Corneal erosion and clouding were noted, as well as excessive grooming and ulceration of the scrotum. Animals which

survived the exposure, especially at the higher concentrations of either HCl gas or aerosol, had bloody discharges from their nostrils and exhibited audible difficulty in breathing (producing a laboured 'clicking'. The fur had a 'singed' appearance and was discoloured to a greenish hue. Decrease in food consumption and weight loss following exposure was also noted.

Gross examination of the animals which died during or at some time following exposure showed that the respiratory tract was the main target for the HCl damage. Moderate to severe alveolar emphysema, atelectasis and oedema of the lungs were observed, and occasional 'spotting' of the lung tissue was also noted. The upper respiratory tract was severely irritated with severe damage of the epithelia tissue of nose and trachea. Animals surviving up to terminal sacrifice (7 days after exposure) showed that recovery was not complete with abnormally coloured grey lungs failing to collapse upon opening the chest cavity. There was also evidence of consolidation of lung tissue.

Histopathological examination confirmed the damage of respiratory tract while no abnormality was detected in other tissues.

5.3 Conclusion

Toxic signs during exposure to HCl gas or aerosol were essentially identical. HCl was severely irritating to the eyes, mucous membranes and exposed areas of skin. The calculated LC_{50} values were the following:

HCl gas (5 min exposure): 40989 ppm (34803-48272)

HCl gas (30 min exposure): 4701 ppm (4129-5352)

HCl aerosol (5 min exposure): 45.6 mg/L (39.5-52.8) equivalent to 31008 ppm (26824-35845)

HCl aerosol (30 min exposure): 8.3 mg/L (7.2-9.7) equivalent to 5666 ppm (4855-6614)

5.3.1 Reliability: 2

5.3.2 Deficiencies: Minor reporting deficiencies. (Substance purity, bodyweight data, individual data not reported). Not GLP. However, reporting is in most respects fully adequate for this endpoint, and study design exceeds guideline requirement in many respects.

Doc. IIIA/ Section A6.1.3/01

Acute Toxicity

Acute inhalation toxicity in the rat

BPD Data set IIA/ Annex Point VI.6.1.3

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*22.05.2009.*
Materials and Methods	*Applicant's version is acceptable. Based on the publication in "American Industrial Hygiene Association Journal"1974, 35:623-631 "Acute toxicity in rats and mice exposed to hydrogen chloride gas and aerosols". For evaluation of acute inhalation toxicity in the rat a group of 10 male rats were used and exposed to 5 and 30 min. inhalation test in whole-body exposure chamber applying different gas and aerosols concentrations. Animals were observed for 7 days for clinical signs and mortality.*
Results and discussion	*Applicant's version is adopted. The lowest concentrations used (see Tables A6.1.3/01-1, A6.1.3/01-2, A6.1.3/01-3 and A6.1.3/01-4) are not associated with mortality The calculated LC_{50} values were the following:* *HCl gas (5 min exposure): 40989 ppm (34803-48272)* *HCl gas (30 min exposure): 4701 ppm (4129-5352)* *HCl aerosol (5 min exposure): 45.6 mg/L (39.5-52.8) equivalent to 31008 ppm (26824-35845)* *HCl aerosol (30 min exposure): 8.3 mg/L (7.2-9.7) equivalent to 5666 ppm (4855-6614)* *Histopathological examination confirmed the damage of respiratory tract as the main cause for mortality. No abnormality detected in other organs.*
Conclusion	*Agree with applicant's explanation of the study results and conclusions.*
Reliability	*2*
Acceptability	*In general, acceptable.*
Remarks	*The study serves as an informative evidence of HCl acute inhalation toxicity only, which can be applied for other conclusions in evaluation of preparations with HCl as an active substance.*
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A6.1.3/01-1: HCl gas (5 min exposure) Acute Inhalation Toxicity in Rats

Concentration (ppm)	Mortality ratio	Time of deaths (No./day)							
		0 (during exposure)	1	2	3	4	5	6	7
30000	0/10								
32255	1/10			1					
39850	6/10		2	3			1		
45200	7/10		5	2					
57290	9/10		5	4					
LC_{50} value: 40989 ppm (34803-48272)									

Table A6.1.3/01-2: HCl gas (30 min exposure) Acute Inhalation Toxicity in Rats

Concentration (ppm)	Mortality ratio	Time of deaths (No./day)							
		0 (during exposure)	1	2	3	4	5	6	7
2078	0/10								
2678	1/10	1							
3071	0/10								
5180	5/10	2	1			1	1		
6068	8/10	7	1						
6681	10/10	7		1		2			
LC_{50} value: 4701 ppm (4129-5352)									

Table A6.1.3/01-3: HCl aerosol (5 min exposure) Acute Inhalation Toxicity in Rats

Concentration		Mortality ratio	Time of deaths (No./day)							
mg/L	ppm		0 (during exposure)	1	2	3	4	5	6	7
9.7	6571	0/10								
28.4	19312	1/10			1					
37.3	25324	3/10		2		1				
43.6	29648	6/10		1	4	1				
57.0	38746	6/10		2	1			3		
60.1	40810	7/10		2	4				1	
91.3	62042	10/10		8	1	1				
LC_{50} value: 45.6 mg/L (39.5-52.8) equivalent to 31008 ppm (26824-35845)										

Table A6.1.3/01-4: HCl aerosol (30 min exposure) Acute Inhalation Toxicity in Rats

Concentration		Mortality ratio	Time of deaths (No./day)							
mg/L	ppm		0 (during exposure)	1	2	3	4	5	6	7
4.3	2910	1/10			1					
6.6	4481	0/10								
9.0	6078	6/10	1	3	1			1		
9.8	6640	8/10	3	1	2		2			
LC_{50} value: 8.3 mg/L (7.2-9.7) equivalent to 5666 ppm (4855-6614)										

Doc. IIIA/ Section A6.1.3/02

BPD Data set IIA/ Annex Point VI.6.1.3

Acute Toxicity

Acute inhalation toxicity in the mouse

Official use only

1 REFERENCE

1.1	**Reference**	Darmer K.I. Jr., Kinkead E.R. and DiPasquale L.C. (1974) Acute Toxicity in Rats and Mice Exposed to Hydrogen Chloride Gas and Aerosol. American Industrial Hygiene Association Journal **35**: 623-631 Published
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Companies with letters of access	None
1.2.3	Criteria for data protection	No data protection claimed.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	No, but conducted according to the "Guide for Laboratory Animal Facilities and Care" (1965), prepared by the Committee on the Guide for Laboratory Animal Resources, Natl. Acad. Sci./Natl. Research Council: and Public Law 89-544, "Laboratory Animal Welfare Act," (1967)
2.2	**GLP**	No, GLP was not compulsory at the time the study was conducted
2.3	**Deviations**	Not applicable

3 MATERIALS AND METHODS

3.1	**Test material**	HCl gas or HCl aerosol
3.1.1	Lot/Batch number	Not stated
3.1.2	Specification	HCl gas supplied in a cylinder obtained from Matheson Company. HCl aerosol was obtained by introducing HCl gas into an exposure chamber filled with saturated water droplet mist generated using a DeVilbiss modified ultrasonic nebulizer.
3.1.2.1	Description	Not stated
3.1.2.2	Purity	Not stated
3.1.2.3	Stability	Not stated
3.2	**Test Animals**	
3.2.1	Species	Mice
3.2.2	Strain	CF-1 (ICR derived)
3.2.3	Source	Carworth Farms Inc.
3.2.4	Sex	Male
3.2.5	Age/weight at study initiation	Age not specified, bodyweight: 25 - 30 g

Doc. IIIA/ Section A6.1.3/02

BPD Data set IIA/ Annex Point VI.6.1.3

Acute Toxicity

Acute inhalation toxicity in the mouse

3.2.6	Number of animals per group	10 or 15 mice/group
3.2.7	Control animals	No
3.3	**Administration/ Exposure**	Inhalation
3.3.1	Post exposure period	7-8 days
		Inhalation
3.3.2	Concentrations	Gas concentrations (5 min exposure): 3200, 5060, 6145, 6410, 7525, 8065, 9276, 13655, 26485, and 30000 ppm Gas concentrations (30 min exposure): 410, 1134, 2678, 2721, 2942, 3071, 4045, 4076 and 5363 ppm Aerosol concentrations (5 min exposure): 13.3, 14.8, 17.7, 22.0, 25.0 and 27.6 mg/litre (equivalent to 9058, 10059, 12104, 14913, 17000 and 18773 ppm) Aerosol concentrations (30 min exposure): 1.8, 3.1, 3.8, 4.0, 4.3, 4.5 and 6.5 mg/litre (equivalent to 1204, 2127, 2557, 2720, 2910, 3036 and 4432 ppm) Concentrations were measured continuously during exposures using a chloride ion specific electrode with double distilled water as an absorber.
3.3.3	Particle size	The nebulizer was evaluated to confirm the production of droplets in the range specified by the manufacturer (i.e. 0.5 to 9 microns). Particle size distribution was determined by measuring 456 droplets which were rended visible in the filter by adding a 5% congo red solution. Results obtained were as follows:

Droplet size range (µm)	Number counted	Percentage Of droplets	Cumulative percentage of droplets
≤ 1	292	64.0	64.0
1 – 2	134	29.4	93.4
2 – 5	30	6.5	99.9
> 5	0		

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Acute Toxicity

Acute inhalation toxicity in the mouse

3.3.4	Type or preparation of particles	HCl Gas was metered through a corrosion resistant gas regulator and a flow-meter and introduced into a modified Rochester chamber. The input air to the chamber was pre-dried and supplied at the constant rate of 10 cfm (ca. 283.169 L/min). HCl Aerosol was produced introducing HCl gas into a Longley chamber which was filled with a saturated water droplet mist. Water was supplied to the DeVilbiss ultrasonic nebulizer at the flow rate of 6.8 mL/min while predried air was maintained at the constant rate of 10 cfm (ca. 283.169 L/min). Animals were introduced into the chamber when the desired concentration was obtained by means of sliding cage "drawers" in the walls of the chamber. Concentrations were measured continuously during exposures using a chloride ion specific electrode with double distilled water as an absorber.
3.3.5	Type of exposure	Whole body
3.3.6	Vehicle	-
3.3.7	Concentration in vehicle	Not applicable
3.3.8	Duration of exposure	5 minutes or 30 minutes
3.3.9	Controls	No control animals were used
3.4	**Examinations**	Clinical signs and mortality were observed during exposure and up to 7-8 days post-exposure. Gross and histopathological examinations were made of representative samples of tissues from the animals.
3.5	**Method of determination of LC_{50}**	Not stated
3.6	**Further remarks**	None

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Acute Toxicity

Acute inhalation toxicity in the mouse

4 RESULTS AND DISCUSSION

4.1 Clinical signs

See tables A6.1.3/01-1 to A6.1.3/01-4. Mortalities were observed at all the doses, with the exception of the lowest ones. Toxic signs during exposure to HCl gas or aerosol were essentially identical. HCl was severely irritating to the eyes, mucous membranes and exposed areas of skin. Animals usually exhibited a rapid and shallow breathing pattern by the end of the exposure period. Corneal erosion and clouding were noted, as well as excessive grooming and ulceration of the scrotum. Animals which survived the exposure, especially at the higher concentrations of either HCl gas or aerosol, had bloody discharges from their nostrils and exhibited audible difficulty in breathing (producing a laboured 'clicking'). The fur had a 'singed' appearance and was discoloured to a greenish hue. Decrease in food consumption and weight loss following exposure was also noted.

4.2 Pathology

Gross examination of the animals which died during or at some time following exposure showed that the respiratory tract was the main target for the HCl damage. Moderate to severe alveolar emphysema, atelectasis and oedema of the lungs were observed, and occasional 'spotting' of the lung tissue was also noted. The upper respiratory tract was severely irritated with severe damage of the epithelia tissue of nose and trachea. Animals surviving up to terminal sacrifice (7 days after exposure) showed that recovery was not complete with abnormally coloured grey lungs failing to collapse upon opening the chest cavity. There was also evidence of consolidation of lung tissue.

Histopathological examination confirmed the damage of respiratory tract while no abnormality was detected in other tissues.

4.3 Other

None

4.4 LC_{50}

HCl gas (5 min exposure): 13745 ppm (10333-18283)

HCl gas (30 min exposure): 2644 ppm (2264-3086)

HCl aerosol (5 min exposure): 16.5 mg/L (14.8-18.5) equivalent to 11238 ppm (10006-12547)

HCl aerosol (30 min exposure): 3.2 mg/L (2.6-3.8) equivalent to 2142 ppm (1779-2580)

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

In an acute inhalation study, 10 or 15 male CD-1 mice/group were exposed for 5 or 30 minutes to different concentrations of either HCl gas or HCl aerosol in a whole-body exposure chamber. Particle size distribution indicated the aerosol to be entirely respirable. Animals were observed for 7 days for clinical signs and mortality. Gross and histopathological examinations were made of representative samples of tissues from the animals.

5.2 Results and discussion

Mortalities were observed at all the doses. HCl was severely irritating to the eyes, mucous membranes and exposed areas of skin. Animals usually exhibited a rapid and shallow breathing pattern by the end of the exposure period. Corneal erosion and clouding were noted, as well as excessive grooming and ulceration of the scrotum. Animals which survived the exposure, especially at

		the higher concentrations of either HCl gas or aerosol, had bloody discharges from their nostrils and exhibited audible difficulty in breathing (producing a laboured 'clicking'). The fur had a 'singed' appearance and was discoloured to a greenish hue. Decrease in food consumption and weight loss following exposure was also noted. Gross examination of the animals which died during or at some time following exposure showed that the respiratory tract was the main target for the HCl damage. Moderate to severe alveolar emphysema, atelectasis and oedema of the lungs were observed, and occasional 'spotting' of the lung tissue was also noted. The upper respiratory tract was severely irritated with severe damage of the epithelia tissue of nose and trachea. Animals surviving up to terminal sacrifice (7 days after exposure) showed that recovery was not complete with abnormally coloured grey lungs failing to collapse upon opening the chest cavity. There was also evidence of consolidation of lung tissue. Histopathological examination confirmed the damage of respiratory tract while no abnormality was detected in other tissues.
5.3	**Conclusion**	Toxic signs during exposure to HCl gas or aerosol were essentially identical. HCl was severely irritating to the eyes, mucous membranes and exposed areas of skin. The calculated LC_{50} values were the following: HCl gas (5 min exposure): 13745 ppm (10333-18283) HCl gas (30 min exposure): 2644 ppm (2264-3086) HCl aerosol (5 min exposure): 16.5 mg/L (14.8-18.5) equivalent to 11238 ppm (10006-12547) HCl aerosol (30 min exposure): 3.2 mg/L (2.6-3.8) equivalent to 2142 ppm (1779-2580)
5.3.1	Reliability	2
5.3.2	Deficiencies	Minor reporting deficiencies. (Substance purity, bodyweight data, individual data not reported). Not GLP. However, reporting is in most respects fully adequate for this endpoint, and study design exceeds guideline requirement in many respects.

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BPD Data set IIA/ Annex Point VI.6.1.3

Acute Toxicity

Acute inhalation toxicity in the mouse

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*25.05.2009.*
Materials and Methods	*Applicant's version is acceptable. Based on the publication in "American Industrial Hygiene Association Journal" 1974, 35:623-631 "Acute toxicity in rats and mice exposed to hydrogen chloride gas and aerosols". For evaluation of acute inhalation toxicity in the mice a group of 10 or 15 male mice were used and exposed to 5 and 30 min. inhalation test in whole-body exposure chamber applying different gas and aerosols concentrations. Animals were observed for 7-8 days for clinical signs and mortality.*
Results and discussion	*Applicant's version is adopted. The lowest concentrations used (see Tables A6.1.3/02-1, A6.1.3/02-2, A6.1.3/02-3 and A6.1.3/02-4) are associated with a minor mortality The calculated LC_{50} values were the following:* *HCl gas (5 min exposure): 13745 ppm (10333-18283)* *HCl gas (30 min exposure): 2644 ppm (2264-3086)* *HCl aerosol (5 min exposure): 16.5 mg/L (14.8-18.5) equivalent to 11238 ppm (10006-12547)* *HCl aerosol (30 min exposure): 3.2 mg/L (2.6-3.8) equivalent to 2142 ppm (1779-2580)* *Histopathological examination confirmed the damage of respiratory tract as the main cause for mortality. No abnormality detected in other organs.*
Conclusion	*Agree with applicant's explanation of the study results and conclusions*
Reliability	*2*
Acceptability	*In general, acceptable.*
Remarks	*The study serves as an informative evidence of HCl acute inhalation toxicity only, which can be applied for other conclusions in evaluation of preparations with HCl as an active substance.*
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A6.1.3/02-1: HCl gas (5 min exposure) Acute Inhalation Toxicity in Mice

Concentration (ppm)	Mortality ratio	Time of deaths (No./day)							
		0 (during exposure)	1	2	3	4	5	6	7
3200	1/10						1		
5060	1/10				1				
6145	2/10			1		1			
6410	0/10								
7525	6/10			1	2		3		
8065	2/10				2				
9276	5/10				2	3			
13655	6/10		2		3		1		
26485	13/15	1	3	2	1	2	4		
30000	13/15	3	4		1	1	4		
LC_{50} value: 13745 ppm (10333-18283)									

Table A6.1.3/02-2: HCl gas (30 min exposure) Acute Inhalation Toxicity in Mice

Concentration (ppm)	Mortality ratio	Time of deaths (No./day)								
		0 (during exposure)	1	2	3	4	5	6	7	8
410	0/15									
1134	2/15				2					
2678	8/15		4		2		1			
2721	4/15		1	2	1					
2942	12/15	1			2	4	5			
3071	6/15		2	2	2					
4045	11/15		4			1	1		3	2
4076	13/15		4	1	1		3	4		
5363	14/15	3	5	2		1	2	1		
LC_{50} value: 2644 ppm (2264-3086)										

Table A6.1.3/02-3: HCl aerosol (5 min exposure) Acute Inhalation Toxicity in Mice

Concentration		Mortality ratio	Time of deaths (No./day)							
mg/L	ppm		0 (during exposure)	1	2	3	4	5	6	7
13.3	9058	3/10				1	2			
14.8	10059	3/10						2	1	
17.7	12104	5/10			1		1	1	2	
22.0	14913	9/10		1		2		1	4	1
25.0	17000	9/10		2	1	2	4			
27.6	18773	10/10		2	1	5		2		
LC_{50} value: 16.5 mg/L (14.8-18.5) equivalent to 11238 ppm (10006-12547)										

Table A6.1.3/02-4: HCl aerosol (30 min exposure) Acute Inhalation Toxicity in Mice

Concentration		Mortality ratio	Time of deaths (No./day)							
mg/L	ppm		0 (during exposure)	1	2	3	4	5	6	7
1.8	1204	2/10				1		1		
3.1	2127	5/10		3				1		1
3.8	2557	5/10					3		2	
4.0	2720	5/10		3		2				
4.3	2910	9/10	1	4	1		1	2		
4.5	3036	7/10	1	4	1	1				
6.5	4432	10/10	4	3	2		1			
LC_{50} value: 3.2 mg/L (2.6-3.8) equivalent to 2142 ppm (1779-2580)										

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Acute Toxicity

Acute inhalation toxicity in the guinea pig

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	1 REFERENCE	
1.1	**Reference**	Burleigh-Flayer H., Wong K.L. and Alarie Y. (1985) Evaluation of the Pulmonary Effects of HCl Using CO_2 Challenges in Guinea Pigs. Fundam. and Appl. Toxicol. **5**: 978-985 Published
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Companies with letters of access	None
1.2.3	Criteria for data protection	No data protection claimed.
	2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	No
2.2	**GLP**	No, GLP was not compulsory at the time the study was conducted
2.3	**Deviations**	Not applicable
	3 MATERIALS AND METHODS	
3.1	**Test material**	HCl gas
3.1.1	Lot/Batch number	Not stated
3.1.2	Specification	HCl from Matheson Company
3.1.2.1	Description	Not stated
3.1.2.2	Purity	Not stated
3.1.2.3	Stability	Not stated
3.2	**Test Animals**	
3.2.1	Species	Guinea pig
3.2.2	Strain	English smooth-haired
3.2.3	Source	Hilltop Lab Animals Inc. (USA)
3.2.4	Sex	Male
3.2.5	Age/weight at study initiation	Age not specified, bodyweight: 330 - 450 g
3.2.6	Number of animals per group	4 guinea pigs for the control and the two lower dose level groups; 8 guinea pigs for the two higher dose level groups
3.2.7	Control animals	Yes, air
3.3	**Administration/ Exposure**	Inhalation
3.3.1	Post exposure	2 or 15 days

	period	
		Inhalation
3.3.2	Concentrations	Gas concentrations: 320, 680, 1040, and 1380 ppm
3.3.3	Exposure chamber	The exposure chamber was a rectangular Plexiglas chamber which had a volume of 10.4 litres with four body plethysmographs composed of Plexiglas cylinders (9 cm internal diameter) attached to the sides. The guinea pigs were secured in each of the four plethysmographs with their heads protruding through a perforated latex dam into the exposure chamber. The latex dam provided an airtight seal around the animal's neck. Rubber stoppers were used to seal each body plethysmograph and prevented the guinea pig from escaping.
3.3.4	Type or preparation of particles	HCl exposure mixtures were obtained by metering 20000 ppm HCl in N_2 into the exposure chamber and simultaneously diluting with room air at a known flow rates. The gas flow through the exposure chamber was maintained at 20 L/min. Hydrochloric acid concentrations were determined colorimetrically using Osterreichische Stickstoffwertke method of analysis (Leithe, 1971). Four animals were exposed at a time in a head-only procedure for 30 minutes.
3.3.5	Type of exposure	Nose-only
3.3.6	Vehicle	-
3.3.7	Concentration in vehicle	Not applicable
3.3.8	Duration of exposure	30 minutes
3.3.9	Controls	Control animals were exposed to air only
3.4	**Examinations**	
3.4.1	Respiratory frequency and type of irritation	A differential pressure transducer was used to measure changes in pressure due to the respiration of the animal in each plethysmograph. The pressure variations were converted into electrical signals, amplified, and then recorded on an oscillograph. From these recording, the effects of HCl on respiratory frequency (*f*) was evaluated. The wave pattern was analysed to determine the type of irritation (sensory *vs* pulmonary): sensory irritation was denoted by both a decrease in respiratory rate and a lengthened expiratory phase due to stimulation of the trigeminal nerve. Characteristics of pulmonary irritation include an initial increase in respiratory rate in guinea pigs followed by a decrease due to a pause following each expiration as a result of stimulation of irritant receptors within the lung.
3.4.2	Evaluation of pulmonary effect	The pulmonary effect of HCl was evaluated using the ventilatory response to CO_2. The animals were weighed and then challenged with 10% CO_2, 20% CO_2, and 70% N_2 before exposure and at 0.5 and 3 hrs, 1, 3, 5, 10 and 15 days following exposure. The animals were placed in a whole-body plethysmograph where respiration-produced changes in chamber pressure (ΔP) were measured. ΔP is proportional to tidal volume in normal animals while breathing

		10% CO_2. Respiratory frequency (*f*) was obtained from the fluctuations in ΔP, with each wave representing a breath. These parameters were monitored during a 5-min baseline period breathing room air, 7-min "CO_2 period" during which the 10% CO_2 mixture was inhaled, and a 5-min recovery period. The average ΔP and *f* during the baseline period were used to determine the effects of HCl on baseline respiration while the mean ΔP or *f* from 4 to 7 min into the CO_2 period were employed as the measurements of the ventilatory response to CO_2.
3.4.3	Lung histopathology	4 animals from the 1040-ppm group were sacrificed 2 days following exposure and another 4 were sacrificed 15 days after exposure. The lungs were removed and fixed by infusion of 10% buffered formalin. Sections 5 μm thick were prepared and stained with hematoxylin and eosin for light microscopic examination.
3.5	**Statistics**	One-way analysis of variance was used to compare the mean of ΔP and *f* during the baseline and CO_2 challenge of each HCl concentration at the various times following exposure to control animals. If a significant result was obtained, a multiple comparison of the means was performed using Dunnett's test. The level of significance chosen was $p<0.05$ in all cases. For data in which a HCl concentration-response relationship was suspected, an analysis to check the linearity of the concentration-response curves was done according to Armitage (1971). If the curve was indeed linear, the slope was obtained via least-squares liner regression and whether the slope was significantly different from zero was tested according to Armitage.
3.6	**Further remarks**	As two animals of the 1040-ppm group died following exposure, it is considered likely that microscopic examination of lungs carried out 2 days after exposure included these two animals (i.e. 2 dead animals + 2 sacrificed animals examined at day 2 after exposure, 4 animals sacrificed and examined at 15 days following exposure). Moreover, it is considered that the number of animals surviving 15 days postexposure (3rd column, 4th line of Table 1 of the original paper, i.e. 6) should read 4.
		4 RESULTS AND DISCUSSION
4.1	**Clinical observations and body weight**	During exposure 1 and 2 animals, respectively, died following exposure to 1380 and 1040 ppm HCl. Body weight was significantly reduced in the group exposed to 1380 ppm HCl, but only at 1 day following exposure. Corneal opacities were observed in 4 out of 6 animals that survived throughout the study in the 1040-ppm group and in all 5 survivors of the 1380-ppm group. One case of corneal opacity was also detected out of 4 animals in the 680-ppm group while all animals in the 320-ppm group appeared normal. The ratios of lung weights versus body weights of all the groups were similar at 15 days following exposure.
4.2	**Respiratory frequency and type of irritation**	Exposures to HCl at the three higher concentrations almost immediately (less than 1 min) led to sensory irritation, while it took 6 min for sensory irritation to appear at 320 ppm. As inhalation of HCl continued, the respiratory pattern of sensory irritation turned into the pattern of pulmonary irritation, with a linear relationship

for concentration-response for time of onset.

4.3 Evaluation of pulmonary effect

Baseline ΔP was significantly higher at 0.5 h following exposure for the 1380-ppm group, but returned to pre-exposure value at 3 hrs. 1 day after exposure this group again showed a significantly higher baseline ΔP. The 1040-ppm group showed a significantly higher baseline ΔP at 5 days post exposure. During the next 10 days recovery occurred.

During the CO_2 challenge, ΔP was not affected in any exposed group at any time point following exposure. In contrast, baseline *f* and maximal *f* achieved during CO_2 challenges were markedly affected. Guinea pigs exposed to all concentrations of HCl breathed significantly lower at 0.5 h. Following this time point, the two highest concentration groups followed a similar time course, with *f* significantly lower than controls for the entire 15-day post exposure period. All exposure groups showed a significant reduction in maximal *f* achieved during the CO_2 challenge at 0.5 h following exposure. The groups exposed to 1040 or 1380 ppm continued to show this effect up to 10 days after exposure, while no difference compared to control was noted at 15 days.

4.4 Lung histopathology

Multifocal acute alveolitis along with congestion and mild haemorrhage was observed at histopathology of lung of animals exposed to 1040 ppm HCl 2 days post exposure. Squamous metaplasia with loss of cilia and submucosal infiltration of acute inflammatory cells were also noted in the larger conducting airways. Fifteen days after exposure to 1040 ppm HCl, mild lymphoid hyperplasia in the parenchyma and interstitial infiltration of mixed inflammatory cells were present. Besides, goblet cell hyperplasia and mild bronchitis were noted in the larger conducting airways, suggesting tissue damage in both the airway and alveolar regions not completely recovering at that time.

4.3 Other

None

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

Pulmonary effects of 30 min inhalation exposures to hydrochloric acid at 0, 320, 680, 1040 or 1380 ppm were evaluated during and following exposure in male guinea pigs. During exposure the respiratory rate and the time of onset of sensory or pulmonary irritation as evidenced by the change in respiratory pattern were measured. Following exposure to HCl, animals were evaluated using a pulmonary performance test based on their ventilation response (respiratory rate and tidal volume) during challenge with 10% CO_2. Microscopic examination of lungs of animals exposed to 1040 ppm HCl was also carried out at 2 or 15 days following exposure.

5.2 Results and discussion

Mortalities were observed during exposure to the highest concentration (1380 ppm, 2 out 8 animals). Following exposure another animal in this group died, and 2 out of 8 animals of the 1040-ppm group died. Body weight was significantly reduced compared to pre-exposure in animals at 1380 ppm, but only at 1 day after exposure. Corneal opacities were observed in 4 out of 6 animals that survived throughout the study in the 1040-ppm group and in all 5 survivors of the 1380-ppm group. One case of corneal

opacity was also detected out of 4 animals in the 680-ppm group while all animals in the 320-ppm group appeared normal.

The ratios of lung weights versus body weights of all the groups were similar at 15 days following exposure.

HCl exposure resulted in both sensory and pulmonary irritation. The onset of sensory irritation was immediate at 680, 1040, 1380 ppm, while it took 6 min during exposure to 320 ppm. The onset of pulmonary irritation showed a concentration-response relationship, the higher the concentration the earlier the onset.

The maximal respiratory frequency achieved during the CO_2 challenge was lower in HCl-exposed animals than in controls with dose-relationship, but HCl exposure had no apparent effect on the maximal tidal volume. Guinea pigs exposed to all concentrations of HCl breathed significantly lower at 0.5 h. Following this time point, the two highest concentration groups followed a similar time course, with frequency of respiration significantly lower than controls for the entire 15-day post exposure period. All exposure groups showed a significant reduction in maximal frequency of respiration achieved during the CO_2 challenge at 0.5 h following exposure. The groups exposed to 1040 or 1380 ppm continued to show this effect up to 10 days after exposure, while no difference compared to control was noted at 15 days.

Tissue damage in both the airway and alveolar regions was noted both after 2 or 15 days following exposure, with multifocal acute alveolitis along with congestion and mild haemorrhage and squamous metaplasia with loss of cilia and submucosal infiltration of acute inflammatory cells noted at the earlier time point and mild lymphoid hyperplasia in the parenchyma and interstitial infiltration of mixed inflammatory cells and goblet cell hyperplasia and mild bronchitis noted in the larger conducting airways at the later time point, indicating complete recovery was not attained.

5.3 Conclusion

Hydrochloric acid inhalation 30 min exposure resulted in both sensory and pulmonary irritation of guinea pigs at doses including the lowest dose tested (320 ppm). The maximal respiratory frequency achieved during the CO_2 challenge was lower in HCl-exposed animals than in controls with dose-relationship, but HCl exposure had no apparent effect on the maximal tidal volume. Corneal opacities were noted in animals at the two higher dose levels, and in a single animal at 680 ppm. Tissue damage in both the airway and alveolar regions was noted both after 2 or 15 days following exposure, indicating complete recovery was not attained in animals exposed to 1040 ppm.

5.3.1 Reliability

2

5.3.2 Deficiencies

Purity not reported; not GLP or guideline. Study however complies with modern methods to demonstrate respiratory irritation, without methodological flaw.

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Acute Toxicity

Acute inhalation toxicity in the guinea pig

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*26.05.2009.*
Materials and Methods	*Applicant's version is acceptable. Based on the publication in: Fundamental and applied Toxicology (1985) "Evaluation of the pulmonary effects of HCl using CO_2 challenges in guinea pigs" A group of 4-8 male guinea pigs were used exposed to HCl gas (nose only). Duration of exposure time was 30 min. A control group of 4 male guinea pigs exposed to air were used. Respiratory frequency and type of irritation (sensory and pulmonary) as well as pulmonary effect and lung histopathology was determined. Assessing respiratory frequency one-way analysis of variance was used to compare effects of each HCl concentration at the various times following exposure to control animals.*
Results and discussion	*Mortalities were observed during exposure to the highest concentration (1380 ppm, 2 out 8 animals). Following exposure another animal in this group died, and 2 out of 8 animals of the 1040-ppm group died. Body weight was significantly reduced compared to pre-exposure in animals at 1380 ppm, but only at 1 day after exposure. Hydrochloric acid inhalation 30 min exposure resulted in both sensory and pulmonary irritation of guinea pigs at doses including the lowest dose tested (320 ppm). The maximal respiratory frequency achieved during the CO_2 challenge was lower in HCl-exposed animals than in controls with dose-relationship, but HCl exposure had no apparent effect on the maximal tidal volume. Corneal opacities were noted in animals at the two higher dose levels. Applicant's version is adopted.*
Conclusion	*Both sensory and pulmonary irritation was observed. Tissue damage in both the airway and alveolar regions was noted both after 2 or 15 days following exposure, indicating complete recovery was not attained in animals exposed to 1040 ppm.. Agree with applicant's conclusion.*
Reliability	*2*
Acceptability	*Acceptable*
Remarks	*The study serves as an informative evidence of HCl acute inhalation toxicity only, which can be applied for other conclusions in evaluation of preparations with HCl as an active substance. The highest dose of HCl not inducing sensory and pulmonary irritation was not determined.*

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BPD Data set IIA/ Annex Point VI.6.1.3

Acute Toxicity

Acute inhalation toxicity in the guinea pig

	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	

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BPD Data set IIA/ Annex Point VI.6.1.3

Acute Toxicity

Acute inhalation toxicity in the baboon

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1 REFERENCE

1.1	**Reference**	Kaplan H.L. (1987) Effects of irritant gases on avoidance/escape performance and respiratory response of the baboon. Toxicology **47**: 165-179 Published
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Companies with letters of access	None
1.2.3	Criteria for data protection	No data protection claimed.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	No
2.2	**GLP**	No
2.3	**Deviations**	Not applicable

3 MATERIALS AND METHODS

3.1	**Test material**	HCl gas
3.1.1	Lot/Batch number	Not stated
3.1.2	Specification	Not stated
3.1.2.1	Description	Not stated
3.1.2.2	Purity	Not stated
3.1.2.3	Stability	Not stated
3.2	**Test Animals**	
3.2.1	Species	Baboon
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	Age: juvenile, bodyweight: not specified
3.2.6	Number of animals per group	A total of 8 baboons were used (i.e. one animal per concentration)
3.2.7	Control animals	No control animals used
3.3	**Administration/ Exposure**	Inhalation
3.3.1	Post exposure	None

	period	
		Inhalation
3.3.2	Concentrations	Gas concentrations: 190, 810, 890, 940, 2780, 11400, 16570 and 17290 ppm
3.3.3	Exposure chamber and escape performance	A recirculating gas mixing/exposure system and a test apparatus were developed for measuring the effects of the gas on baboon escape performance. The animals were trained to depress an appropriate lever in order to open an escape door and then exit through the door into an adjacent chamber within 30 seconds. For each exposure, the gas bypass loop was closed, and the test gas recirculated from the gas mixing chamber through the animals' exposure chamber. After 5 min exposure, the escape performance test was presented to the animals. If the animal did not exit within 10 sec, shock was applied to the bars of the cage and maintained for 20 sec. If the animal depressed the correct lever and exit within 10 sec, the response was designated as "avoidance" response; if the animal exited after 10 seconds but within 30 sec, the response was designated an "escape".
3.3.5	Type of exposure	Not stated; presumably whole-body
3.3.6	Vehicle	-
3.3.7	Concentration in vehicle	Not applicable
3.3.8	Duration of exposure	5 minutes
3.3.9	Controls	No control animals were used, but pre-exposure performances were taken into consideration
3.4	**Examinations**	
3.4.1	Performance parameters measured	- whether the response was an avoidance, escape, or failure response; - the time to first lever press; - the time to first correct lever press; - the time to exit the chamber; - the number of correct and incorrect lever presses; - the number of intertrial lever presses (ITIs = the number of presses made prior to presentation of the escape performance test)
3.6	**Further remarks**	None.
		4 RESULTS AND DISCUSSION
4.1	**Observations**	In eight experiments in which baboons were exposed for 5 min to HCl at concentrations of 190 to 17290 ppm, 6 animals made avoidance responses and 2 animals made escape responses (escapes at 11400 and 17290 ppm). The exposure did not affect any of the performance measurements in the baboon, except that the number of ITI responses increased with increasing concentrations of the gas. The two animals exposed to the highest concentrations (16570 and

		17290 ppm) expired several weeks later from bacterial pneumonia.
4.3	**Other**	None
		5 APPLICANT'S SUMMARY AND CONCLUSION
5.1	**Materials and methods**	In a study of escape performance, for which the animals had been trained, juvenile baboons were exposed for 5 minutes to HCl at concentrations of 190 to 17290 ppm and then presented to the performance test.
5.2	**Results and discussion**	6 animals made avoidance responses and 2 animals made escape responses (escapes at 11400 and 17290 ppm). The exposure did not affect any of the performance measurements in the baboon, except that the number of ITI responses (ITI = the number of presses of lever made prior to presentation of the escape performance test) increased with increasing concentrations of the gas. The two animals exposed to the highest concentrations (16570 and 17290 ppm) expired several weeks later from bacterial pneumonia.
5.3	**Conclusion**	Exposure to hydrochloric acid for 5 minutes evokes avoidance/escaping responses in trained animals, with an increase of attempts to escape, as demonstrated by the increased number of ITI responses (ITI = the number of presses of lever made prior to presentation of the escape performance test) recorded with increasing concentrations of the gas. The study demonstrated that also baboons, like rodents, can survive to short exposures to high concentrations of this gas.
5.3.1	Reliability	3
5.3.2	Deficiencies	Observations other than those related to escape performance are not reported.

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Acute Toxicity

Acute inhalation toxicity in the baboon

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*27.05.2009.*
Materials and Methods	*Based on publication from Toxicology (1987) – Kaplan H.L. Effects of irritant gases on avoidance/escape performance and respiratory response of the. 8 juvenile baboons without control group exposed for 5 min to HCl gas with the concentration from 190 – 17290ppm. One baboon was tested per one HCl concentration from the concentration`s range. Avoidance/escaping responses were determined*
Results and discussion	*6 animals made avoidance responses and 2 animals made escape responses (escapes at 11400 and 17290 ppm). The two animals exposed to the highest concentrations (16570 and 17290 ppm) expired several weeks later from bacterial pneumonia. Only observations of the avoidance /escape performances are reported.*
Conclusion	*Not agree with applicant`s version that animals can survive from short exposure to high concentrations of the HCl gas, because two animals exposed to the highest concentrations expired several weeks later from bacterial pneumonia. However, as one test animal was used per one certain HCl concentration only, it is impossible to state sure what the indirect reason is for death of animals.*
Reliability	*4*
Acceptability	*Not acceptable, because the highest concentration of HCl not inducing the avoidance/escaping responses is determined. Respiratory response of the baboons exposed to HCl is not reported.*
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	

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Acute Toxicity

Acute inhalation toxicity in the baboon

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1 REFERENCE

1.1	**Reference**	Kaplan H.L., Anzueto A., Switzer W.G. and Hinderer R.K. (1988) Effects of hydrogen chloride on respiratory response and pulmonary function of the baboon. J. Toxicol. & Environ. Hlth. **23**: 473-493 Published
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Companies with letters of access	None
1.2.3	Criteria for data protection	No data protection claimed.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	No, but the guidelines provided in the National Research Council's Guide for the Care and Use of Laboratory Animals were followed throughout all the phases of the study.
2.2	**GLP**	No
2.3	**Deviations**	Not applicable

3 MATERIALS AND METHODS

3.1	**Test material**	HCl gas
3.1.1	Lot/Batch number	Not stated
3.1.2	Specification	Not stated
3.1.2.1	Description	Not stated
3.1.2.2	Purity	Not stated
3.1.2.3	Stability	Not stated
3.2	**Test Animals**	
3.2.1	Species	Baboon (*Papio cynocephalus*)
3.2.2	Strain	Not stated
3.2.3	Source	Not stated
3.2.4	Sex	Males
3.2.5	Age/weight at study initiation	Age: adults, bodyweight: 7.1 to 13.1 kg
3.2.6	Number of animals per group	A total of 12 baboons were used (i.e. 3 animals/group)
3.2.7	Control animals	Yes, air-exposed

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Acute Toxicity

Acute inhalation toxicity in the baboon

3.3	**Administration/ Exposure**	Inhalation
3.3.1	Post exposure period	Up to 3 months
		Inhalation
3.3.2	Concentrations	Nominal concentrations: 0, 500, 5000 and 10000 ppm Analytical concentrations (mean ± SD): 586 ± 22, 582 ± 16, and 518 ± 53; 4190 ± 125, 4606 ± 149, and 3460 ± 376; 11566 ± 376, 8500 ± 172, and 10444 ± 199
3.3.3	Preparation of atmosphere	The HCl exposure atmospheres were generated from cylinders of pure HCl. The gas was introduced continuously through a glass and Teflon rotameter and Teflon control valve into an inlet air stream, which was drawn through the exposure system at a flow rate of approx. 40 L/min by an exhaust blower. The flow rate was monitored by the pressure drop across an orifice plate mounted in the exhaust duct. The concentration of HCl was maintained at a fairly constant level (± 10% of the average concentration) by continuously monitoring the concentration in the exposure chamber and adjusting the rate of flow as necessary.
3.3.5	Type of exposure	Head-only. Animals were anesthetized with Ketamine at the initial dose of 13 mg/kg, supplemented as necessary to maintain an adequate level of anaesthesia during the 15-min exposure.
3.3.6	Vehicle	-
3.3.7	Concentration in vehicle	Not applicable
3.3.8	Duration of exposure	15 minutes
3.3.9	Controls	Air exposure
3.4	**Examinations**	
3.4.1	Measurements of respiratory parameters	An inductive plethysmography system was used to measure and record respiratory rate (*f*), tidal volume (V_T), and minute volume (MV) prior to, during, and after exposure of the anesthetized baboons. After calibration and validation of the Respitrace system, baseline respiratory measurements (*f*, V_T and MV) were recorded from the animal in a supine position next to the exposure chamber. After 5 min of baseline recording the animal's head was placed inside the headbox containing air or the HCl atmosphere and recording of respiratory parameters was continued during the 15-min exposure. At the end of the exposure, the animal's head was removed from the headbox and post-exposure measurements were recorded for an additional 15 min. Arterial blood samples (0.5 mL) were obtained from a catheter in the femoral artery once prior to initiation of exposure, every minute during exposure and every 5 min post-exposure until the animal's appearance was normal. Blood samples were analyzed for pH, PaO_2, and $PaCO_2$ using an IL 1302 blood gas analyzer.

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Acute Toxicity

Acute inhalation toxicity in the baboon

3.4.2 Pulmonary function studies

Pulmonary function tests were conducted with each animal at three time points: 1) during the week prior to exposure, 2) 3 days after exposure and 3) 3 months after exposure. Each animal was anesthetized with Ketamine at the initial dose of 13 mg/kg, supplemented as necessary to maintain an adequate level of anaesthesia. The trachea was intubated with a number 7 cuffed endotracheal tube, and a thin-walled latex balloon, 10 cm length, was positioned in the middle third of the esophagus, just cephalad to the point of maximum cardiac artefact. The esophageal balloon was connected to one side of a pressure transducer for measurement of esophageal pressure to estimate the pleural pressure (P_L). The other side of the transducer was used to measure mouth pressure (P_M) for calculation of transpulmonary pressure ($P_{TP} = P_M - P_L$). Inspiratory capacity (IC) was determined by inflating the lungs to a transpulmonary pressure of +40 cm of water. Pressure measurements were recorded. Pulmonary volumes, the diffusing capacity of the lungs for carbon monoxide (DL_{CO}), the diffusing capacity per unit lung volume (DL/VA), and capillary blood flow (Q_C) were also determined by making the animals rebreathing a gas mixture containing helium, acetylene, oxygen, and nitrogen by forcing IC volumes into the lungs with a 2-L syringe for a period of 15 sec. Functional residual capacity (FRC) also was measured during rebreathing of the gas mixture and was used to calculate total lung capacity (TLC = FRC + IC). Vital capacity (VC) is defined as the sum of IC + expiratory residual volume ERV. The measurements of these pulmonary function parameters were obtained from computer processing of mass spectrometric analytical data during the rebreathing of the gas mixture that was repeated twice to obtain an average value for each parameter. Pulmonary static compliance (C_S) was calculated using a method of analysis of pressure-volume curves obtained during stepwise deflation of the lungs from TLC to below FRC.

Anteroposterior and lateral chest radiographs were obtained in all animals in conjunction with the pulmonary function tests as well as within 1 h following exposure. The radiographs were taken with the lung inflated to an airway pressure of +40 cm of water using a constant tube to film distance and with identical settings for all subsequent films for any individual animal.

3.4.3 CO_2 challenge response studies

Carbon dioxide challenge response studies of each of the control and treated animals were conducted on the same days as the pulmonary function tests. Baseline respiratory parameters (f, V_T, and MV) were recorded with the Respitrace system for 5 min prior to exposure to CO_2, with the animal in a supine position. The head of the animal was then placed inside the same chamber used for exposure, an air flow of room air maintained, and respiratory parameters measured for an other 5 min prior to introduction of CO_2. At the end of 5 min, CO_2 was metered into the chamber from a cylinder containing 99.99% minimum CO_2 at a sufficient rate to achieve a 10% concentration within the chamber at the end of 5 min and to maintain this concentration for an additional 5 min. Simultaneously, O_2 was metered into the chamber at a sufficient flow rate to maintain a concentration of 20.5 ± 1% within the

chamber. At the end of the 10 min exposure to CO_2, the animal's head was removed from the chamber and respiratory recording was continued for an additional 5 min.

3.5 Statistics

- Effects of HCl on respiratory response and atrial blood gases: an average ratio of responses in each respiratory parameter (*f*, V_T, and MV) during the exposure to the average 5-min baseline value was obtained for each animal. Mean values of the average ratios for the three animals in each of the four groups were compared between groups by means of a one-way analysis of variance. If significance ($p \leq 0.05$) was obtained, the four groups means were compared using Duncan's multiple comparison test. Mean arterial blood gas values of the three animals in each group at each minute of exposure and at 5 and 10 min post exposure were compared against mean pre exposure values and to each other across groups for significance ($P \leq 0.05$), using a two-way analysis of variance.

- Effects of HCl on pulmonary function and blood gases: pulmonary function and blood gas values were compared within groups at the three time points (pre exposure and 3 days and 3 months post exposure) and across exposure groups using a two-way analysis of variance.

- Effects of HCl on CO_2 challenge response: the rate of change (slope) of each respiratory parameter (*f*, V_T, and MV) was obtained for each animal by fitting a least-squares line to the changes in the parameter from the first minute during each of the next 5 min of the CO_2 challenge test. The resultant slopes of the 3 animals in each of the 4 groups were compared across the three CO_2 challenge periods (pre exposure and 3 days and 3 months post exposure) using a two-way repeated-measures analysis of the variance. When significance was found, multiple comparisons of the means were made between and within the four exposure groups across the three time periods. Similarly, ratios of the maximum response values of each parameter (*f*, V_T, and MV) during the CO_2 challenge to the average baseline value prior to exposure to CO_2 were obtained for each animal. The resultant ratios of the 3 animals in each of the 4 groups were compared across the three CO_2 challenge periods (pre exposure and 3 days and 3 months post exposure) using a two-way repeated-measured analysis of the variance. When significance was found, multiple comparisons of the means were made between and within the four exposure groups across the three time periods.

3.6 Further remarks None.

4 RESULTS AND DISCUSSION

4.1 Observations

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Acute Toxicity

Acute inhalation toxicity in the baboon

4.1.1	Effects on respiratory response and arterial blood gases	The animals responded to HCl with a concentration-related increase in respiratory frequency. At 500 ppm there was a small but rapid increase, which was maintained at a fairly stable level during the remainder of 15-min exposure, averaging approx. to 50% of baseline. At the two higher levels the animals held their breath for approx. 10-20 sec, after which respiratory frequency rapidly increased and continued to increase over several minutes. At 1000 ppm the increase was 100%. The mean ratios of the average frequency during the 15-min exposure to the average baseline frequency were significantly different between the control and the 5000- and 10000-ppm groups. The difference between the 10000 and the 500-ppm group was also statistically significant. Comparison of mean ratios of average tidal volume during exposure to average baseline values did not show any significant difference. The increased *f* and unchanged V_T were reflected in an increased respiratory minute volume (MV), concentration related, and whose mean of the ratios during exposure to baseline MV attained statistical significance between the control and the 10000-ppm group at Duncan's analysis. Despite the increased respiratory frequency and minute volume the arterial PaO_2 value decreased rapidly at the two higher HCl concentrations, with average values at 5, 10 and 15 min during exposure and at 5 and 10 min post exposure statistically different from pre exposure values and corresponding exposure values of the control and 500-ppm animals. The lowest PaO_2 value occurred after exposure to 10000 ppm HCl, and hypoxemia persisted for at least 10 min after exposure in the animals at the two higher concentrations. Concurrently with the decreases in blood PaO_2, blood $PaCO_2$ and pH appeared to increase and decrease, respectively, without attaining statistical significance compared to pre exposure values.
4.1.2	Effects on pulmonary function and arterial blood gases	Comparison of the mean values obtained at pulmonary function test of four groups carried out prior to exposure, and at 3 days and 3 months after exposure did not show any statistically significant difference, either in any parameter or for any time point. Blood pH and arterial blood gases also were not significantly different.
4.1.3	Effects on CO_2 challenge response	There was considerable variability in respiratory response among the animals of each group during the 5-min ramping to 10% CO_2; the slopes of the change in frequency response at 3 days and 3 months were not significantly different from the pre exposure values for both the control and the 500-ppm animals while the slopes appeared to increase with time following exposure for the 5000- and 10000-ppm animals. The changes in maximal response in *f*, V_T, and MV during the 5-min exposure to CO_2 also showed considerable variability among animals of each group.
4.3	**Other**	None

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	In a study on respiratory response and pulmonary function, groups of 3 male anaesthetized baboons were head-only exposed for 15 minutes to HCl at concentrations of 0, 500, 5000 or 10000 ppm. Respiratory parameters were determined (respiratory rate *f*, tidal

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Acute Toxicity

Acute inhalation toxicity in the baboon

		volume V_T, and minute volume MV) prior to, during, and after exposure. Arterial blood samples were obtained once prior to initiation of exposure, during exposure and every 5 min post-exposure until the animal's appearance was normal and analyzed for pH, PaO_2, and $PaCO_2$. Pulmonary function tests, including response to challenge with 10% CO_2, were conducted with each animal at three time points: during the week prior to exposure, 3 days and 3 months after exposure.
5.2	**Results and discussion**	The acute respiratory response consisted of a concentration-related increase in frequency and minute volume, preceded by a transient breath-holding reflex possibly caused by irritation of the nerve receptors of the nasal and oral mucosa, together with a marked decrease in blood PaO_2 at the two higher concentrations. The exposure did not cause significant alterations in any of the pulmonary function parameters measured at 3 days and 3 months after exposure, suggesting that most of HCl was trapped by the moist tissues of the nasal and oral mucosa and upper respiratory tract, limiting the penetration to the lower respiratory tract. The results of CO_2 challenge response test could not be interpreted with confidence because of the high inter-animal variability in respiratory response.
5.3	**Conclusion**	The study demonstrates that baboons can survive to exposure to very high concentrations of HCl for 15 min and that probably humans are much less sensitive than the mouse.
5.3.1	Reliability	3
5.3.2	Deficiencies	Non-standard method; results not directly applicable to EU C&L procedures.

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Acute Toxicity

Acute inhalation toxicity in the baboon

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*27.05.2009.*
Materials and Methods	*Applicant`s version is acceptable –based on the publication in Journal Toxicology and environmental Health (1988) – Effects of hydrogen chloride on respiratory response and pulmonary function of the baboon. Groups of 3 adult male anaesthetized baboons were head-only exposed for 15 minutes to HCl at concentrations of 0, 500, 5000 or 10000 ppm (so, the control group was tested). A number of respiratory response`s and pulmonary functions` parameters were determined. Statistical analysis determining statistical significance in relation to different test groups and parameters measured was implemented.*
Results and discussion	*Applicant's version is adopted. The acute respiratory response consisted of a concentration-related increase in frequency and minute volume, preceded by a transient breath-holding reflex possibly caused by irritation of the nerve receptors of the nasal and oral mucosa, together with a marked decrease in blood PaO_2 at the two higher concentrations. Other parameters showed no statistical significance in values among different test groups.*
Conclusion	*Agree with applicant's version – the baboons can survive to exposure to very high concentration of HCl for 15min. and probably humans are much less sensitive than mice, as well.*
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	

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Acute Toxicity

Acute inhalation toxicity in the mouse

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1 REFERENCE

1.1	**Reference**	Lucia H.L., Barrow C.S., Stock M.F. and Alarie Y. (1977) A semi-quantitative method for assessing anatomic damage sustained by the upper respiratory tract of the laboratory mouse, *Mus musculus*. J. Combust. Toxicol. **4**: 472-486 Published
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Companies with letters of access	None
1.2.3	Criteria for data protection	No data protection claimed.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	No.
2.2	**GLP**	No
2.3	**Deviations**	Not applicable

3 MATERIALS AND METHODS

3.1	**Test material**	HCl gas
3.1.1	Lot/Batch number	Not stated
3.1.2	Specification	Not stated
3.1.2.1	Description	Not stated
3.1.2.2	Purity	Not stated
3.1.2.3	Stability	Not stated
3.2	**Test Animals**	
3.2.1	Species	Mouse
3.2.2	Strain	Swiss-Webster
3.2.3	Source	Hilltop Labs, USA
3.2.4	Sex	Males
3.2.5	Age/weight at study initiation	Age: not specified, bodyweight: 25 to 30 g
3.2.6	Number of animals per group	4 animals/group
3.2.7	Control animals	No control animals used

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Acute Toxicity

Acute inhalation toxicity in the mouse

3.3	**Administration/ Exposure**	Inhalation
3.3.1	Post exposure period	24 hours
		Inhalation
3.3.2	Concentrations	Nominal concentrations: 17, 131, 280, 493, 723, 1088, 1973, 3110 and 7279 ppm (equivalent to 0.025, 0.19, 0.41, 0.73, 1.06, 1.60, 2.90, 4.57 and 10.70 mg/L)
3.3.3	Preparation of atmosphere	The HCl exposure atmospheres were generated from a cylinder of 49000 ppm HCl in N_2, diluted with room air, and passing through the exposure chamber at the constant flow rate of 20 litres/min.
3.3.5	Type of exposure	Not mentioned: presumably whole-body.
3.3.6	Vehicle	-
3.3.7	Concentration in vehicle	Not applicable
3.3.8	Duration of exposure	10 minutes
3.3.9	Controls	No control animals used
3.4	**Examinations**	
3.4.1	Histopathology	24 hours after exposure the mice were killed by cervical dislocation. The head was cut-off, and the skin, jaw, musculature and brain were removed for complete fixation in 10% buffered aqueous formalin, followed by treatment in 5% nitric acid until the bone was decalcified (generally 36 to 48 h). Then, 4 transverse sections, 1.5 to 2 mm apart, were made across the nose beginning from the external nares and proceeding caudated to the lateral canthi of the eyes. Sections 1, 2 and 3 are respiratory in function while section 4 is olfactory. Section 1 is the external nares and is lined by stratified squamous epithelium, which is a continuation of the mucosa seen externally at the tip of the nose. Sections 2 and 3 have mainly pesudostratified columnar epithelium that has no olfactory function and overly two longitudinally oriented turbinates. Stratified squamous epithelium lines the floor of this passage, which is posterior extension of the mucosa seen in Section 1. There are also small areas of specialised olfactory epithelium seen in the roof of Section 3. Section 4 is an almost separate chamber with the olfactory stratified epithelium overlaying a complex pattern of multiply-folded turbinates. Each portion of tissue was then labelled and processed separately. The section was washed overnight under running tap water, dehydrated thru graded ethanol, cleared in xylene and embedded in Paraplast II. Sections at 5 µm were obtained and stained with hematoxylin & eosin. Lesions were graded according to the following scale: 0 No damage seen at 24 h 1+ 1-50% of the mucosa is damaged, but underlying tissues are intact 2+ 25-75% of the mucosa is destroyed, and some damage to

the submucosa is noted

3+ 50-99% % of the mucosa is destroyed, and there is damage to the submucosa and underlying support structures

4+ 100% of the mucosa is destroyed and there is extensive destruction of all underlying tissues

3.4 Statistics None.

3.6 Further remarks None.

4 RESULTS AND DISCUSSION

4.1 Observations

No effect on tissue in Sections 1, 3 and 4 was noted at 17 ppm. In Section 2, small superficial ulcerations of the mucosa appeared at the inferior-most extent of the respiratory epithelium, at its junction with squamous epithelium. As the concentration of HCl was increased, the mucosal ulcerations seen in Section 2 increased in extent, in a contiguous fashion, gradually extending up the sides and the septum of the nasal cavity. At 723 ppm, this damage involved more than the lower 2/3 of the chamber. However, the strip of squamous epithelium on the floor of the nose remained intact until 1088 ppm. At 1973 ppm the entire mucosa of Section 2 was destroyed. Damage to the squamous epithelium of Section 1 first occurred when the animals were exposed to 493 ppm. Damage to the mucosa in Section 3, again starting in the inferior-most pseudostratified columnar epithelium, was first noted at 131 ppm and at 3110 ppm it involved the lower ½ of the mucosa, except for the squamous epithelium. Even at 7279 ppm there was preservation of the superior-most pseudostratified columnar epithelium, and the inferior-most squamous epithelium. Damage to the sinus mucosa in Section 4 was not seen until 3110 ppm was reached, and even then only 50% of the animals had damage, consisting always to small ulcerations of the inferior-most turbinate mucosa. However, the mucosa of the midline passage was much more vulnerable and became ulcerated at 1088 ppm. Damage to the underlying support structures was first noted in Section 2 at 1088 ppm, when the cartilage of the septum was necrotic, and the bone of the delicate maxilloturbinate was eroded. At 1973 ppm the septal cartilage of Section 1 was destroyed. At 7279 ppm all animals had total destruction of the mucosa and support structures in Sections 1 and 2, and most of the mucosa of Section 3. The ethmoid sinus was spared, except for some small ulcerations on the most-inferior turbinate. These animals has also their eyes totally destroyed, were awkwardly attempting to mouth breath, swallowing large amounts of air, and were unable to eat or drink.: they would have died, in any case, shortly after the 24 hours post-exposure period.

The numerical rating given to the damage produced by HCl is reported in table A6.1.3/06-01.

4.3 Other None

5 APPLICANT'S SUMMARY AND CONCLUSION

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Acute Toxicity

Acute inhalation toxicity in the mouse

5.1	**Materials and methods**	A histopathological study was carried out in mice. Groups of 4 mice were exposed to HCl at increasing concentrations ranging from 17 ppm (0.025 mg/L) to 7279 ppm (10.7 mg/L) for 10 minutes. 24 hours following exposure the animals were sacrificed, their heads were processed and slides from 4 Sections of the upper respiratory tract were obtained and stained with hematoxylin & eosin. Lesions observed were graded according to a specific scale evaluating both the area of interest and the degree of damage.
5.2	**Results and discussion**	The range of HCl concentrations tested resulted in injury of the different sections from minimal ulcerations to complete destruction. Effects were noted on Section 2 (anterior nasal turbinate) before the other sections.
5.3	**Conclusion**	The study accurately describes histopathological lesions observed following exposure to increasing concentrations of HCl for 10 minutes. HCl caused tissue destruction (corrosion) in the respiratory tract of the mouse at high concentrations.
5.3.1	Reliability	2
5.3.2	Deficiencies	Non-standard method. Results however appear scientifically valid.

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Acute Toxicity

Acute inhalation toxicity in the mouse

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*27.05.2009.*
Materials and Methods	*Agree with applicant`s version based on the publication of J. Combustion Toxicology (1977) – Lucia H.L., Barrow C.S., Stock M.F. and Alarie Y. – A semi – quantitative method for assessing anatomic damage sustained by the upper respiratory tract of the laboratory mouse Mus musculus. Groups of 4 mice were exposed to HCl at increasing concentrations ranging from 17 ppm (0.025 mg/L) to 7279 ppm (10.7 mg/L) for 10 minutes. 24 hours following exposure the animals were sacrificed, their heads were processed and slides from 4 sections of the upper respiratory tract were* histopathologically *studied.*
Results and discussion	*The range of HCl concentrations tested resulted in injury of the different sections from minimal ulcerations to complete destruction. Effects were noted on Section 2 (anterior nasal turbinate) before the other sections. Agree with applicant`s version. Practically no damage caused only at lowest HCl concentration – 17 ppm (see table A6.1.3/06-01).*
Conclusion	*Agree with applicant`s version. HCl caused tissue destruction (corrosion) in the respiratory tract of the mouse at high concentrations.*
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 A6.1.3/06-01: Summary of effects observed following exposure to HCl

Exposure (ppm)	Concentration (mg/L)	Section 1	Section 2	Section 3	Section 4
17	0.025	0	0-1+	0	0
131	0.19	0-1+	1+	0-1+	0
280	0.41	0-1+	1+	1+	0
493	0.73	1+	1-2+	1+	0
723	1.06	1+	2+	1+	0
1088	1.60	2+	3+	1+	0
1973	2.90	2+	4+	1+	0-1+
3110	4.57	4+	4+	2+	1+
7279	10.70	4+	4+	3+	1+

Doc. IIIA/ Section A6.1.3/07

Acute Toxicity

Acute inhalation toxicity in the mouse

BPD Data set IIA/ Annex Point VI.6.1.3

Official use only

		1 REFERENCE
1.1	**Reference**	Barrow C.S., Lucia H. and Alarie Y.C. (1979) A comparison of the acute inhalation toxicity of hydrogen chloride versus the thermal decomposition products of polyvinylchloride. Journal of Combustion Toxicology **6**: 3-12 Published
1.2	**Data protection**	No
1.2.1	Data owner	Not applicable
1.2.2	Companies with letters of access	None
1.2.3	Criteria for data protection	No data protection claimed.
		2 GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	No
2.2	**GLP**	No, GLP was not compulsory at the time the study was conducted
2.3	**Deviations**	Not applicable
		3 MATERIALS AND METHODS
3.1	**Test material**	a. Products from thermal decomposition of PVC b. Hydrogen chloride
3.1.1	Lot/Batch number	Not stated
3.1.2	Specification	Not stated
3.1.2.1	Description	Not stated
3.1.2.2	Purity	Not stated
3.1.2.3	Stability	Not stated
3.2	**Test Animals**	
3.2.1	Species	Mouse
3.2.2	Strain	Swiss-Webster
3.2.3	Source	Hilltop Laboratories
3.2.4	Sex	Male
3.2.5	Age/weight at study initiation	Age not specified, bodyweight: 25 - 30 g
3.2.6	Number of animals per group	4 mice/group
3.2.7	Control animals	No