Section A2.10(2b)
Annex Point IIA2.10

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

Product Type 2 - Hard Surface Disinfection Hospitals and Industrial Areas (PT2.01)

2.10.2	**Environmental exposure towards active substance**	
2.10.2.1	**Production**	**Refer to Justification for non-submission of data TNG Section 2.10.2.1**
	(i) Releases into water	
	(ii) Releases into air	
	(iii) Waste disposal	
2.10.2.2	**Intended use(s)**	[redacted]
	Affected compartment(s):	
	water	100% of the emission is to waste water
	sediment	-
	air	-
	soil	-
	Predicted concentration in the affected compartment(s)	**Partitioning within a Sewage Treatment Plant (STP)**
	water	4.64 % will partition into water
	sediment	Not applicable
	air	2.43E-03 will enter the air
	Soil	2.86% will partition into sludge. Nevertheless there is no indirect exposure of soil via the application of sludge. Glutaraldehyde is very reactive with organic matter, therefore unlikely to reach the soil via sludge amendment of soils, and in consequence groundwater.

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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

Product Type 2 - Hard Surface Disinfection Hospitals and Industrial Areas (PT2.01)

Assessment		PEC
Scenario 1 - Hard Surface Disinfection Hospitals and Industrial Areas (PT2.01)	PEC for micro-organisms in the STP (mg/l)	2.61E-03
	Local PEC in surface water during emission episode (dissolved) (mg/l)	2.61E-04
	Local PEC in fresh-water sediment during emission episode (mg/kg wwt)	2.05E-03
	Local PEC in groundwater under agricultural soil (mg/l)	n.a
	Local PEC in agricultural soil (total) averaged over 30 days (mg/kg/wwt)	n.a
	Local PEC in agricultural soil (total) averaged over 180 days (mg/kg/wwt)	n.a

Soil will not be exposed to glutaraldehyde, as there is no indirect exposure via the application of sludge. Glutaraldehyde was not detected in sludge, in line with its high reactivity with functional groups such as amines present in activated sludge.

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	November 25th, 2012
Materials and methods	2.10.1.2 Intended use(s) Human and environmental exposure assessments were also performed by the RMS - please refer to Doc IIB.
Conclusion	The uses are as described by the applicants. Please see the human and environmental exposure assessments in Doc IIB.
Reliability	Not applicable
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*

Section A2.10(2b) **Annex Point IIA2.10**	**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** **Product Type 2 - Hard Surface Disinfection Hospitals and Industrial Areas (PT2.01)**

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

Table A2.10(2): Workplace exposure / inhalation exposure

Exposure scenario	Workplace operation	PPE	Year(s) of measurement	Number of measurements	Type of measurements	Exposure concentration
[redacted]	[redacted]					
Formulation	Production of PT 02 products	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available			refer to section 2.10.1.2

MG/PT Application	Application of PT 02 products: professionals	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available	refer to section 2.10.1.2
MG/PT Application	Application of PT 02 products: non-professionals	No PPE used	No measurements available	refer to section 2.10.1.2

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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

Product Type 3 - Poultry Farm Disinfection (PT3)

Subsection		Official use only
2.10.1 Human exposure towards active substance		
2.10.1.1 Production	**Refer to Justification for non-submission of data TNG Section 2.10.1.1**	
i) Description of process		
ii) Workplace description		
iii) Inhalation exposure		
iv) Dermal exposure		
2.10.1.2 Intended use(s)		
1. Professional Users	[redacted] is a biocidal product used in veterinary hygiene to disinfect areas in which animals are housed. The product is used to control pathogenic micro-organisms in industrial poultry barns, other intensive livestock farming installations and similar facilities i.e. hatcheries, incubators, stables. Poultry farm disinfection is presented here as the worst case.	
i) Description of application process	Scenario 6 – Mixing and Loading Solution for Disinfection of a Poultry Farm by Spraying or Fogging This scenario represents the task of handling containers of 50% [redacted] Scenario 7 - Disinfection of a Poultry Farm by Spraying This scenario represents the task of application by spraying. [redacted] Scenario 8 - Disinfection of a Poultry Farm by Fogging This scenario represents application by fogging. [redacted]	

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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

Product Type 3 - Poultry Farm Disinfection (PT3)

[redacted]

ii) Workplace description	Scenario 6 – Mixing and Loading Solution for Disinfection of a Poultry Farm by Spraying or Fogging ConsExpo has been used to perform the exposure assessment calculations. Using the default model in ConsExpo Version 4.1: - *Disinfectants → Veterinary hygiene biocidal products → Disinfectant milking machine → Mixing and Loading liquid* and adapting this model to suit this scenario the likely exposure to the worker was estimated. Scenario 7 - Disinfection of a Poultry Farm by Spraying Using the default model in ConsExpo Version 4.1:- *Disinfectants → Veterinary Hygiene Biocidal Products → Animal Transports → Spraying*, and adapting this model to suit this scenario, the likely exposure to the worker was estimated. Scenario 8 - Disinfection of a Poultry Farm by Fogging No worker exposure during fogging. Scenario 6 covers the potential exposure during mixing and loading of solution into fogging machine.
iii) Inhalation exposure	Scenario 6 – Mixing and Loading Solution for Disinfection of a Poultry Farm by Spraying or Fogging: Inhalation exposure is considered to be negligible. Scenario 7 - Disinfection of a Poultry Farm by Spraying:- Tier 3 wit 95% effective PPE: 0.00247 mg/m^3 (mean event); ; 0.000411 mg/m^3 (daily mean) ***Scenario 8 - Disinfection of a Poultry Farm by Fogging:*** Inhalation exposure is considered to be negligible.
iv) Dermal exposure	Scenario 6 – Mixing and Loading Solution for Disinfection of a Poultry Farm by Spraying or Fogging:- 0.00833 mg/kg bw/day (acute); external dose 0.0233 mg/cm^2. Scenario 7 – Disinfection of a Poultry Farm by Spraying:- Tier 3 with 95% effective PPE: 0.00054 mg/kg bw/day(acute); external dose 0.0015 mg/cm^2 Scenario 8 - Disinfection of a Poultry Farm by Fogging:- Dermal exposure is considered to be negligible.
2. Non-professional Users including the general public	Scenario 9 - Indirect exposure could occur if a child was to enter the barn immediately after it has been sprayed or fogged. This is unlikely and it would be restricted to children that live on the farm. Indirect exposure could result from one of the following:- inhalation of volatilised residues (acute/ sub-chronic) dermal contact of contaminated surfaces (acute) ingestion from hand to mouth contact (acute)

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Product Type 3 - Poultry Farm Disinfection (PT3)

(i) via inhalational contact	Inhalation exposure negligible.
(ii) via skin contact	6.0E-04 mg/kg bw; external dose 4.6E-05 mg/cm^2
(iii) via drinking water	Not applicable
(iv) via food	Not applicable
(v) indirect via environment	Not applicable
Oral contact from mouthing fingers	6.1E-04 mg /kg bw

2.10.2 Environmental exposure towards active substance

2.10.2.1 Production **Refer to Justification for non-submission of data TNG Section 2.10.2.1**

(i) Releases into water	
(ii) Releases into air	
(iii) Waste disposal	

2.10.2.2 Intended use(s) **Scenario 1 - Poultry Farm Disinfection**

[redacted]

Affected compartment(s):	
water	-
sediment	-
air	Emissions to air
soil	Emissions to slurry are calculated to reach the soil.
Predicted concentration in the affected compartment(s)	The Predicted concentrations are presented in Doc II B
water	

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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

Product Type 3 - Poultry Farm Disinfection (PT3)

sediment	
air	
Soil	Glutaraldehyde will undergo rapid dissipation in matrixes with high concentration of bacteria and organic matter.

Assessment		PEC
Scenario 1 - Sow in groups and Laying hens in free range	Manure / Concentration of the active ingredient in soil based on the nitrogen immission standard for grassland (mg/kg)	2.3E-06
	Manure / Concentration of the active ingredient in soil based on the nitrogen immission standard for arable land (mg/kg)	2.3E-06
	Slurry Concentration of the active ingredient in soil based on the nitrogen immission standard for grassland (mg/kg)	3.8E-06
	Slurry Concentration of the active ingredient in soil based on the nitrogen immission standard for arable land (mg/kg)	3.8E-06

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	November 28th, 2012
Materials and methods	2.10.1.2 Intended use(s) Human and environmental exposure assessments were also performed by the RMS - please refer to Doc IIB.
Conclusion	The uses are as described by the applicants. Please see the human and environmental exposure assessments in Doc IIB.
Reliability	Not applicable
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.*

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Annex Point IIA2.10

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

Product Type 3 - Poultry Farm Disinfection (PT3)

	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 A2.10(6): Workplace exposure / inhalation exposure

Exposure scenario	Workplace operation	PPE	Year(s) of measurement	Number of measurements	Type of measurements	Exposure concentration
[redacted]	[redacted]					
Formulation	Production of PT 03 products	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available			refer to section 2.10.1.2

MG/PT Application	Application of PT 03 products: professionals	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available	refer to section 2.10.1.2

MG/PT Application	Application of PT 03 products: non-professionals	No PPE used	No measurements available	refer to section 2.10.1.2

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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

Product Type 4 – Food Vessels

Subsection		Official use only
2.10.1 Human exposure towards active substance		
2.10.1.1 Production	**Refer to Justification for non-submission of data TNG Section 2.10.1.1**	
i) Description of process		
ii) Workplace description		
iii) Inhalation exposure		
iv) Dermal exposure		
2.10.1.2 Intended use(s)		
1. Professional Users	In many countries glass bottles are re-used. The bottles are washed and disinfected prior to being re-used. Since chlorine does not work well under alkaline conditions and in the presence of organic residues, non-oxidizers are preferred for this application. Cold food processing vessels (e.g.: industrial mayonnaise mixers, yoghurt producing facilities, fermenters for beer or other fermented products, etc.) are periodically disinfected after use by spraying with a solution of 0.1% Glutaraldehyde.	
	[redacted]	
i) Description of application process	[redacted]	
ii) Workplace description	Scenario 11 -Connecting drum to pump [redacted]	

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Product Type 4 – Food Vessels

	Scenario 35 Maintenance of machinery [redacted]
iii) Inhalation exposure	Scenario 11 -Connecting drum to pump0.00713 mg/m^3 (event mean); 3.71E-06 mg/m^3 (daily mean) Scenario 35 Maintenance of machinery; negligible.
iv) Dermal exposure	Scenario 11 -Connecting drum to pump:- 0.0233 mg/cm^2 (external dose) Scenario 35 Maintenance of machinery – Tier 1 0.0234 mg/cm^2 (external dose) Scenario 35 Maintenance of machinery – Tier 2 0.0234 mg/cm^2 (external dose)
2. Non-professional Users including the general public	This application is for professional use only.
(i) via inhalational contact	Not applicable
(ii) via skin contact	Not applicable
(iii) via drinking water	Not applicable
(iv) via food	Not applicable
(v) indirect via environment	Not applicable

2.10.2 Environmental exposure towards active substance

2.10.2.1 Production	**Refer to Justification for non-submission of data TNG Section 2.10.2.1**
(i) Releases into water	
(ii) Releases into air	
(iii) Waste disposal	
2.10.2.2 Intended use(s)	[redacted]

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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

Product Type 4 – Food Vessels

[redacted]

Scenario 1 – Disinfection of Food Vessels

Using the model presented and described in the ESD for Product Types 2, 3 and 4 (AEA Technology (Report No.AEAT/ED48587/R1(2006), Table 16) emission scenario for calculating the releases of disinfectants used in entire plants (e.g. breweries, dairies, beverage processing plants)), the emission to waste water was calculated as shown below and used as an input to EUSES Version 2.0.3.

[redacted]

Affected compartment(s):	
water	100% of the emission is to waste water
sediment	-
air	-
soil	-
Predicted concentration in the affected compartment(s)	**Partitioning within a Sewage Treatment Plant (STP)**
water	4.64% will partition into water
sediment	Not applicable
air	2.43E-03 will enter the air
Soil	2.86% will partition into sludge. Nevertheless there is no indirect exposure of soil via the application of sludge. Glutaraldehyde is very reactive with organic matter, therefore unlikely to reach the soil via sludge amendment of soils, and in consequence groundwater.

Please refer to the Doc IIB for the detailed exposure calculations and Predicted Environmental Concentrations.

Assessment		PEC

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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

Product Type 4 – Food Vessels

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	November 28th, 2012
Materials and methods	2.10.1.2 Intended use(s) Human and environmental exposure assessments were also performed by the RMS - please refer to Doc IIB. 2.10.2.2 (Environmental exposure): [redacted]
Conclusion	The uses are as described by the applicants. Please see the human and environmental exposure assessments in Doc IIB.
Reliability	Not applicable
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 A2.10(10):Workplace exposure / inhalation exposure

Exposure scenario	Workplace operation	PPE	Year(s) of measurement	Number of measurements	Type of measurements	Exposure concentration
[redacted]	[redacted]					
Formulation	Production of PT 04 products	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available			refer to section 2.10.1.2

MG/PT Application	Application of PT 04 products: professionals	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available	refer to section 2.10.1.2

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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

Product Type 4 – Food Processing Surface Disinfection (PT4)

Subsection		Official use only
2.10.1 Human exposure towards active substance		
2.10.1.1 Production	**Refer to Justification for non-submission of data TNG Section 2.10.1.1**	
i) Description of process		
ii) Workplace description		
iii) Inhalation exposure		
iv) Dermal exposure		
2.10.1.2 Intended use(s)		
1. Professional Users	Walls of slaughter houses and other rooms where food is processed/stored need to be disinfected on a regular basis (in the absence of food) with the idea to avoid the contamination of the food that is further processed and to avoid spreading of pathogenic micro-organisms (e.g.: Foot and Mouth Disease, Viruses or Salmonella Bacteria).	
i) Description of application process	[redacted]	
ii) Workplace description	Scenario 12 - Application of Disinfectant in a Slaughter House TNsG, Human Exposure, Report 2002, Part 2, p.158, Disinfection Model 9 has been used to calculate the exposure to a worker following disinfection of a slaughter House.	
iii) Inhalation exposure	Scenario 12 - Application of Disinfectant in a Slaughter House:- 0.002 mg/m^3 (mean event)	
iv) Dermal exposure	Scenario 12 - Application of Disinfectant in a Slaughter House:- Tier 2 0.0134 mg/cm2 (external dose)	

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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

Product Type 4 – Food Processing Surface Disinfection (PT4)

2. Non-professional Users including the general public	This application is for professional use only.
(i) via inhalational contact	Not applicable
(ii) via skin contact	Not applicable
(iii) via drinking water	Not applicable
(iv) via food	Not applicable
(v) indirect via environment	Not applicable

2.10.2 Environmental exposure towards active substance

2.10.2.1 Production **Refer to Justification for non-submission of data TNG Section 2.10.2.1**

(i) Releases into water

(ii) Releases into air

(iii) Waste disposal

2.10.2.2 Intended use(s)

[redacted]

Scenario: Food Processing Surface Disinfection

[redacted]

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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

Product Type 4 – Food Processing Surface Disinfection (PT4)

Affected compartment(s):	
water	100% of the emission is to waste water
sediment	-
air	-
soil	-
Predicted concentration in the affected compartment(s)	**Partitioning within a Sewage Treatment Plant (STP)**
water	4.64 % will partition into water
sediment	Not applicable
air	2.43E-03 will enter the air
Soil	2.86% will partition into sludge. Nevertheless there is no indirect exposure of soil via the application of sludge. Glutaraldehyde is very reactive with organic matter, therefore unlikely to reach the soil via sludge amendment of soils, and in consequence groundwater.

Please refer to the Doc IIB for the detailed exposure calculations and Predicted Environmental Concentrations.

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

Section A2.10(11)
Annex Point IIA2.10

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

Product Type 4 – Food Processing Surface Disinfection (PT4)

Date	November 28th, 2012
Materials and methods	2.10.1.2 Intended use(s) Human and environmental exposure assessments were also performed by the RMS - please refer to Doc IIB.
Conclusion	The uses are as described by the applicants. Please see the human and environmental exposure assessments in Doc IIB.
Reliability	Not applicable
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 A2.10(11):Workplace exposure / inhalation exposure

Exposure scenario	Workplace operation	PPE	Year(s) of measurement	Number of measurements	Type of measurements	Exposure concentration
[redacted]	[redacted]					
Formulation	Production of PT 04 products	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available			refer to section 2.10.1.2

MG/PT Application	Application of PT 04 products: professionals	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available	refer to section 2.10.1.2

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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

Product Type 6 – Preservatives for Detergents (PT6.01)

Subsection		Official use only
2.10.1 Human exposure towards active substance		
2.10.1.1 Production	**Refer to Justification for non-submission of data TNG Section 2.10.1.1**	
i) Description of process	[redacted]	
ii) Workplace description		
iii) Inhalation exposure		
iv) Dermal exposure		
2.10.1.2 Intended use(s)		
1. Professional Users	Laundry softener, liquid detergents and other aqueous systems require an in-can preservative to protect them against bio-spoilage during their shelf life. These systems are prone to microbial growth (both moulds and bacteria). A preservative must be added to these aqueous formulations during their production in the manufacturing plant and the added preservative must prevent the bio-deterioration of these systems until they are used, namely a few months (up to 1 year) after production. Product formulation and product use (laundry softener, liquid detergent, wax emulsion and car polish) by professional workers has been evaluated. The maximum Glutaraldehyde present in the product was 0.1%.	
i) Description of application process	Scenario 29– Formulation - Connecting a drum to a pump [redacted] Scenario 30 – Loading Laundry Softener [redacted] Scenario 31 - Mixing and Loading Liquid Detergent [redacted]	

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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

Product Type 6 – Preservatives for Detergents (PT6.01)

Scenario 32 - Applying Liquid Detergent

[redacted]

Scenario 33 - Applying Wax Emulsion

[redacted]

Scenario 34 - Applying Car Polish

[redacted]

ii) Workplace description

Scenario 29– Connecting a drum to a pump

This scenario used the default scenario in ConsExpo Version 4.1:- Cleaning & washing → Dishwashing → Machine liquid: rinse aid → Loading, the exposure to the worker is calculated.

Scenario 30 – Loading Laundry Softener

This scenario used the default model for Cleaning & Washing → Laundry products → Fabric conditioner.

Scenario 31 - Mixing and Loading Liquid Detergent

This scenario used the default model for Cleaning & Washing → Dishwashing products → Hand dishwashing liquid → mixing & loading.

Scenario 32 - Applying Liquid Detergent

This scenario used the default model for Cleaning & Washing → Dishwashing products → Hand dishwashing liquid → Application. Tier 1 does not consider use of PPE while Tier 2 considers use of gloves.

Scenario 33 - Applying Wax Emulsion

This scenario used the default model for Cleaning & Washing → Floor, Carpet and Furniture Products → Floor polish. Tier 1 does not consider use of PPE, Tier 2 considers use of gloves, and Tier 3 considers use of gloves with RPE.

Scenario 34 - Applying Car Polish

This scenario used the default model for Cleaning & Washing → Floor, Carpet and Furniture Products → Floor polish.

iii) Inhalation exposure

Scenario 29 Formulation Tier 1- neglible exposure.

Scenario 30 Loading laundry softener Tier 1 - 3.56E-05 mg/m^3 (event mean); 1.85E-07 mg/m^3 (daily mean).

Scenario 31 Mixing detergent Tier 1- 1.42E-05 mg/m^3 (event mean); 7.48E-08 mg/m^3 (daily mean).

Scenario 32 Applying detergent Tier 1- 8.46E-04 mg/m^3 (event mean); 3.52E-04 mg/m^3 (daily mean).

Scenario 32 Applying detergent Tier 2 8.46E-04 mg/m^3 (event mean); 3.52E-04 mg/m^3 (daily mean).

Scenario 33 Applying wax emulsion Tier 1 – 0.0521 mg/m^3 (event mean); 0.013 mg/m^3 (daily mean).

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Scenario 33 Applying wax emulsion Tier 2 – 0.0521 mg/m^3 (event mean); 0.013 mg/m^3 (daily mean).

Scenario 33 Applying wax emulsion Tier 3 – 0.0521 mg/m^3 (event mean); 0.0013 mg/m^3 (daily mean).

Scenario 34 Applying car polish Tier 1 – 0.0358 mg/m3 (event mean); 0.00298 mg/m3 (daily mean).

Scenario 34 Applying car polish Tier 2 – – 0.0358 mg/m3 (event mean); 0.00298 mg/m3 (daily mean).

iv) Dermal exposure

Scenario 29 Formulation Tier 1- 0.0233 mg/cm^2 (external dose).

Scenario 30 Loading laundry softener Tier 1 – 4.65E-05 mg/cm^2

Scenario 31 Mixing detergent Tier 1- 4.65E-05 mg/cm^2.

Scenario 32 Applying detergent Tier 1- 0.0076 mg/cm^2.

Scenario 32 Applying detergent Tier 2 0.0076 mg/cm^2.

Scenario 33 Applying wax emulsion Tier 1 0.0128 mg/cm^2.

Scenario 33 Applying wax emulsion Tier 2 – 0.0128 mg/cm^2.

Scenario 33 Applying wax emulsion Tier 3 – 0.0128 mg/cm^2.

Scenario 34 Applying car polish Tier 1 - 0.0014 mg/cm^2.

Scenario 34 Applying car polish Tier 2 - 0.0014 mg/cm^2.

2. Non-professional Users including the general public

Four different consumer products which contain Glutaraldehyde as an in-can preservative have been assessed. These include laundry softener, liquid detergent, wax emulsion and car polish. ConsExpo has been used to perform the exposure assessment calculations. The maximum Glutaraldehyde present in the product was 0.1%.

Scenario 13 –Loading Laundry Softener

The amount of human exposure to laundry softeners has been estimated using ConsExpo Version 4.1. The calculations are based on the default model for Cleaning & Washing → Laundry products → Fabric conditioner.

Scenario 14 - Mixing and Loading Liquid Detergent

The amount of human exposure to liquid dish washing detergent has been estimated using ConsExpo Version 4.1. The calculations are based on the default model for Cleaning & Washing → Dishwashing products → Hand dishwashing liquid → mixing & loading.

Scenario 15 - Applying Liquid Detergent

The calculations are based on the default model for Cleaning & Washing → Dishwashing products → Hand dishwashing liquid → Application. The maximum percentage Glutaraldehyde present in the product is 0.1%.

Scenario 16 - Applying Wax Emulsion

The calculations are based on the default model for Cleaning & Washing → Floor, Carpet and Furniture Products → Floor polish.

Scenario 17 - Applying Car Polish

The calculations are based on the USEPA standard scenario for

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		applying car wax.. It is assumed that the non-professional user polishes their car six times a year. **Scenario 18 - Indirect Exposure to Laundry Softener** The calculations are based on the default model for Cleaning & Washing → Laundry products → Fabric conditioner → Post application. **Scenario 19 - Indirect Exposure to Liquid Detergent** Indirect exposure from consuming residues of liquid detergent present on crockery following washing have been determined. The calculations are based on the default model for Cleaning & Washing → Dishwashing products → Hand dishwashing liquid → Post Application.
	(i) via inhalational contact	Scenario 13 –Loading Laundry Softener 3.56E-05 mg/m^3 (event mean); 1.86E-05 mg/m^3 (daily mean) Scenario 14 - Mixing and Loading Liquid Detergent - 1.42E-05 mg/m^3 (event mean); 8.64E-09 mg/m^3 (daily mean) Scenario 15 - Applying Liquid Detergent – 8.46E-04 mg/m^3 (event mean); 4.11E-05 mg/m^3 (daily mean) Scenario 16 - Applying Wax Emulsion – 0.0521 mg/m^3 (event mean); 0.00217 mg/m^3 (daily mean) Scenario 17 - Applying Car Polish – negligible. Scenario 18 - Indirect Exposure to Laundry Softener – negligible. Scenario 19 - Indirect Exposure to Liquid Detergent – negligible.
	(ii) via skin contact	Scenario 13 –Loading Laundry Softener 4.65E-05mg/cm^2 (external dose) Scenario 14 - Mixing and Loading Liquid Detergent - 4.65E-05mg/cm^2 Scenario 15 - Applying Liquid Detergent – 0.0076 mg/cm^2 Scenario 16 - Applying Wax Emulsion – 0.0128 mg/cm^2 Scenario17 - Applying Car Polish – 0.0033 mg/cm^2 Scenario 18 - Indirect Exposure to Laundry Softener – 0.00029 mg/cm^2 Scenario19 - Indirect Exposure to Liquid Detergent – negligible.
	(iii) via drinking water	Not applicable
	(iv) via food	Not applicable
	(v) indirect via environment	Not applicable
Oral Exposure		Scenario 19 - Indirect Exposure to Liquid Detergent – 6.9E-6 mg/kg bw/day

2.10.2 Environmental exposure towards active substance

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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

Product Type 6 – Preservatives for Detergents (PT6.01)

2.10.2.1 Production	**Refer to Justification for non-submission of data TNG Section 2.10.2.1**
(i) Releases into water	
(ii) Releases into air	
(iii) Waste disposal	
2.10.2.2 Intended use(s)	[redacted]
	Scenario 2 - Detergent Disposed via the Drain As a worst case scenario, it is assumed that 100% of the product is discharged to a STP. The emission to waste water was calculated based on the emission scenario for PT1 Table 3.4 'Emission scenario for calculating the release of disinfectants used in human hygiene biocidal products (private use) based on an average consumption for products containing the biocide' (Royal Haskoning Document, Environmental Emission Scenarios for biocides used as human hygiene biocidal products (PT1), Jan 2004 as recommended in Royal Haskoning Document, Environmental Emission Scenarios for biocides used as in-can preservatives (PT6), Jan 2004).
Affected compartment(s):	
water	100% of the emission is to waste water
sediment	-
air	-
soil	-
Predicted concentration in the	**Partitioning within a Sewage Treatment Plant (STP)**

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Product Type 6 – Preservatives for Detergents (PT6.01)

affected compartment(s)	
water	4.64% will partition into the water
sediment	Not applicable
air	2.43E-03 will enter the air
Soil	2.86% will partition into sludge. Nevertheless there is no indirect exposure of soil via the application of sludge. Glutaraldehyde is very reactive with organic matter, therefore unlikely to reach the soil via sludge amendment of soils, and in consequence groundwater. Please refer to the Doc IIB for the detailed exposure calculations and Predicted Environmental Concentrations.

Compartment	Value

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	November 28th, 2012
Materials and methods	2.10.1.2 Intended use(s) Human and environmental exposure assessments were also performed by the RMS - please refer to Doc IIB.
Conclusion	The uses are as described by the applicants. Please see the human and environmental exposure assessments in Doc IIB.
Reliability	Not applicable
Acceptability	Acceptable
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*

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Product Type 6 – Preservatives for Detergents (PT6.01)

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 A2.10(14):Workplace exposure / inhalation exposure

Exposure scenario	Workplace operation	PPE	Year(s) of measurement	Number of measurements	Type of measurements	Exposure concentration
[redacted]	[redacted]					
Formulation	No formulation for PT 06 products	-	No measurements available			refer to section 2.10.1.2
MG/PT Application	Application of PT 06 products: professionals	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available			refer to section 2.10.1.2
MG/PT Application	Application of PT 06 products: non-professionals	No PPE used	No measurements available			refer to section 2.10.1.2

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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

Product Type 6 – Paper Wet-end Additives Preservation and Paper Coatings Preservation (PT6.02)

Subsection		Official use only
2.10.1 Human exposure towards active substance		
2.10.1.1 Production	**Refer to Justification for non-submission of data TNG Section 2.10.1.1**	
i) Description of process		
ii) Workplace description		
iii) Inhalation exposure		
iv) Dermal exposure		
2.10.1.2 Intended use(s)		
1. Professional Users	Additives containing Glutaraldehyde as an in-can preservative are used by professionals in the paper-making process. These additives (e.g. kaolin slurry used in the wet-end stage of paper production) generally contain 0.01 to 0.05% Glutaraldehyde (100-500g Glutaraldehyde per tonne of additive) which are produced by diluting 50% Glutaraldehyde.	
i) Description of application process	[redacted]	
ii) Workplace description	Scenario 20 - Loading and unloading slurry tanks Using the EASE model within EUSES version 2.0.3 the potential exposure to the operator is calculated. [redacted]	

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Annex Point IIA2.10

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

Product Type 6 – Paper Wet-end Additives Preservation and Paper Coatings Preservation (PT6.02)

[redacted]

iii) Inhalation exposure	0.087 mg/m^3 (mean event)
iv) Dermal exposure	Negligible
2. Non-professional Users including the general public	This application is for professional use only.
(i) via inhalational contact	Not applicable
(ii) via skin contact	Not applicable
(iii) via drinking water	Not applicable
(iv) via food	Not applicable
(v) indirect via environment	Not applicable

2.10.2 Environmental exposure towards active substance

2.10.2.1 Production **Refer to Justification for non-submission of data TNG Section 2.10.2.1**

(i) Releases into water

(ii) Releases into air

(iii) Waste disposal

2.10.2.2 Intended use(s) **– Emissions to the Environment from the use of wet-paper additives**

[redacted]

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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

Product Type 6 – Paper Wet-end Additives Preservation and Paper Coatings Preservation (PT6.02)

[redacted]

	Affected compartment(s):	
	water	100% of the emission is to waste water
	sediment	-
	air	-
	soil	-
the	Predicted concentration in affected compartment(s)	**Partitioning within a Sewage Treatment Plant (STP)**
	water	4.64 % will partition into water
	sediment	Not applicable
	air	2.43E-03 will enter the air
	Soil	2.86% will partition into sludge. Nevertheless there is no indirect exposure of soil via the application of sludge. Glutaraldehyde is very reactive with organic matter, therefore unlikely to reach the soil via sludge amendment of soils, and in consequence groundwater.

Please refer to DocIIB for detailed information on Predicted Environmental Concentrations.

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	November 28th, 2012

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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

Product Type 6 – Paper Wet-end Additives Preservation and Paper Coatings Preservation (PT6.02)

Materials and methods	2.10.1.2 Intended use(s) Human and environmental exposure assessments were also performed by the RMS - please refer to Doc IIB.
Conclusion	The uses are as described by the applicants. Please see the human and environmental exposure assessments in Doc IIB.
Reliability	Not applicable
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 A2.10(17):Workplace exposure / inhalation exposure

Exposure scenario	Workplace operation	PPE	Year(s) of measurement	Number of measurements	Type of measurements	Exposure concentration
[redacted]	[redacted]					
Formulation	Production of PT 06 products	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available			refer to section 2.10.1.2

MG/PT Application	Application of PT 06 products: professionals	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available	refer to section 2.10.1.2

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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

Product Type 11 – Closed Recirculated Cooling Systems (PT11.03)

Subsection		Official use only
2.10.1 Human exposure towards active substance		
2.10.1.1 Production	**Refer to Justification for non-submission of data TNG Section 2.10.1.1**	
i) Description of process		
ii) Workplace description		
iii) Inhalation exposure		
iv) Dermal exposure		
2.10.1.2 Intended use(s)		
1. Professional Users	Glutaraldehyde is used as a preservative in closed recirculated systems. The water in the closed system contains 0.01% Glutaraldehyde (100g Glutaraldehyde per m^3 of cooling water) which is produced by diluting 50% Glutaraldehyde.	
i) Description of application process	[redacted]	
ii) Workplace description	Scenario 21 – Filling a closed system Using the TNsG Model 7 mixing and loading 'pump liquid' data the potential exposure to the operator is calculated. Scenario 22 – Draining a closed system Using the TNsG Model 7 mixing and loading 'pump liquid' data the potential exposure to the operator is calculated.	
iii) Inhalation exposure	Scenario 21 – Filling a closed system Inhalation uptake has not been considered in this scenario as it is considered that there will be no vapour or respirable droplets produced during the process. Scenario 22 – Draining a closed system Inhalation exposure is 0.0022 mg/m^3 (mean event and daily mean)	
iv) Dermal exposure	Scenario 21 – Filling a closed system Using TNsG Model 7 mixing and loading 'pump liquid data' the	

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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

Product Type 11 – Closed Recirculated Cooling Systems (PT11.03)

	potential Tier 2 dermal exposure has been estimated to be:0.008 mg/cm^2 (external dose) Scenario 22 – Draining a closed system Using TNsG Model 7 mixing and loading 'pump liquid data' the potential dermal exposure has been estimated to be: 4.68E-04 mg/cm^2 (external dose)
2. Non-professional Users including the general public	This application is for professional use only.
(i) via inhalational contact	Not applicable
(ii) via skin contact	Not applicable
(iii) via drinking water	Not applicable
(iv) via food	Not applicable
(v) indirect via environment	Not applicable
2.10.2 Environmental exposure towards active substance	
2.10.2.1 Production	**Refer to Justification for non-submission of data TNG Section 2.10.2.1**
(i) Releases into water	
(ii) Releases into air	
(iii) Waste disposal	
2.10.2.2 Intended use(s)	**Scenario 15 – Emissions to the Environment from Closed Recirculated Cooling Systems** [redacted]

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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

Product Type 11 – Closed Recirculated Cooling Systems (PT11.03)

[redacted]

Affected compartment(s):	
water	100% of the emission is to waste water
sediment	-
air	-
soil	-
Predicted concentration in the affected compartment(s)	**Partitioning within a Sewage Treatment Plant (STP)**
water	4.64 % will partition into water
sediment	Not applicable
air	2.43E-03 will enter the air
Soil	2.86% will partition into sludge. Nevertheless there is no indirect exposure of soil via the application of sludge. Glutaraldehyde is very reactive with organic matter, therefore unlikely to reach the soil via sludge amendment of soils, and in consequence groundwater.

Please refer to the Doc IIB for the detailed exposure calculations and Predicted Environmental Concentrations.

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	November 28th, 2012
Materials and methods	2.10.1.2 Intended use(s) Human and environmental exposure assessments were also performed by the RMS - please refer to Doc IIB.
Conclusion	The uses are as described by the applicants. Please see the human and environmental exposure assessments in Doc IIB.
Reliability	Not applicable
Acceptability	Acceptable
Remarks	

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Annex Point IIA2.10

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

Product Type 11 – Closed Recirculated Cooling Systems (PT11.03)

	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 A2.10(20):Workplace exposure / inhalation exposure

Exposure scenario	Workplace operation	PPE	Year(s) of measurement	Number of measurements	Type of measurements	Exposure concentration
[redacted]	[redacted]					
Formulation	Production of PT 11 products	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available			refer to section 2.10.1.2

MG/PT Application	Application of PT 11 products: professionals	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available	refer to section 2.10.1.2

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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

Product Type 11 – Open Evaporative Recirculated Cooling Towers, small (PT11.02)

Subsection		Official use only
2.10.1 Human exposure towards active substance		
2.10.1.1 Production	**Refer to Justification for non-submission of data TNG Section 2.10.1.1**	
i) Description of process		
ii) Workplace description		
iii) Inhalation exposure		
iv) Dermal exposure		
2.10.1.2 Intended use(s)		
1. Professional Users	Glutaraldehyde is used as a preservative in cooling tower water. The cooling tower water contains 0.01% Glutaraldehyde (100g Glutaraldehyde per m^3 of cooling water) which is produced by diluting 50% Glutaraldehyde.	
i) Description of application process	[redacted]	
ii) Workplace description	Scenario 25 – disconnecting/reconnecting drums Using the TNsG Model 7 mixing and loading 'pump liquid' data the potential exposure to the operator is calculated.	
iii) Inhalation exposure	Inhalation uptake has not been considered in this scenario as it is considered that there will be no vapour or respirable droplets produced during the process.	
iv) Dermal exposure	Using TNsG Model 7 mixing and loading 'pump liquid data' the potential dermal exposure has been estimated to be: 0.008 mg/cm^2 (external dose)	
2. Non-professional Users including the general public	Scenario 26 - This application is for professional use only, however the possibility of bystander exposure through inhalation of spray drift was considered.	
(i) via inhalational	Adult = 0.001 mg/m^3 (mean event)	

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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

Product Type 11 – Open Evaporative Recirculated Cooling Towers, small (PT11.02)

contact	Child = 0.001 mg/m^3 (mean event)Infant = 0.001 mg/m^3 (mean event)
(ii) via skin contact	Not applicable
(iii) via drinking water	Not applicable
(iv) via food	Not applicable
(v) indirect via environment	Not applicable

2.10.2 Environmental exposure towards active substance

2.10.2.1 Production	**Refer to Justification for non-submission of data TNG Section 2.10.2.1**
(i) Releases into water	
(ii) Releases into air	
(iii) Waste disposal	

2.10.2.2 Intended use(s)	**Scenario14 – Emissions to the Environment from Cooling towers**
	[redacted]
Affected compartment(s):	
water	100% of the emission is to waste water
sediment	-
air	-
soil	-
Predicted concentration in the affected compartment(s)	**Partitioning within a Sewage Treatment Plant (STP)**
water	4.64 % will partition into water
sediment	Not applicable
air	2.43E-03 will enter the air

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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

Product Type 11 – Open Evaporative Recirculated Cooling Towers, small (PT11.02)

Soil	2.86% will partition into sludge. Nevertheless there is no indirect exposure of soil via the application of sludge. Glutaraldehyde is very reactive with organic matter, therefore unlikely to reach the soil via sludge amendment of soils, and in consequence groundwater. Please refer to the Doc IIB for the detailed exposure calculations and Predicted Environmental Concentrations. 4.64 % will partition into water

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	November 28th, 2012
Materials and methods	2.10.1.2 Intended use(s) Human and environmental exposure assessments were also performed by the RMS - please refer to Doc IIB.
Conclusion	The uses are as described by the applicants. Please see the human and environmental exposure assessments in Doc IIB.
Reliability	Not applicable
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 A2.10(19):Workplace exposure / inhalation exposure

Exposure scenario	Workplace operation	PPE	Year(s) of measurement	Number of measurements	Type of measurements	Exposure concentration
[redacted]	[redacted]					
Formulation	Production of PT 11 products	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available			refer to section 2.10.1.2

MG/PT Application	Application of PT 11 products: professionals	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available	refer to section 2.10.1.2
MG/PT Application	Application of PT 11 products: non-professionals	No PPE used	No measurements available	refer to section 2.10.1.2

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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

Product Type 12 – Slimicides for Paper; de-inking (PT12.01)

Subsection		Official use only
2.10.1 Human exposure towards active substance		
2.10.1.1 Production	**Refer to Justification for non-submission of data TNG Section 2.10.1.1**	
i) Description of process		
ii) Workplace description		
iii) Inhalation exposure		
iv) Dermal exposure		
2.10.1.2 Intended use(s)		
1. Professional Users	Slimicides containing Glutaraldehyde are used by professionals in the paper de-inking process. Slimicides are added to the pulper water in the de-inking process and generally contain a maximum of 0.02% Glutaraldehyde (based on a maximum addition of 250g Glutaraldehyde per tonne of pulp produced, using on average 1.3 m^3 of water to produce one tonne of pulp) which is produced by diluting 50% Glutaraldehyde.	
i) Description of application process	[redacted]	
ii) Workplace description	Scenario 27 - disconnect empty container/reconnect full container Using the TNsG Model 7 mixing and loading 'pump liquid' data the potential exposure to the operator is calculated. Scenario 28 - exposure during cleaning/maintenance of pulp tanks Using a combination of the TNsG and ConsExpo background documents a suitable scenario was developed to calculate the potential exposure during cleaning and maintenance.	
iii) Inhalation exposure	Inhalation uptake has not been considered in this scenario as it is considered that there will be no vapour or respirable droplets	

Section A2.10(24)
Annex Point IIA2.10

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

Product Type 12 – Slimicides for Paper; de-inking (PT12.01)

	produced during the process.
iv) Dermal exposure	Scenario 27 - disconnecting/reconnecting drums Using TNsG Model 7 mixing and loading 'pump liquid data' the potential Tier 2 dermal exposure has been estimated to be: 0.008 mg/cm2 (external dose) Scenario 28 - cleaning/maintenance of machines and pulp tanks the potential Tier 2 dermal exposure has been estimated to be: 4.5E-05 mg/cm2 (external dose)
2. Non-professional Users including the general public	This application is for professional use only.
(i) via inhalational contact	Not applicable
(ii) via skin contact	Not applicable
(iii) via drinking water	Not applicable
(iv) via food	Not applicable
(v) indirect via environment	Not applicable

2.10.2 Environmental exposure towards active substance

2.10.2.1 Production	**Refer to Justification for non-submission of data TNG Section 2.10.2.1**
(i) Releases into water	
(ii) Releases into air	
(iii) Waste disposal	
2.10.2.2 Intended use(s)	**Scenario 19 – Emissions to the Environment during Paper De-inking** [redacted]

Section A2.10(24)
Annex Point IIA2.10

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

Product Type 12 – Slimicides for Paper; de-inking (PT12.01)

[redacted]

Affected compartment(s):	
water	100% of the emission is to waste water
sediment	-
air	-
soil	-
Predicted concentration in the affected compartment(s)	**Partitioning within a Sewage Treatment Plant (STP)**
water	4.64 % will partition into water
sediment	Not applicable
air	2.43E-03 will enter the air
Soil	2.86% will partition into sludge. Nevertheless there is no indirect exposure of soil via the application of sludge. Glutaraldehyde is very reactive with organic matter, therefore unlikely to reach the soil via sludge amendment of soils, and in consequence groundwater. Please refer to the Doc IIB for the detailed exposure calculations and Predicted Environmental Concentrations.
	4.64 % will partition into water

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	November 28th, 2012
Materials and methods	2.10.1.2 Intended use(s) Human and environmental exposure assessments were also performed by the RMS - please refer to Doc IIB.
Conclusion	The uses are as described by the applicants. Please see the human and environmental exposure assessments in Doc IIB.
Reliability	Not applicable
Acceptability	Acceptable

Section A2.10(24)
Annex Point IIA2.10

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

Product Type 12 – Slimicides for Paper; de-inking (PT12.01)

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 A2.10(24):Workplace exposure / inhalation exposure

Exposure scenario	Workplace operation	PPE	Year(s) of measurement	Number of measurements	Type of measurements	Exposure concentration
[redacted]	[redacted]					
Formulation	Production of PT 12 products	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available			refer to section 2.10.1.2

MG/PT Application	Application of PT 12 products: professionals	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available	refer to section 2.10.1.2

Section A2.10(23)
Annex Point IIA2.10

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

Product Type 12 – Slimicides for Paper; Wet-end (PT12.01)

Subsection		Official use only
2.10.1	**Human exposure towards active substance**	
2.10.1.1	**Production**	**Refer to Justification for non-submission of data TNG Section 2.10.1.1**
	i) Description of process	
	ii) Workplace description	
	iii) Inhalation exposure	
	iv) Dermal exposure	
2.10.1.2	**Intended use(s)**	
	1. Professional Users	Slimicides containing Glutaraldehyde are used by professionals in the paper-making industry. Slimicides are added to the process water in the wet-end stage of paper production: • A one-off shock dose of 75 ppm (100% glutaraldehyde) providing a defouling treatment • A continuous or semi-continuous dose of 37.5 ppm (100% glutaraldehyde) providing a maintenance treatment
	i) Description of application process	[redacted]
	ii) Workplace description	Scenario 23 - disconnecting/reconnecting drums Using the TNsG Model 7 mixing and loading 'pump liquid' data the potential exposure to the operator is calculated. Scenario 24 - cleaning/maintenance of machines and pulp tanks Using a combination of the TNsG and ConsExpo background documents a suitable scenario was developed to calculate the potential exposure during cleaning and maintenance.

Section A2.10(23)
Annex Point IIA2.10

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

Product Type 12 – Slimicides for Paper; Wet-end (PT12.01)

	There is no exposure from the end product.
iii) Inhalation exposure	Inhalation uptake has not been considered in these scenarios as it is considered that there will be no vapour or respirable droplets produced during the process.
iv) Dermal exposure	Scenario 23 - disconnecting/reconnecting drums Using TNsG Model 7 mixing and loading 'pump liquid data' the potential Tier 2 dermal exposure has been estimated to be: 0.008 mg/cm^2 (external dose) Scenario 24 - cleaning/maintenance of machines and pulp tanks The potential Tier 2 dermal exposure has been estimated to be1.76E-04 mg/cm^2 (external dose)
2. Non-professional Users including the general public	This application is for professional use only.
(i) via inhalational contact	Not applicable
(ii) via skin contact	Not applicable
(iii) via drinking water	Not applicable
(iv) via food	Not applicable
(v) indirect via environment	Not applicable

2.10.2 Environmental exposure towards active substance

2.10.2.1 Production	**Refer to Justification for non-submission of data TNG Section 2.10.2.1**
(i) Releases into water	
(ii) Releases into air	
(iii) Waste disposal	

2.10.2.2 Intended use(s)

Scenario 18 – Emissions to the Environment during Paper Manufacturing

[redacted]

Section A2.10(23)
Annex Point IIA2.10

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

Product Type 12 – Slimicides for Paper; Wet-end (PT12.01)

[redacted]

	Affected compartment(s):	
	water	100% of the emission is to waste water
	sediment	-
	air	-
	soil	-
the	Predicted concentration in affected compartment(s)	**Partitioning within a Sewage Treatment Plant (STP)**
	water	4.64 % will partition into water
	sediment	Not applicable
	air	2.43E-03 will enter the air
	Soil	2.86% will partition into sludge. Nevertheless there is no indirect exposure of soil via the application of sludge. Glutaraldehyde is very reactive with organic matter, therefore unlikely to reach the soil via sludge amendment of soils, and in consequence groundwater.

Tier 2 realistic scenario is presented here:

Assessment		PEC
Slimicides: Paper Wet-end (PT12.01)-defouling Tier 4	PEC for micro-organisms in the STP (mg/l)	2.47E-03
	Local PEC in surface water during emission episode (dissolved) (mg/l)	2.47E-04

Assessment		PEC
Slimicides: Paper Wet-end (PT12.01)-Maintenance Tier 4	PEC for micro-organisms in the STP (mg/l)	1.24E-03
	Local PEC in surface water during emission episode (dissolved) (mg/l)	1.24E-04

Section A2.10(23)
Annex Point IIA2.10

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

Product Type 12 – Slimicides for Paper; Wet-end (PT12.01)

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	November 28th, 2012
Materials and methods	2.10.1.2 Intended use(s) Human and environmental exposure assessments were also performed by the RMS - please refer to Doc IIB.
Conclusion	The uses are as described by the applicants. Please see the human and environmental exposure assessments in Doc IIB.
Reliability	Not applicable
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 A2.10(23):Workplace exposure / inhalation exposure

Exposure scenario	Workplace operation	PPE	Year(s) of measurement	Number of measurements	Type of measurements	Exposure concentration
[redacted]	[redacted]					
Formulation	Production of PT 12 products	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available			refer to section 2.10.1.2

MG/PT Application	Application of PT 12 products: professionals	- Chemical goggles consistent with EN 166 or equivalent. - CE approved air-purifying respirato (full-face, organic vapor cartridge with a particulate pre-filter, type AP2), when material is heated, when aerosols/mists are generated, when ventilation is not adequate. - Protective clothing chemically resistant to this material. - Chemical resistant gloves classified under Standard EN374 (protective gloves against chemicals and micro-organisms), preferably butyl rubber. - Selection of specific items such as face shield, boots, apron, or full body suit will depend on the task.	No measurements available	refer to section 2.10.1.2

Section A3	Physical and Chemical Properties of Active Substance							
Subsection (Annex Point)	Method	Purity/ Specification	Results Give also data on test pressure, temperature, pH and concentration range if necessary	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.1 Melting point, boiling point, relative density (IIA3.1)								
3.1.1 Melting point								
Melting pt. 1 IUCLID 2.1/01	OECD Guideline 102	50% Glutaraldehyde [redacted]	***result:*** -18°C and -21.2°C ***pressure:*** performed at atmospheric pressure.	The freezing point was determined by monitoring the temperature drop while cooling the test item in a dry ice/alcohol bath with continuous stirring	Y	1	[redacted] (2000a) Freezing Point / Melting Point of [redacted] Unpublished.	
3.1.2 Boiling point								
Boiling pt. 1 IUCLID 2.2/01	OECD Guideline 103	50% Glutaraldehyde [redacted]	**result:** 100.7°C **pressure:** 1013 hPa	The boiling point was determined using Buchi 510 GS-1 melting point apparatus.	Y	1	[redacted] (2000b) Boiling Point of [redacted] Unpublished	
3.1.3 Bulk density/ relative density								

	Bulk/rel. density 1 IUCLID 2.3/01	OECD Guideline 109	50% Glutaraldehyde [redacted]	**result:** 1.129 g/ml (=1.129 kg/dm^3) **temperature:** 20±0.05°C	The pycnometer method was used.	Y	1	[redacted] (2000c) Density of [redacted] Unpublished	
3.2	**Vapour pressure (IIA3.2)**								
	Vapour pressure 1 IUCLID 2.4/01	ASTM E-1719	50% glutaraldehyde (commercially available source) batch number not reported. (A pure glutaraldehyde sample was produced by evaporation of an aqueous solution at reduced pressure).	**temperature:** 20°C **result:** 0.3mmHg; 44 Pa for 50% Glutaraldehyde	The vapour pressure experiments were carried out as successive P-T (pressure – temperature) runs on one sample of glutaraldehyde charged to the ebulliometer. Extrapolation between the 50% solution and working concentrations of Glutaraldehyde cannot be made as the relationship is not linear. A linear relationship is however possible	N	2	Olson, J.D. (1998) The vapor pressure of pure and aqueous glutaraldehyde. *Fluid Phase Equilibria*, 713-720 Published. [redacted] (2006), A Critical Evaluation of Vapor Pressure Measurements for Aqueous Glutaraldehyde Formulations [redacted]	

				at concentrations between 0-2% and temperatures between 20-35°C. Refer to Table 3.2.1-2 for calculated vapour pressures.				
3.2.1 Henry´s Law Constant (Pt. I-A3.2) IUCLID 2.14/03	Technical Guidance Document (TGD)	50% glutaraldehyde (commercially available source) batch number not reported.	**Measured/calculated:** Calculated **Result:** 5.86E-02 $Pa.m^3.mol^{-1}$	Calculated using the TGD from the vapour pressure and solubility reported in Sections 3.2 and 3.5, respectively. Refer to Table 3.2.1-1 for details of the calculations performed. RMS information on calculation of the Henry's Law Constant, see below Table 3.2.1-1	N	2	Technical Guidance Document (TGD), Environmental Risk Assessment, p 45-46	
3.3 Appearance (IIA3.3) IUCLID 1.1.1/01	-	-	-	-	-	-	-	
3.3.1 Physical state	OPPTS 830.6303	50% glutaraldehyde, [redacted]	Clear colourless liquid	Determination carried out on a 5mL sample at 26°C	Y	1	[redacted] 2007, Determination of pH, odour, colour, physical state and acidity of glutaraldehyde, [redacted] Unpublished, 28	

							September 2007.	
3.3.2 Colour	OPPTS 830.6302	50% glutaraldehyde, [redacted]	Gardner scale: Colour <1 Hazen NSA Scale: Colour <5	The colour was measured using a Lovibond 2000 Comparator MK II and a 10mL sample of the test substance.	Y	1	[redacted] 2007, Determination of pH, odour, colour, physical state and acidity of glutaraldehyde, [redacted] Unpublished, 28 September 2007.	
3.3.3 Odour	OPPTS 830.6304	50% glutaraldehyde, [redacted]	Not tested as glutaraldehyde is currently classified as a respiratory sensitiser	Glutaraldehyde is known to have a pungent 'green apple' adour.	Y	1	[redacted] 2007, Determination of pH, odour, colour, physical state and acidity of glutaraldehyde, S[redacted] Unpublished, 28 September 2007.	
3.4 Absorption spectra (IIA3.4) IUCLID 1.1.2								
UV/VIS	Method not reported	50% glutaraldehyde [redacted]	Wavelength Absorbance 374.5 0.0031 282 0.1618 234 0.6357 Refer to Figure 3.4-1 for a typical spectrum.	None	N	2	[redacted] (2000) Ultra Violet/Visible (UV/vis) Spectrometry of 50% Glutaraldehyde [redacted] (unpublished)	

IR	Method not reported	50% glutaraldehyde [redacted]	• 3478.7 O-H stretch (mostly from water, but some contribution from hydrated glutaraldehyde possible) • 2956.3 C-H stretch (symmetric, from CH_2) • 2876.63 C-H stretch (asymmetric, from CH_2) • 1712.74 C=O Stretch (from aldehyde) • 1646.75 O-H bend • 1463.75 & 1444.4 C-H bend • 683.238 O-H bend Refer to Figure 3.4-2 for a typical spectrum.	None	N	2	[redacted] Fourier Transform Infrared Spectrometry (FT-IR) of 50% Glutaraldehyde [redacted] (unpublished)	
NMR	Method not reported	50% glutaraldehyde [redacted]	See the line below	None	Y	1	[redacted] (1999), Analytical Characterization, [redacted]	

							[redacted] (unpublished), 25 May 1999	

The spectrum (Figure 3.4-3) shows: 1) aldehydic protons at 9.64 ppm, 2) multiplets at 53 and 5.0 ppm which probably arise from the protons that were originally aldehydic but have been hydrated to form -$CH(OH)_2$ groups and related cyclic structures. 3) multiplets near 2.6 ppm for the protons on carbon adjacent to the aldehydic carbonyl groups. 4) simple aliphatic methylene groups which all appear within the complex pattern between 1.1 and 1.9 ppm. 5) 4.8 ppm resonance due to exchangeable protons from the hydroxyl groups and water (now in the sample, and 6) minor resonances between 14 and 3.3 ppm which may be due to methanol and various hemiacetals or acetals which could form fromt methanol and glutaraldehyde. This spectrum is appropriate for an aqueous solution of glutaraldehyde.

Figure 3.4-4 shows the $^{13}C(^{1}H)$ NMR spectrum for the same sample. The six largest resonances in this spectrum are probably due to the two expected 2.6-dihydoxytetrahydropyrans (Figure 3.4-5; Structures 4and5): pairs of acetal carbons at 97.0 and 94.2ppm, methylene carbons adjacent to the acetal carbons at 33.7 and 33.0 ppm, and the unique methylene in each isomer at 21.4 and 18.9 ppm. The remaining resonances are probably due to the acyclic species as follows: 1) two aldehydic carbon resonances at 211.0 and 210.3 ppm (Figure 3.4-5; Structures 1 and 2); 2) aldehyde-hydrate resonances at 93.6 and 93.4 ppm (Figure 3.4-5; Structures 2 and 3); 3) aliphatic resonances at 45.4 and 44.9 ppm due to the methylene groups bound to the two types of aldehyde carbons (Figure 3.4-5; Structures 1 and .2); 4) resonances near.39.3 and 38.9 ppm (of similar intensity to the 93.6 and 93.4 ppm peaks) from the methylenes adjacent to the two types of hydrated aldehyde carbons (Figure 3.4-5; Structures 2 and 3); and 5) three resonances at 22.2, 19.5, and 16.6 ppm which are probably the central methylene groups (bound to two other methylenes) of the three acyclic compounds present in these solutions (Figure 3.4-5; Structures l, 2 and 3). The NMR spectra are consistent with the samples being aqueous glutaraldehyde, which exists in solution as five different main compounds which can readily interconvert. The proposed five compounds are: glutaraldehyde, glutaraldehyde monohydrate, glutaraldehyde dihydrate, and the two geometric isomers of 2,6- dihydroxytetrahydropyran (Figure 3.4-5; Structures 1-5). The methanol and its derivatives suggested in the ^{1}H spectrum were not concentrated enough to detect clearly in this ^{13}C NMR spectrum. The ^{1}H and ^{13}C NMR spectra are totally consistent with the sample being aqueous glutaraldehyde that contains no major unexpected organic impurities. Because these five species interconvert so readily it would not be surprising for them to simply decompose to Structure 1 in a chromatographic injection port and to be undetected by non-spectroscopic analytical techniques.

MS	Method not reported	50% glutaraldehyde [redacted]	See the line below	None	Y	1	[redacted] (1999), [redacted] Analytical Characterization, [redacted]	

							(unpublished), 25 May 1999	
The EI total ion current chromatogram (summed over m/z 11 to m/z 310) for the sample is shown in Figure 3.4-6. Identifications annotated on the chromatogram are based on the EI and CI spectra of the components. Both the EI and CI spectra of the major component are consistent with glutaraldehyde (or, 1,5-pentanedial, MW 100, $C_5H_8O_2$). The other components identified in the sample are: water, methanol (MW = 32, CH_4O, several MW = 182 components and a MW = 200 component. Both the EI and CI spectra of the MW = 182 components appear consistent with isomers of "glutaraldehyde dimer minus water" ($C_{10}H_{14}O_3$). The EI and CI spectra of the MW = 200 component appear consistent with glutaraldehyde dimer ($C_{10}H_{16}O_4$). Reference spectra for glutaraldehyde, water and methanol were obtained from the National Institute of Standards and Technology (NIST) mass spectral library.								
3.5 Solubility in water (IIA3.5) Water solubility 1 IUCLID 2.6.1/01	*including effects of pH (5-9)* EC A.6 Water Solubility	51.3% glutaraldehyde [redacted]	**result:** 51.3 % glutaraldehyde is miscible with water and is therefore considered to be fully (100%) soluble. **temperature:** 21°C **pH:** not measured	The measured value expressed as 100 % glutaraldehyde was ≥ 51.3g/100ml. One guideline deviation was noted during this study. The pH of the samples was not measured. Glutaraldehyde is not expected to ionize in water based on its chemical structure, therefore testing of the solubility at different pH values was not considered necessary. Refer to Justification for	Y	1	[redacted] (1994a) Determination of the Solubility in Water and Selected Solvents. [redacted] Unpublished	

					Non-submission of Data A3.5. In that the predicted (EUSES ver 2.0.3) solubilities at 10 °C and 30 °C were 0.81E+06 and 1.07E+6. respectively.				
3.6	**Dissociation constant (-)**	-	-	-	Refer to TNG Justification for Non-submission of Data A3.6. See also 3.5.	-	-	-	
3.7	**Solubility in organic solvents, including the effect of temperature on solubility (IIIA3.1)** IUCLID 2.6.1/02	Not stated	51.3% glutaraldehyde [redacted]	**result:** Acetone and isopropanol: 51.3% glutaraldehyde is miscible with acetone and isopropanol and is therefore considered to be fully (100%) soluble. Dichloromethane: 51.3% glutaraldehyde is soluble at 70g/100ml Ethyl acetate: 51.3% glutaraldehyde is soluble at 59g/100ml n-hexane: 51.3% glutaraldehyde is soluble at 0.19g/100ml Toluene: 51.3% glutaraldehyde is	For acetone and isopropanol the measured value expressed as 100 % glutaraldehyde was ≥ 51.3g/100ml. For dichloromethane, ethyle acetate, n-hexane and toluene the measured values expressed as 100% glutaraldehyde are 36, 30, 0.096 and 4.4 respectively.	Y	1	[redacted] (1994a) Determination of the Solubility in Water and Selected Solvents. [redacted] Unpublished	

			soluble at 8.5g/100ml **temperature:** 21°C					
3.8	**Stability in organic solvents used in b.p. and identity of relevant breakdown products (IIIA3.2)**	-	-	-	Refer to TNG Justification for Non-submission of Data A3.8	-	-	-	
3.9	**Partition coefficient n-octanol/water (IIA3.6)** log Pow 1 IUCLID 2.5/01	*including effects of pH (5-9)* OECD Guideline 107	50% Glutaraldehyde [redacted]	**result:** -0.3324 **temperature:** 25°C **pH:** see remarks	The partition coefficient of glutaraldehyde is not pH dependent. For additional information, see App 2.	Y	2	[redacted] (1996) Partition coefficient (n-octanol/deionized water) of [^{14}C]glutaraldehyde. [redacted] Unpublished	
3.10	**Thermal stability, identity of relevant breakdown products (IIA3.7)** IUCLID 2.14/01	FIFRA Guideline Subdivision D, § 63-13	51.3% glutaraldehyde [redacted]	14-day elevated temperature stability – no visible changes were noted after incubation at 50°C for 14 days. However there was a statistical change in the measured amount of glutaraldehyde. Purity at start 98.4%, purity at termination 90.3%.	Analysis of the samples was by GC-FID. The applicant has provided a further amendment, (see comm # 54): (Accelerated study:) We agree that the wording "statistical	Y	1	[redacted] (1994b) Stability of Glutaraldehyde, [redacted] Unpublished	

			28-day room temperature stability - no visible changes were noted after incubation at room temperature (approximately 20-21°C) for 28 days. Glutaraldehyde was found to be stable under these conditions. Stability to sunlight - no visible changes were noted after exposure to natural sunlight for 24 hours. Glutaraldehyde was found to be stable under these conditions.	change" we provided in the A3 template is misleading. The change from 90.3% purity to 98.4% purity is significant and leads to the conclusion that Glutaraldehyde is not stable upon accelerated storage at 50 deg.C. The report (see A3_10(1) in Doc IV-A) indicates on page 17 that : "A student t-test for the comparison of means was performed comparing the purity of Glutaraldehyde before and after the exposure period. The means were statistically different." 2) Concerning the 28-day room temperature stability, here as				

				well the reporting we did in the A3 template is not complete. Indeed, the same report indicates on page 18 that : "At test initiation, the mean percent purity of [redacted] was 98.6%, and at test termination, the mean purity was 98.3%. A student t-test comparison of means found no statistical difference between the measured purities"				
3.11 Flammability, including auto-flammability and identity of combustion products (IIA3.8) IUCLID 2.9	EPA 63-15	50% Glutaraldehyde [redacted]	Not flammable	Refer to TNG Justification for Non-submission of Data A3.11	N	2	[redacted] 1989, End-Use Product Chemistry [redacted]	

3.12 Flash-point (IIA3.9)	ASTM D-3278 Setaflash closed cup apparatus	Glutaralhyde 50 wt% [redacted]	184.8 °F = 85 °C	Additional data were supplied to the Finnish RMS to confirm that there is no flash as per the ASTM D-3278 test method, and that no Flash Point is detected up to the point that the water evaporates. This has already been agreed by the RMS. No flash with the flame extinguished at 184.8 deg F			[redacted] 3.12	
3.13 Surface tension (IIA3.10) IUCLID 2.6.2/01 Surface tension 1	OECD Guideline 115	50% Glutaraldehyde [redacted]	**result:** 72.4 mN/m (1g/L) **temperature:** 20°C	Determination carried out using a DeNuoy Tensiometer	Y	1	[redacted] (2000e) Surface Tension of [redacted] Unpublished	
3.14 Viscosity (-)	OECD guideline 114	50% Glutaraldehyde	**result:** 20.15 mPa/s	Determination carried out using a	Y	1	[redacted] (2000f) Viscosity of	

	IUCLID 2.13		[redacted]	**temperature:** 20°C	Ubbelohde Viscometer, ASTM method D88-94			[redacted] Unpublished	
3.15	**Explosive properties (IIA3.11)** IUCLID 2.10	EPA 63-16	50% Glutaraldehyde [redacted]	Not explosive	Refer to TNG Justification for Non-submission of Data A3.15	N	2	[redacted] 1989, End-Use Product Chemistry [redacted] e Corporation.	
3.16	**Oxidizing properties (IIA3.12)** IUCLID 2.11	EPA 63-14	50% Glutaraldehyde [redacted]	Not oxidising	Refer to TNG Justification for Non-submission of Data A3.16	N	2	[redacted] 1989, End-Use Product Chemistry U[redacted]	
3.17	**Reactivity towards container material (IIA3.13)** IUCLID 8.8	Not stated	50% Glutaraldehyde [redacted]	Metals **For stainless steel and nickel**: corrosion rate is nil and there is no reactivity or colour change in the product. **For carbon steel, copper, aluminium, zinc, tin plate**: not recommended. Coatings and Plastic	Compatibility tests are carried out for 90 days at 45°C. Metals are visually examined for localised corrosion and corrosion rates are measured. The coatings are visually examined to determine if they have softened,	N	2	[redacted] 2000, Shipping and Storage compatibility for 50% Glutaraldehyde, [redacted] September 8, 2000 and laboratory information appendices.	

			For polyethylene and polyethylene lined drums and plastic 9570: recommended. **For phenolic lining, Plasite 7122 and Phenguard 368**: not recommended. Elastomers **For silicone and Kalrez**: recommended.	blistered or show no apparent attack. Elastomers and plastics are examined visually and changes in weight, hardness and thickness are measured.				

eCA FI note August 2014:

The Information has been updated and revised by the end of 2012 and thereafter for point 3.5 and 3.10 July/August 2014.

3.5 The applicant has reminded the eCA on the contents of a separate 3.5. Justification with updates in it.

3.10 Information on Temperature of decomposition cannot be replaced with information on stability studies at lower temperatures where stability is maintained. However, according to Information requirements determination of temperature of decomposition is not an absolute requirement if temperature of boiling and melting are known.

No data gaps exist.

See the earlier (2012 and 2014) comments below, pp 23 and onwards.

Table 3.2.1-1 Calculation of Henry's Law Constant

Based on the calculation in the TGD the Henry's Law Constant is calculated as follows:-

$$HENRY = \frac{VP * MOLW}{SOL}$$

Vapour pressure = 44 Pa at 20°C which is 62.1 Pa at 25°C
Solubility = 1E+05 at 20°C which is 1.06E+05 Pa at 25°C (set to maximum acceptable value for EUSES)

$$HENRY = \frac{62.1 * 100.1}{1.06E+05}$$

HENRY = 5.86E-02 $Pa.m^3.mol^{-1}$

Additional RMS information on Calculation of Henry's Law Constant: (November 2012)

RMS: For a chemical in aqueous solution requiring water for stability it is not possible to measure solubility in water with accuracy. The estimation should be expressed as g/L. The substance might be soluble at considerably higher concentrations, but due to the instability, this information would not be relevant as the substance would not be (monomeric) glutaraldehyde.

The H's constant was calculated in risk assessment for both dossiers in Doc II A level as follows:

Vapour pressure (VP) =
44 Pa at 20 °C (Olson 1998, A3.2)
Molecular weight (MOLW)= 100.1 g/mol
Solubility (SOL)=
51.3 g/100ml at 21°C (Dow A3.5)
In risk assessment, the RMS has used the value 0.0086 Pa×m3/mol.

The applicant Dow has made the same calculation using different values for solubility and temperature.

Table 3.2.1-2 Conversion of Vapour Pressure for Temperature and Concentration of Glutaraldehyde

Appendix Table 1B. Glutaraldehyde partial pressure (mm Hg) in air equilibrated with aqueous glutaraldehyde solutions, converted from data shown in Appendix Table 1A.

Glut-liquid (mass %)	Glutaraldehyde Vapor Pressure (mm Hg)						
	20 °C	25 °C	30 °C	35 °C	40 °C	45 °C	50 °C
0.010	1.52E-05	2.28E-05	3.80E-05	5.84E-05	7.60E-05	1.52E-04	3.04E-04
0.10	1.52E-04	2.28E-04	3.80E-04	5.84E-04	7.60E-04	1.52E-03	3.04E-03
2.0	3.04E-03	5.32E-03	8.36E-03	1.37E-02	2.20E-02	3.50E-02	5.47E-02
15.0	2.43E-02	4.03E-02	6.61E-02	1.07E-01	1.72E-01	2.55E-01	4.19E-01
50.0	9.73E-02	1.57E-01	2.51E-01	3.94E-01	6.10E-01	9.29E-01	1.40E+00

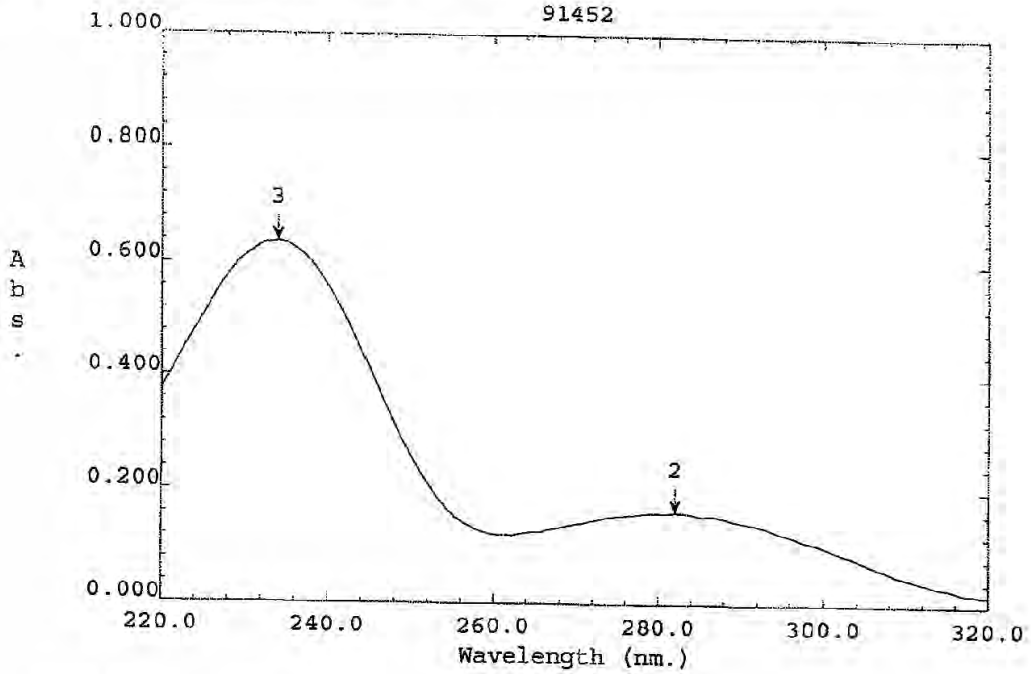
Total Pressure = 760 mm Hg (where, 760 mm Hg = 1 atm = 760 torr = 101.325 kPa)

These values for vapor pressure were calculated from the glutaraldehyde concentrations (ppm) in air from Olson's Table 4 using the following relationship between vapor pressure and air concentration:

(ppm volatile material in air = (partial pressure of material (mm Hg)/760 mm Hg/atm) x 1×10^6 ppm/atm

or, vapor pressure glutaraldehyde, as mm Hg = (ppm of material in air x 760 mm Hg/atm)/1×10^6 ppm/atm

Figure 3.4-1 Typical UV/Visible Sprectrum



File Name: 91452
Ucarcide 250 (ie. 50% glutaraldehyde in water) 200:1 dilutio

Created: 13:21 09/13/00
Data: Original

Measuring Mode: Abs.
Scan Speed: Medium
Slit Width: 1.0
Sampling Interval: 0.5

Figure 3.4-2 Typical IR Sprectrum

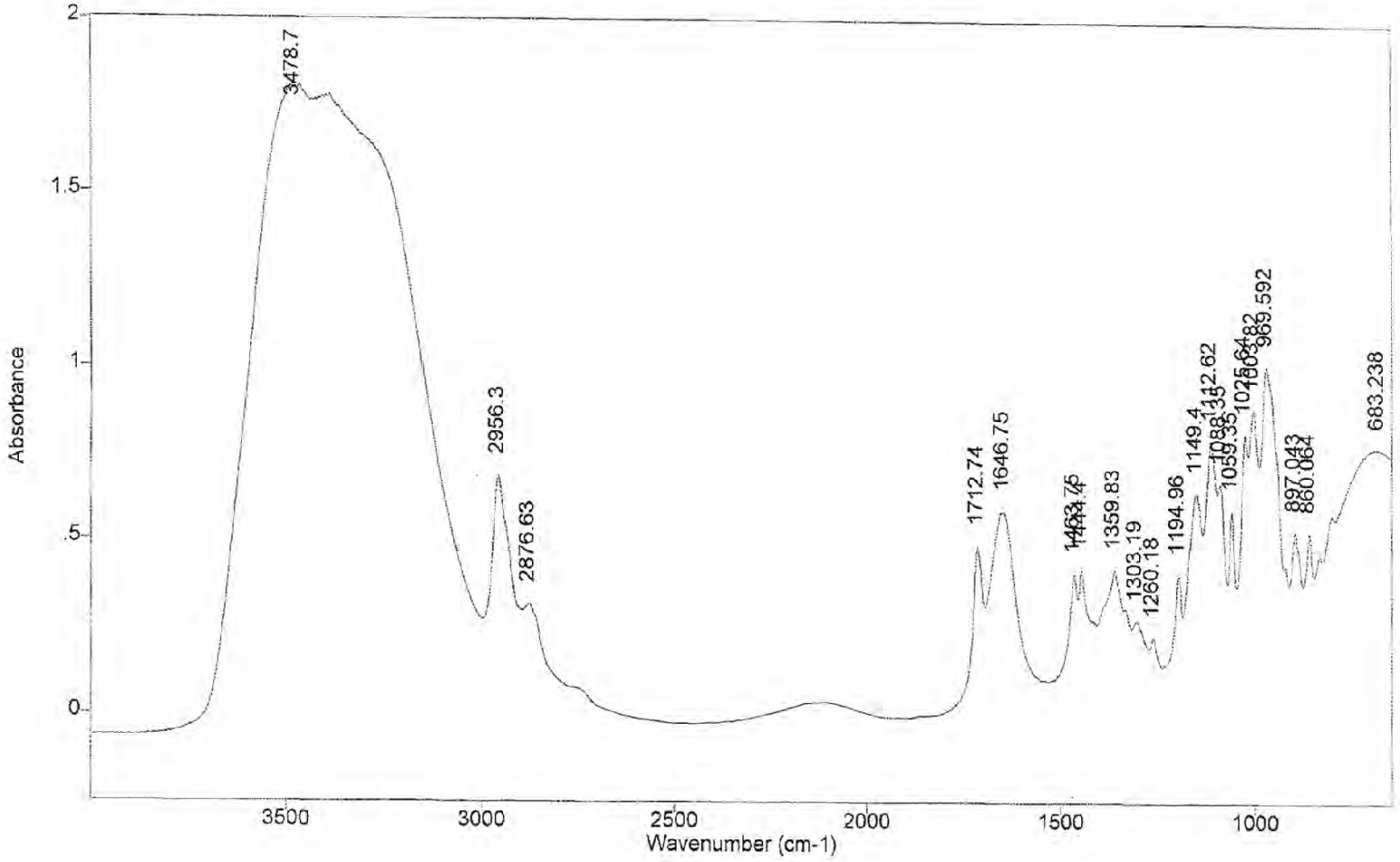


Figure 3.4-3 ^{1}H NMR Sprectum of [redacted] (Prestudy Sample)

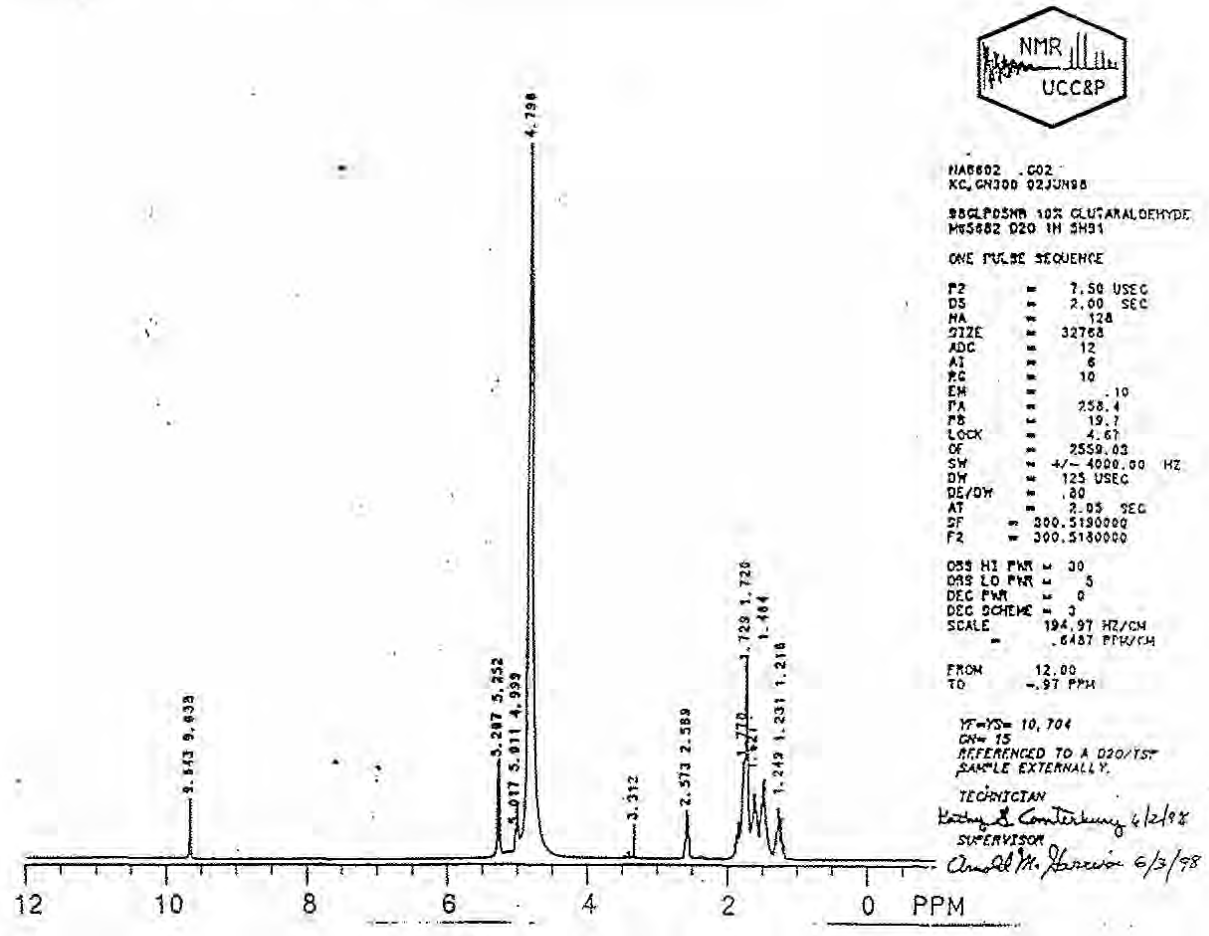


Figure 3.4-4 ^{13}C NMR Sprectum of [redacted] (Prestudy Sample)

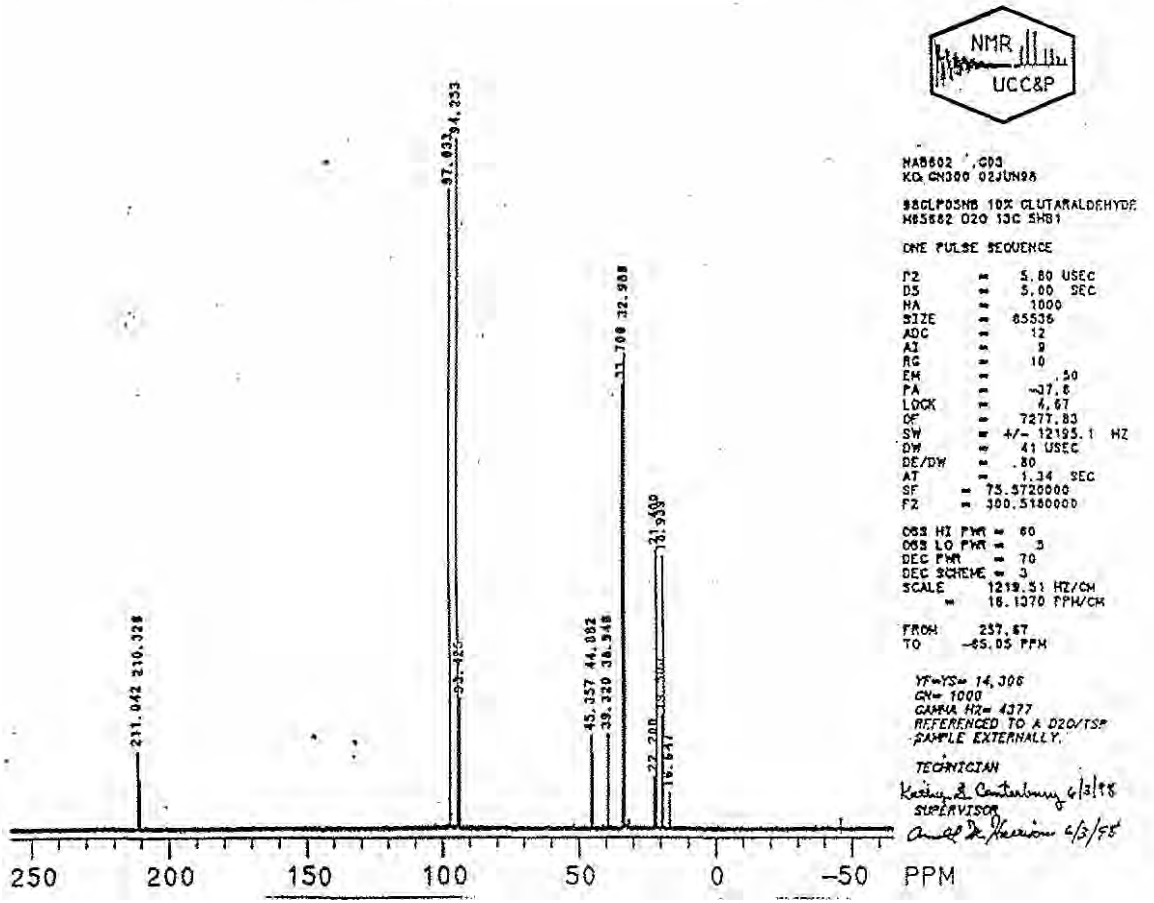


Figure 3.4-5 Structures From the NMR spectra

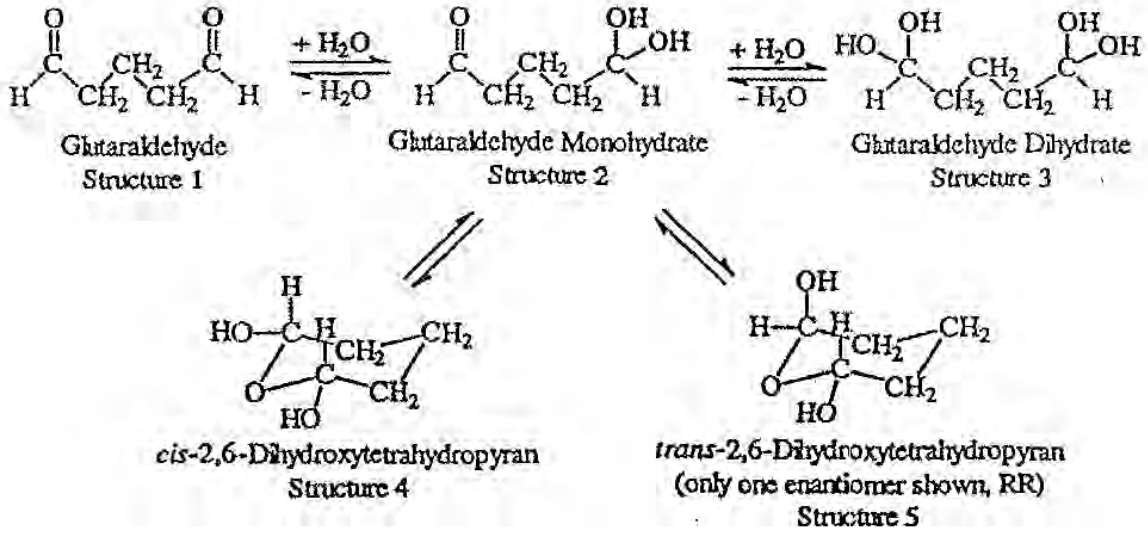
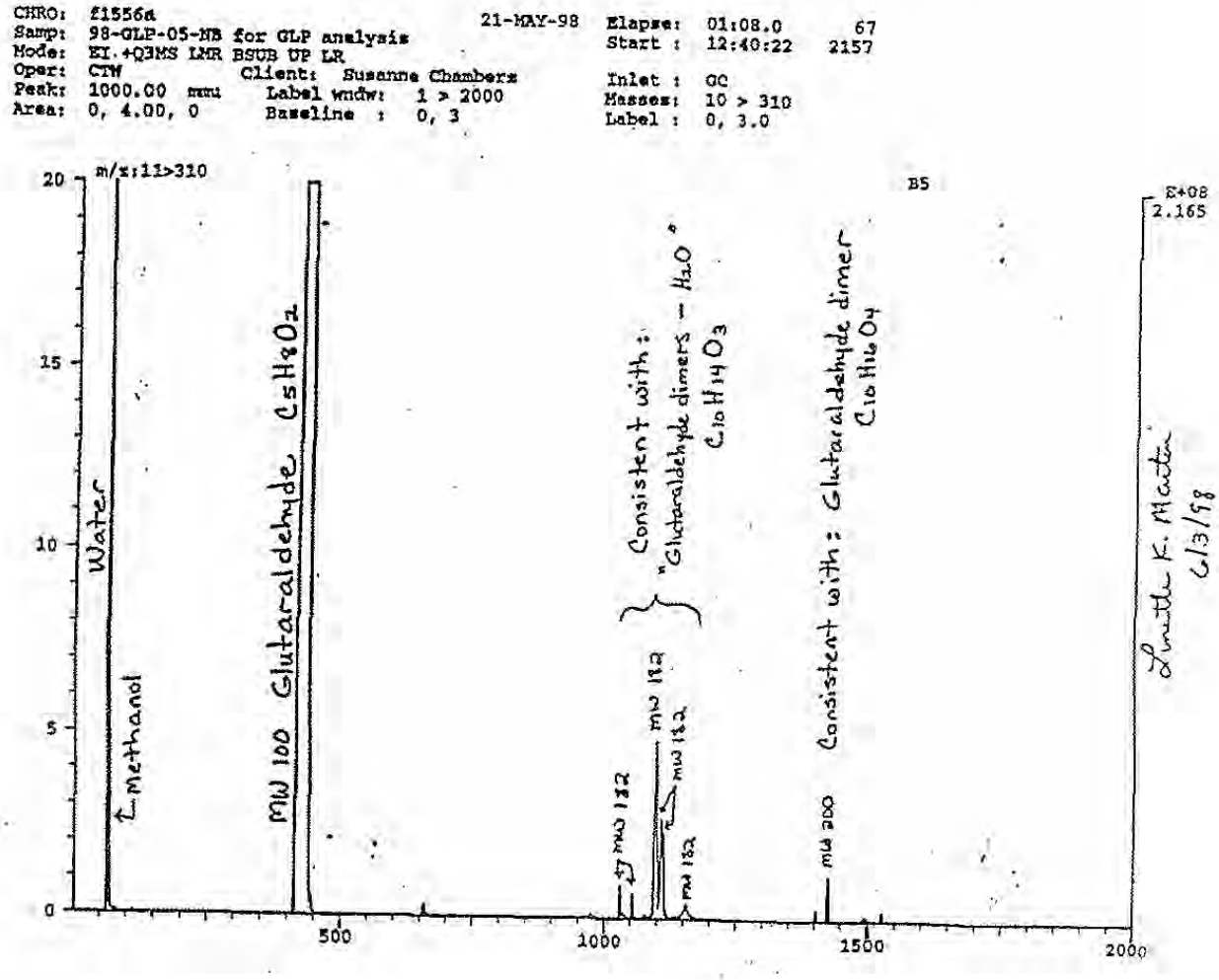


Figure 3.4-6 Capillary GC/MS of [redacted] (Prestudy Sample)



RMS Comments May 2009:

3.2 Vapour pressure, Reported value 44 Pa refer to pure 100% glutaraldehyde (not to 50%) ref: Olson, J.D. (1998) The vapor pressure of pure and aqueous glutaraldehyde.

3.2.1 Henry's Law Constant, Calculation method used is appropriate, but reliability code for the calculated result should not be 1 (no scoring or in this case score 2 is more appropriate).

3.9 Partition coefficient n-octanol/water. The study [redacted]1996) is well done and valid with restrictions. Results clearly and reliable indicate that GA has low potency on bioaccumulation. Calculated values of log kow indicate the same.

The test protocol did not require measuring log Kow values over the pH range 4, 7, 9. Therefore the information requirement is not completely fulfilled. Glutaraldehyde is not dissosiating and therefore the statement "The partition coefficient of glutaraldehyde is not pH dependent" in table A3 can be supported.

Actually the pH values were neglected and not even reported in Shepler study. According to literature, the stability of glutaraldehyde in water is reported to decrease as the pH increases (over pH 5-9) (Jalili et al 1992). The Shepler study reported instability of GA in octanol/water system, but nothing was found from the study report regarding pH values of the test solutions. Stock 50% GA solutions was reported to have pH < 4. Results of standard OECD hydrolysis study could give more information on stability of the substance.

3.12 Flash-point: Justification for not performing test 3.12 on Flash point is not correct and therefore not accepted. Open and closed cup flash points are relevant parameters for flammable substances (pure GA) which can be avaporated from their aquatic solutions to the air (to open or closed space). It can be estimated from Henrys law constant that at equilibrium ca.1800 ppm glutaraldehyde in air mixture (at 50°C) is produced from 50% GA/water. It is not ruled out without testing or other means that flammable GA-air mixture can be formed at higher temperatures.

As a general additional comment, there is in open literature some tested information available on pure glutaraldehyde, which could be reported in the applicant's dossier Reported 50/50% data is not always sufficient/correct input data for modeling. (boiling point 188 °C for pure glutaraldehyde is available, 44 Pa vapour pressure etc. in literature/databases Ref:Experimental database of EpiSuite (USEPA 2008), OVA (2009), Finnish Institute of Occupational Health, OVA-ohje, Glutaraldehydi , Olson, J.D. (1998).

RMS, August 14th 2012:

As agreed at TM III 2012, the absorption spectra (3.4) and Figures 3.4-1 through 3.4-6 have been moved here from the Confidential Annex. It was also agreed to add information on spectra to Doc II A.

Appendix 2, Additional information on Determination of log Pow (End-point 3.9), a staken from the RCOM Table (App1):

Dow Benelux B.V.:

Since Glutaraldehyde does not dissociate (see section 3.6), it's Kow value should not be dependent on pH. Contrary to the RMS comments, the Shepler study did report that "...the pH of the octanol saturated water was between 6 and 7..." on page 24 of the report. The instability of the Glutaraldehyde in the octanol/water test system is not likely due to hydrolytic stability, since reported half-lives for hydrolysis at 25 deg.C reported in the dossier are > 500 days at pH 5, > 100 days at pH 7, and 46 to 64 days at pH 9. These half-lives are much greater than the time-frame for the Kow measurement. The authors of the study suggest that aldehydes can react with excess primary alcohols (octanol in this case) to form acetals and hemicetals under slightly acidic conditions (which is consistent with the reported pH of 6 to 7). This reaction with octanol is the likely source of instability of Glutaraldehyde in the octanol/water test system.

The predicted low log Kow value for Glutaraldehyde, log Kow = -0.18 (KOWWIN, version 1.68), is consistent with the Shepler study attempt to estimate the log Kow value using the HPLC method (OECD 117). In this experiment, the retention time for Gl;utaraldehyde was less than the lowest reference standard in the assay, confirming that the log Kow for Glutaraldehyde was less than 0.

RMS response:

The applicant gives arguments for pH-independency of Kow and on the pH value in Shepler study. It also informs on a suggestion that aldehydes may react with primary alcohol groups of n-octanol. However, it is not shown that (hemi)acetals were formed in the time frame of the test.

All information together support the low dependency of Kow on pH and the conclusion that logKow is below zero.

Section A4.1.3 Analytical Methods for Detection and Identification

Annex Point IIA4.1/4.2 & IIIA-IV.1 **Active Substance Method of Analysis**

Official use only

		1 REFERENCE
1.1	**Reference**	[redacted] (2010), Glutaraldehyde Concentration by Potentiometric Hydroxylamine Hydrochloride Titration, [redacted], Unpublished, 22 June 2010.
1.2	**Data protection**	Yes
1.2.1	Data owner	Dow Benelux B.V.
1.2.2	Company with letter of access	None
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 authorisation]
		2 GUIDELINES AND QUALITY ASSURANCE
2.1	**Guideline study**	No
2.2	**GLP**	No
2.3	**Deviations**	N.A. (not applicable)
		3 MATERIALS AND METHODS
3.1	**Preliminary treatment**	Non-entry field
3.1.1	Enrichment	Titration Procedure Three titration cups for each sample were prepared along with three cups for blanks. To each cup 40 mL of 0.5N hydroxylamine hydrochloride solution, 18 mL of 0.5N triethanolamine solution and a magnetic stir bar were added. For cups containing sample, 0.4 ± 0.1 g of sample were added and weighed to the nearest 0.1 mg. All of the cups were then gently stirred, covered with plastic film and left to stand at room temperature for a minimum of 60 minutes, but not more than 90 minutes for reaction of the reagents. Titration of each cup to a final pH of 3.60 was then carried out using the parameters detailed in Section 3.2.1 (below)
3.1.2	Cleanup	No clean-up required
3.2	**Detection**	Non-entry field
3.2.1	Separation method	Titration is used to determine the concentration of glutaraldehyde present Metrohm Model 719S Titrino, or equivalent Parameters - General Equivalency point Titration (GET) Titration Rate: Slow Pause: 5 seconds EP Criterion: 10 Endpoint A: pH 3.60

Section A4.1.3 **Analytical Methods for Detection and Identification**

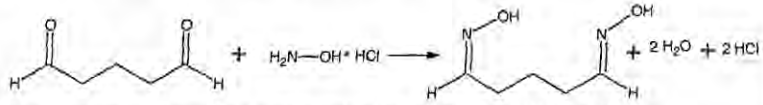
Annex Point IIA4.1/4.2 & IIIA-IV.1 **Active Substance Method of Analysis**

3.2.2	Detector	Potentiometric titration using Metrohm 6.0202.100 (LE) pH electrode
3.2.3	Standard(s)	Titrant = 0.5 N hydrochloric acid Tris(hydroxymethyl)aminomethane (THAM) is used to standardize the 0.5 N HCl N= THAM / HCl x 0.12114 where: N = Normality of the hydrochloric acid THAM = Weight (g) THAM added to the beaker HCl = Volume (mL) of HCl required to reach pH=4.60 0.12114 = Molecular weight correction factor Percent (wt/wt) glutaraldehyde is calculated as follows: GLUT= (B—A) x N x 5.005/ w where: B = Average mL of N normal HCl required for blanks A = mL of N normal HCl required for the sample N = Normality of the HCl W = Mass of the sample in grams 5.005 = Molecular weight correction factor
3.2.4	Interfering substance(s)	Any reactive carbonyl compounds
3.3	**Linearity**	Non-entry field
3.3.1	Calibration range	A single point calibration/standardization was performed.
3.3.2	Number of measurements	3
3.3.3	Linearity	Titrator response was found to be linear over the nominal concentration range of 4.1 to 51% (wt/wt) glutaraldehyde in water (sample weight adjusted to maintain actual glutaraldehyde weight at approximately 0.17 – 0.25 g).
3.4	**Specifity: interfering substances**	Any reactive carbonyl compounds
3.5	**Recovery rates at different levels**	Analysis of four samples at a nominal concentration of 50% (wt/wt) glutaraldehyde and three synthetic mixtures of glutaraldehyde samples containing nominal concentrations of 4, 15 and 25% (wt/wt) glutaraldehyde in water gave the following recoveries – refer to Table A4.1 (1) -1
3.5.1	Relative standard	Refer to Table A4.1 (1) -1

	deviation	
3.6	**Limit of determination**	N.A. (not applicable)
3.7	**Precision**	Non-entry field
3.7.1	Repeatability	Precision data determined from multiple triplicate analyses [n = 10] of a 4% glutaraldehyde formulation and multiple single analyses [n = 15] of the 20% and 50% glutaraldehyde samples are shown in Table A4.1 (1) - 2. The analyses were performed over several days.
3.7.2	Independent laboratory validation	N.A. (not applicable)

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1	**Materials and methods**	Principal: Hydrochloric acid is released as a result of the reaction of hydroxylamine hydrochloride with reactive carbonyl compounds. Glutaraldehyde, having two aldehyde carbonyls, reacts with the hydroxylamine hydrochloride as follows:



The reaction is forced to completion by use of an excess of hydroxylamine hydrochloride. The hydrochloric acid is captured by triethanolamine forming a salt. The excess triethanolamine also acts as a co-solvent for the glutaraldehyde. Back titration with 0.5 N HCl is used to determine the amount of hydrochloric acid released due to the reaction of hydroxylamine hydrochloride with carbonyls in the glutaraldehyde. The method determines all carbonyls as glutaraldehyde.

4.2	**Conclusion**	The method can be considered acceptable for the analysis of glutaraldehyde in aqueous glutaraldehyde formulations
4.2.1	Reliability	1
4.2.2	Deficiencies	Yes, the following deficiency was noted however this is not considered to affect the integrity of the results obtained. The validation study for the method was not GLP compliant

Section A4.1.3 Analytical Methods for Detection and Identification

Annex Point IIA4.1/4.2 & IIIA-IV.1 **Active Substance Method of Analysis**

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	21 September 2011
Materials and methods	Applicant's version is acceptable.
Conclusion	The method can be considered acceptable for the analysis of glutaraldehyde in aqueous glutaraldehyde formulations. As the method detects all carbonyls as glutaraldehyde, it is not specific and hence a confirmatory method of analysis is required.
Reliability	2 (based on non-specificity)
Acceptability	Acceptable
Remarks	The validation study for the method was not GLP compliant.
	COMMENTS FROM ...
Date	21September 2011
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 A4.1(1)-1 Accuracy/Recovery for Glutaraldehyde

Concentration Studied	Average Recovery	Range of Recoveries	Standard Deviation
% (wt/wt)	%	%	%
4.08	99.72	99.11 – 100.10	0.289
15.38	100.02	99.69 - 100.37	0.192
25.74	100.00	99.76 - 100.93	0.355
51.13	100.00	99.29 - 100.90	0.469

Table A4.1(1)-2 Precision for Glutaraldehyde

Sample	n	$t_{(n-1)}$	Average	Standard Deviation s	Estimated Prediction Interval at the 95% Confidence Level for a future result (average of triplicate analyses)
			(%, w,w)	(%, w,w)	(±%, w,w)
4% formulation	10	2.262	4.07	0.012	0.027
[redacted]	15	2.145	20.3	0.13	0.16
[redacted]	15	2.145	50.7	0.17	0..21

Section A4.1.4 Analytical Methods for Detection and Identification

Annex Point IIA4.1/4.2 & IIIA-IV.1 **Determination of Impurity Methanol**

Official use only

1 REFERENCE

1.1	**Reference**	[redacted] (2007), Methanol in Glutaraldehyde, [redacted], Unpublished, 2 October 2007.
1.2	**Data protection**	Yes
1.2.1	Data owner	Dow Benelux B.V.
1.2.2	Company with letter of access	[redacted]
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 authorisation]

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	**Preliminary treatment**	Non-entry field
3.1.1	Enrichment	10.0 ± 0.1 g of sample is mixed with 1.00 ± 0.02 g anhydrous HPLC grade 2-propanol (internal standard).
3.1.2	Cleanup	No clean-up required
3.2	**Detection**	Non-entry field
3.2.1	Separation method	GC-FID was used to determine the concentration of methanol in aqueous glutaraldehyde formulations. Hewlett Packard Model 6890 Gas Chromatograph Column: J&W DB-WAX 30m x 0.32mm x 0.5 µm DF Injection: 1 0 µL, 200:1 Split ratio Injector port temp: 220°C Carrier gas: Helium at 2 ml/min (10 psi constant pressure) Oven Program: 50°C (5 min) - 10°C/min - 230°C (10 min)
3.2.2.	Detector	FID, 230°C Air at 200 mL/min, Hydrogen at 45 mL/min, Makeup (He) at 20 ml/min Range: 0
3.2.3	Standard(s)	10.0 ± 0.5 g anhydrous HPLC grade 2-propanol (internal standard) plus 0.500 ± 0.02 g HPLC grade methanol in 90.0 ± 0.5g g HPLC grade water. Using single point internal standard calibration $Rf_{MeOH} = Area_{IPA}/Area_{MeOH} \times W_{MeOH}/W_{IPA}$

Where:
Rf_{MeOH} = the response factor for methanol
$Area_{IPA}$ = the average peak area of 2-propanol (isopropyl alcohol, IPA) obtained from analysis of the calibration standard
W_{MeOH} = weight (g) of methanol in the calibration stock solution
$Area_{MeOH}$ = the average peak area for methanol, obtained from the analysis of the calibration standard
W_{IPA} = weight (g) of internal standard (isopropyl alcohol) added to the calibration standard

$$C_{MeOH} = Rf_{MeOH} \times Area_{MeOH}/Area_{IPA} \times W_{IPA}/W_{sample} \times 100$$

where:
C_{MeOH} = concentration of methanol in the sample, in % (wt/wt)
Rf_{MeOH} = the response factor for methanol
$Area_{MeOH}$ = the peak area for methanol obtained from analysis of the sample solution
$Area_{IPA}$ = the peak area for isopropanol obtained from analysis of the sample solution
W_{IPA} = weight (g) of internal standard (isopropyl alcohol) added to the sample solution
W_{sample} = weight (g) of sample added to the sample solution

3.2.4	Interfering substance(s)	No direct interferences have been observed in the use of this method.
3.3	**Linearity**	Non-entry field
3.3.1	Calibration range	A single point calibration was preformed
3.3.2	Number of measurements	3
3.3.3	Linearity	Detector response was found to be linear over the range of 0.16 to 2.00% (wt/wt) methanol in solutions of 4 % to 50% glutaraldehyde. Correlation coefficient (r^2) = 0.9957.
3.4	**Specifity: interfering substances**	No direct interferences have been observed in the use of this method.
3.5	**Recovery rates at different levels**	Analysis of 7 solutions of glutaraldehyde aqueous dilutions containing 0.16 to 2.00% (wt/wt) methanol in aqueous glutaraldehyde gave recoveries that averaged 90.02% with a range of 76.29 to 97.92% and a standard deviation of 8.51%. Recoveries were based on the nominal concentration of the analyte in the synthetic mixtures.
3.5.1	Relative standard deviation	±8.5%

Section A4.1.4 **Analytical Methods for Detection and Identification**

Annex Point IIA4.1/4.2 & IIIA-IV.1 **Determination of Impurity Methanol**

3.6	**Limit of determination**	The limit of detection (LOD), defined as three times the baseline noise, was determined to be 0.0014 % (wt/wt) for methanol in 4% glutaraldehyde. The limit of quantitation (LOQ), defined as ten times the baseline noise, was determined to be 0.0046% (wt/wt) for methanol in 4% glutaraldehyde.	
3.7	**Precision**	Non-entry field	
3.7.1	Repeatability	Precision data determined from multiple analyses of two samples of glutaraldehyde are given in Table A4.1(2)-1. The analyses were performed over the data collection period specified in the table - Refer to Table A4.1(2)-1	
3.7.2	Independent laboratory validation	None	
		4 APPLICANT'S SUMMARY AND CONCLUSION	
4.1	**Materials and methods**	A sample of glutaraldehyde is spiked with an internal standard (2-propanol) and injected into a gas chromatograph where the components of interest are separated and detected by aflame ionization detector (FID). Quantitation is by Internal Standard technique based on peak areas. Refer to Figure A4.1(2)-1 for a representative GC chromatogram for the methanol analysis	
4.2	**Conclusion**	The method can be considered acceptable for the analysis of methanol in aqueous glutaraldehyde formulations	
4.2.1	Reliability	1	X
4.2.2	Deficiencies	Yes, the following deficiency was noted however this is not considered to affect the integrity of the results obtained. The validation study for the method was not GLP compliant	

Section A4.1.4 Analytical Methods for Detection and Identification

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

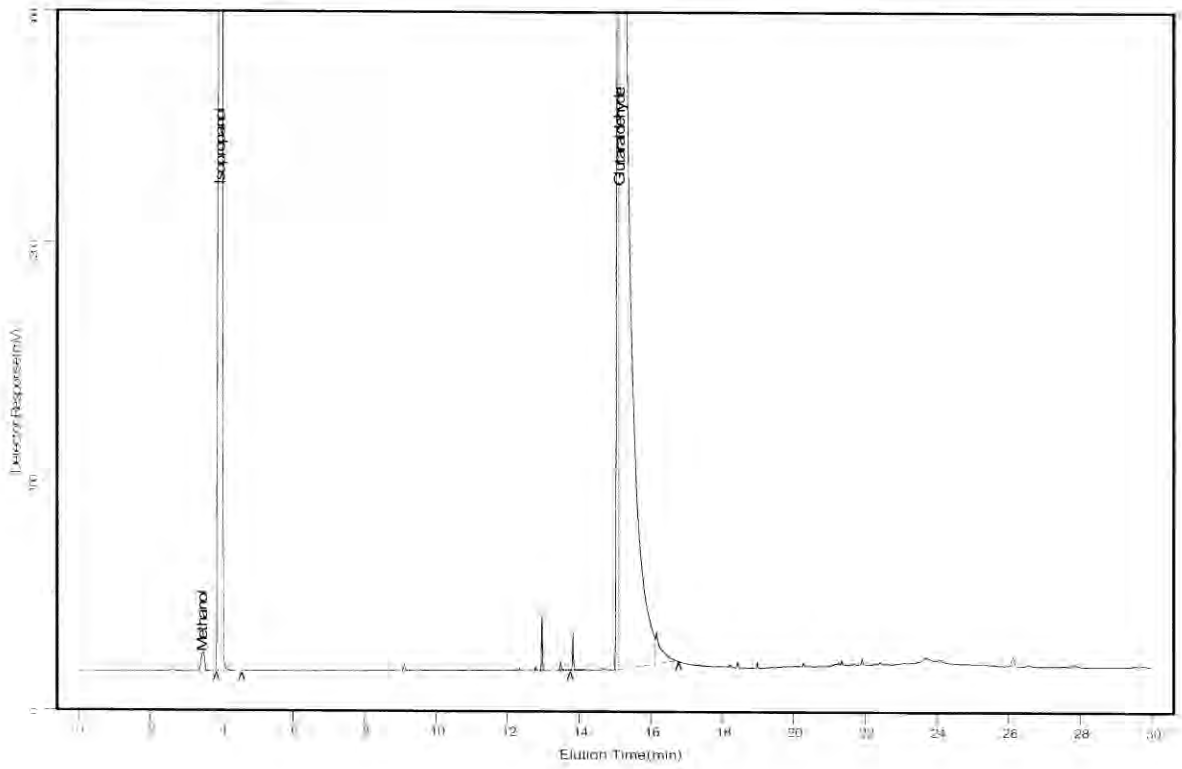
Determination of Impurity Methanol

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	21 September 2011
Materials and methods	Applicant's version is acceptable.
Conclusion	The method can be considered acceptable for the analysis of methanol in aqueous glutaraldehyde formulations. The method is not specific and hence a confirmatory method of analysis is required.
Reliability	2 (based on non-specificity)
Acceptability	Acceptable
Remarks	The validation study for the method was not GLP compliant.
	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 A4.1(2)-1 Precision for Methanol

Sample	Data Collection Period	n	$t_{(n-1)}$	Average x	Standard Deviation SD	Relative Standard Deviation RSD
				% (wt/wt) MeOH	*% (wt/wt)*	*(%)*
1	2 days	10	2.262	0.024	0.001	4.3
2	6 weeks	11	2.093	0.166	0.0046	2.8

Figure A4.1(2)-1 Representative GC Chromatogram for Methanol Analysis in Glutaraldehyde Formulation



Section A4.2(a)
Annex Point IIA4.2
IUCLID5 Section 8

Analytical Methods for Detection and Identification

Method for the determination of Glutaraldehyde in Soil

Official use only

1 REFERENCE

1.1	**Reference**	[redacted] (2008) Glutaraldehyde: Development and Validation of an Analytical Method for the Determination of Glutaraldehyde in Soil, [redacted] (unpublished), 7 July 2008
1.2	**Data protection**	Yes
1.2.1	Data owner	The Dow Chemical Company
1.2.2		
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

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	EC Biocide Directive 98/8/EC Annex IIA, IV. 4.2.(a) and Annex IIB, IV. 4.2.(a) (24/04/98). EC guidance document on residue analytical methods, SANCO/825/00 rev. 7 (17/03/2004).
2.2	**GLP**	Yes
2.3	**Deviations**	None

3 MATERIALS AND METHODS

3.1	**Preliminary treatment**	Non-entry field
3.1.1	Enrichment	<u>Extraction</u> 1. Weigh 20-g of soil into 250-mL screw-capped PE bottle. 2. Fortify specimen with analyte solution, if applicable. 3. Add water to adjust a total extract volume (V_{Ex}) of 100 mL considering the content of water present in the soil. 4. Shake on a horizontal shaker for 30 min (270 rpm). 5. Centrifuge the extract for 2 min (4000 rpm). 6. Decant an aliquot of the raw extract (Vi = 40 mL) and transfer into a 60-mL glass vial with screw cap. 7. Add approx. 0.50 g of potassium hydrogen phthalate for pH adjustment (pH ≈ 4).
3.1.2	Cleanup	Specimen derivatization and extraction procedures should be conducted without stopping. Specimens should be derivatized and extracted in the vessel in which they were collected. Transferring the specimen to another container for derivatization and extraction may cause a loss of analyte. 1. Fortify specimen extract with 50 uL of the internal standard solution (100 µg/mL of $^{13}C_2$-GA). 2. Add 2 mL of freshly prepared 15 mg/mL PFBHA reagent, seal the glass vial with a screw cap and swirl gently to mix. 3. Place the capped vial for 2 hrs in a water bath set at 35°C ± 2°C. 4. After removing the container from the water bath let cool to room

temperature for approx. 40 min.

5. Add 10 drops of concentrated sulphuric acid to the specimen and shake.
6. Add 5 mL of n-hexane, cap the glass vial and shake manually for 1 min.
7. After phase separation, pipette the upper hexane-phase into a 50-mL centrifuge vial containing 5 mL of 0.2 N sulphuric acid.
8. Repeat partition twice with 5 mL portions of n-hexane.
9. Seal the vial with a stop cock, shake manually for 30 sec. and let stand to permit phases to separate.
10. Filter and dry the upper hexane-phase by pipetting the extract over ≈ 10 g anhydrous sodium sulphate held in place with a funnel plugged with silanized glass wool.
11. Collect the dried hexane extract in a pear-shaped 50-mL evaporation flask.
12. Rinse the sodium sulphate with additional ≈ 4 mL of n-hexane.
13. Concentrate the n-hexane extract (at 50°C and 250 mbar) to approx. 1 mL using a rotary evaporator.
14. Evaporate the remaining n-hexane to dryness in a gentle stream of nitrogen.
15. Re-constitute the specimen using 20 mL (VEnd) of methanol / water (1/1 v/v) and sonicate briefly.
16. Analyze final extract by LC/MS/MS.

3.2 Detection

Non-entry field

3.2.1 Separation method

LC-MS/MS was used to quantify the residues. The following RP-HPLC method was used:

HPLC System	Agilent 1100 SL HPLC system (vacuum solvent degasser, binary HPLC pump, column oven), and CTC Analytics HTC-Pal Autosampler.
HPLC Column	YMC J'Sphere C_{18} column (length: 150 mm, i.d.: 3.0 mm, particle size: 4 µm). Column temperature: 20 °C. Pre-column: Phenomenex C_{18} (4 mm, i.d.: 3.0 mm, particle size: 5 µm).
HPLC Injection Volume	30 uL.
HPLC Method	Solvent A: 0.1 % formic acid in water Solvent B: 0.1% formic acid in acetonitrile. Mobile phase composition:

Time (min)	Flow rate (mL/min)	%A	%B
0.0	0.40	50	50
2.0	0.40	50	50
8.0	0.40	0	100
13.0	0.40	0	100
13.1	0.40	50	50
16.0	0.40	50	50

Retention Time	Glutaraldehyde-PFBHA derivative: approx. 11.4 min

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3.2.2 Detector

The following LC/MS/MS method was used for determination of glutaraldehyde:

MS System	Applied Biosystems MDS Sciex API 3000 triple quadrupole LC/MS/MS system with Turbolonspray (ESI) source	
Ion Source Conditions ESI Positive Polarity	Source temperature:	425 °C
	Nebulizer gas:	14 (arbitrary units)
	Curtain gas:	12 (arbitrary units)
	IonSpray voltage:	5500 V
MS/MS Conditions	Declustering potential (DP):	51 V
	Entrance potential (EP):	10V
	Focusing potential (FP):	210 V
	Glutaraldehyde-PFBHA Derivative:	
	Transition 491 m/z > 80 m/z	
	CE:	61V
	CXP:	4.0 V
	CAD:	4
	Transition 491 m/z > 181 m/z (Confirmation)	
	CE:	25 V
	CXP:	16 V
	CAD:	4
	$^{13}C_2$-Glutaraldehyde-PFBHA Derivative:	
	Transition 493 m/z > 181 m/z	
	CE:	25 V
	CXP:	16.0 V
	CAD:	4
	Dwell time per transition:	400 ms

LC/MS/MS employing electron spray ionization in the positive ion mode was used. The following protonated molecular ions [M+H] were monitored:-

Parent Ions: 491 m/z (glutaraldehyde-PFBHA); 493 m/z ($^{13}C_2$-glutaraldehyde)

Daughter Ions: glutaraldehyde derivative (80 m/z and 181 m/z); PFBHA-derivative of the internal standard $^{13}C_2$-glutaraldehyde (181 m/z)

3.2.3 Standard(s)

Internal standards were used. The standards were prepared as follows:-

To prepare the glutaraldehyde-oxime derivative used for LC/MS/MS determination, freshly dosed calibration specimens were processed concurrently with the specimen set.

The following levels of glutaraldehyde (GA) were established by fortifying the aqueous fortification solutions into 40 mL (V_1) of tap water:

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Use solution with [ug/mL] glutaraldehyde	Pipette [mL]	Use solution with [ug/mL] $^{13}C_2$-glutaraldehyde (IS)	Pipette [mL]	Final volume V_{End} [mL]	Obtain [ng/mL] per analyte
1.0	0.080	100	0.050	20	4.0 (GA), 250 (IS)
1.0	0.20	100	0.050	20	10 (GA), 250 (IS)
1.0	0.40	100	0.050	20	20 (GA), 250 (IS)
1.0	1.0	100	0.050	20	50 (GA), 250 (IS)
10	0.25	100	0.050	20	125 (GA), 250 (IS)
10	0.40	100	0.050	20	200 (GA), 250 (IS)
10	1.0	100	0.050	20	500 (GA), 250 (IS)

After fortification of glutaraldehyde (GA) and addition of $^{13}C_2$-glutaraldehyde ($^{13}C_2$-GA) as internal standard at a level of 0.625 mg/kg the calibration specimens were processed according to the analytical procedure used for derivatization of the soil specimens (Refer to point 3.1). The peak areas of the GA versus the internal standard $^{13}C_2$-GA determined in the final extracts were then used to establish the different LC/MS/MS calibration curves.

Refer to Figure A4.2[a]-1 for a typical chromatogram of a calibration standard.

3.2.4	Interfering substance(s)	No substances are expected to interfere.
3.3	**Linearity**	Non-entry field
3.3.1	Calibration range	4.0 to 500 ng/mL of glutaraldehyde (7 levels). The concentration of the internal standard $^{13}C_2$-glutaraldehyde in all calibration solutions was 250 ng/mL.
3.3.2	Number of measurements	Two injections were made of the bottom calibration standard (4.0 ng/ml) and one injection was made of the remaining calibration standards (10, 20, 50, 125, 200 and 500 ng/ml).
3.3.3	Linearity	The correlation coefficients (r) for both MS/MS transitions monitored were > 0.998. Refer to Figure A4.2[a]-5 for a typical calibration line.
3.4	**Specifity: interfering**	No interfering peaks in blank control specimens were detected. Refer to Figure A4.2[a]-4 for a typical chromatogram of a control soil

	substances	sample.
3.5	**Recovery rates at different levels**	Five recovery samples were prepared at each concentration level, 0.05 mg/kg and 0.50 mg/kg (equivalent to the LOQ and 10x LOQ).

Fortification Level	LC/MS/MS Daughter Ion	Glutaraldehyde-PFBHA 491 m/z >	
mg/kg	m/z	80 m/z	181 m/z
Standard Soil 2.2			
0.05	Av.	97%	101%
	RSD	2%	4%
0.50	Av.	89%	84%
	RSD	10%	6%
0.05 and 0.50	Overall Av.	93%	92%
	Overall RSD	8%	11%
RSD: Relative standard deviation			

Refer also to Table A4.2[a]-1.

Refer to Figure A4.2[a]-2 for a Typical Chromatogram of a soil sample fortified at 10xLOQ (0.05 mg/kg).

3.5.1	Relative standard deviation	Refer to point 3.5 (above) and Table A4.2[a]-1
3.6	**Limit of determination**	The limit of determination is 0.05 mg/kg. Refer to Figure A4.2[a]-3 for a Typical Chromatogram of a soil sample fortified at 0.05 mg/kg.
3.7	**Precision**	Non-entry field
3.7.1	Repeatability	The extraction was found to be repeatable, as demonstrated by the relative standard deviation (RSD) values being <10%. Refer to Table A4.1[a]-1.
3.7.2	Independent laboratory validation	Not conducted.

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1	**Materials and methods**	The analytical method to be validated is based on method procedures of EPA Method 556[1] originally developed for the determination of carbonyl compounds (e.g. glutaraldehyde) in water. A related method has recently been developed/reported[2] for water by [redacted] A 20-g soil specimen is extracted with water (V_{Ex} =100 mL) using a mechanical shaker. After centrifugation an aliquot of the raw extract (V_1 = 40 mL) is transferred into a 60-mL glass vial. Then the aqueous extract is fortified with $^{13}C_2$-glutaraldehyde as internal standard. The pH is adjusted with potassium hydrogen phthalate and subsequently the analytes are derivatized with pentafluorobenzylhydroxylamine (PFBHA) at 35 ± 2°C for 2 hrs. After cooling, the reaction mixture is acidified and then partitioned with hexane. The hexane extract is washed with sulphuric acid and evaporated to dryness. The final

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extract is re-constituted in methanol/water (1/1 v/v, VEnd = 20 mL) and subsequently analyzed by LC/MS/MS using two MRM transitions for the glutaraldehyde derivative.

[1] EPA Method 556 Revision 1.0, June 1998: Determination of Carbonyl Compounds in Drinking Water by Pentafluorobenzylhydroxylamine Derivatization and Capillary Gas Chromatography with Electron Capture Detection.

[2] [redacted] 24-Apr-07. Glutaraldehyde: Development and Validation of a Post-Registration Enforcement Method for the Determination of Glutaraldehyde in Surface Water. [redacted]

4.2 Conclusion

An analytical method for the determination of glutaraldehyde in soil was developed, using water extraction, centrifugation, derivatization with pentafluorobenzylhydroxyl amine (PFBHA), and LC/MS/MS determination.

The method was successfully validated for a European standard soil, and thus demonstrated to be applicable for enforcement and monitoring purposes.

The use of LC/MS/MS is considered specific so that no additional confirmatory method is required.

4.2.1 Reliability: 1

4.2.2 Deficiencies: No

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	14 August 2008
Materials and methods	Applicant's version is acceptable.
Conclusion	An analytical method for the determination of glutaraldehyde in soil was developed, using water extraction, centrifugation, derivatization with pentafluorobenzylhydroxyl amine (PFBHA), and LC/MS/MS determination. The method was successfully validated for a European standard soil, and thus demonstrated to be applicable for enforcement and monitoring purposes. The use of LC/MS/MS is considered specific so that no additional confirmatory method is required.
Reliability	1
Acceptability	Acceptable
Remarks	

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	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 A4.2[a]-1 Summary of Recovery Data

Selected extracts (specimen IDs P1236-39, 44, and -47) were injected twice to demonstrate repeatability of LC/MS/MS determination.

Residue R = C_{Ind} x [(V_{Ex} x V_{Fnd}) /(V_I x W)] / 1000 ng/µg = C_{Ind} x M.								
W	V_{Ex}	V_I	V_{End}	Multiplier M				
g	mL	mL	mL	mL/g x µg/ng				
20	100	40	20	0.00250				
Specimen		LC/MS Run	Glutaraldehyde PFBHA Derivative					
ID	R_{Ind}		491 m/z -> 80 m/z		Rec.	491 m/z -> 181 m/z		Rec.
P1236	mg/kg	P1236API#	ng/mL	mg/kg		ng/mL	mg/kg	
Blank Controls								
37	--	142	nd	<20 % of LOQ		nd	<20 % of LOQ	
38	--	143	nd			nd		
LOQ Fortifications								
39	0.050	134	19.9	Mean of 2 inj.		21.1	Mean of 2 inj.	
		135	19.2	0.0489	98%	20.6	0.0521	104%
40	0.050	136	19.3	0.0483	97%	20.6	0.0515	103%
41	0.050	137	19.7	0.0493	99%	20.8	0.0520	104%
42	0.050	138	19.8	0.0495	99%	18.8	0.0470	94%
43	0.050	139	18.8	0.0470	94%	19.9	0.0498	100%
Average (n =5)					97%			101%
RSD (n = 5)					2%			4%
10xLOQ Fortifications								
44	0.50	126	161	Mean of 2 inj.		158	Mean of 2 inj.	
		145	167	0.410	82%	158	0.395	79%
45	0.50	127	176	0.440	88%	165	0.413	83%
46	0.50	128	171	0.428	86%	163	0.408	82%
47	0.50	153	210	Mean of 2 inj.		184	Mean of 2 inj.	
		154	209	0.524	105%	185	0.461	92%
48	0.50	130	173	0.433	87%	167	0.418	84%
Average (n =5)					89%			84%
RSD (n = 5)					10%			6%
Overall Average (n =10)					93%			92%
Overall RSD (n = 10)					8%			11%

nd: Not detected: <4 ng/ml , equivalent to <0.01 mg/kg n: Number of results included in calculation

RSD: Relative standard deviation, Rec.: Recovery.

Figure A4.2[a]-1 Typical LC/MS/MS Chromatogram: Calibration Standard Corresponding to 200 ng/ml Glutaraldehyde

Top: Glutaraldehyde-PFBHA (491 m/z -> 80 m/z)
Middle: Glutaraldehyde-PFBHA (491 m/z -> 181 m/z)
Bottom: $^{13}C_2$-Glutaraldehyde-PFBHA (493 m/z -> 181 m/z, internal standard)

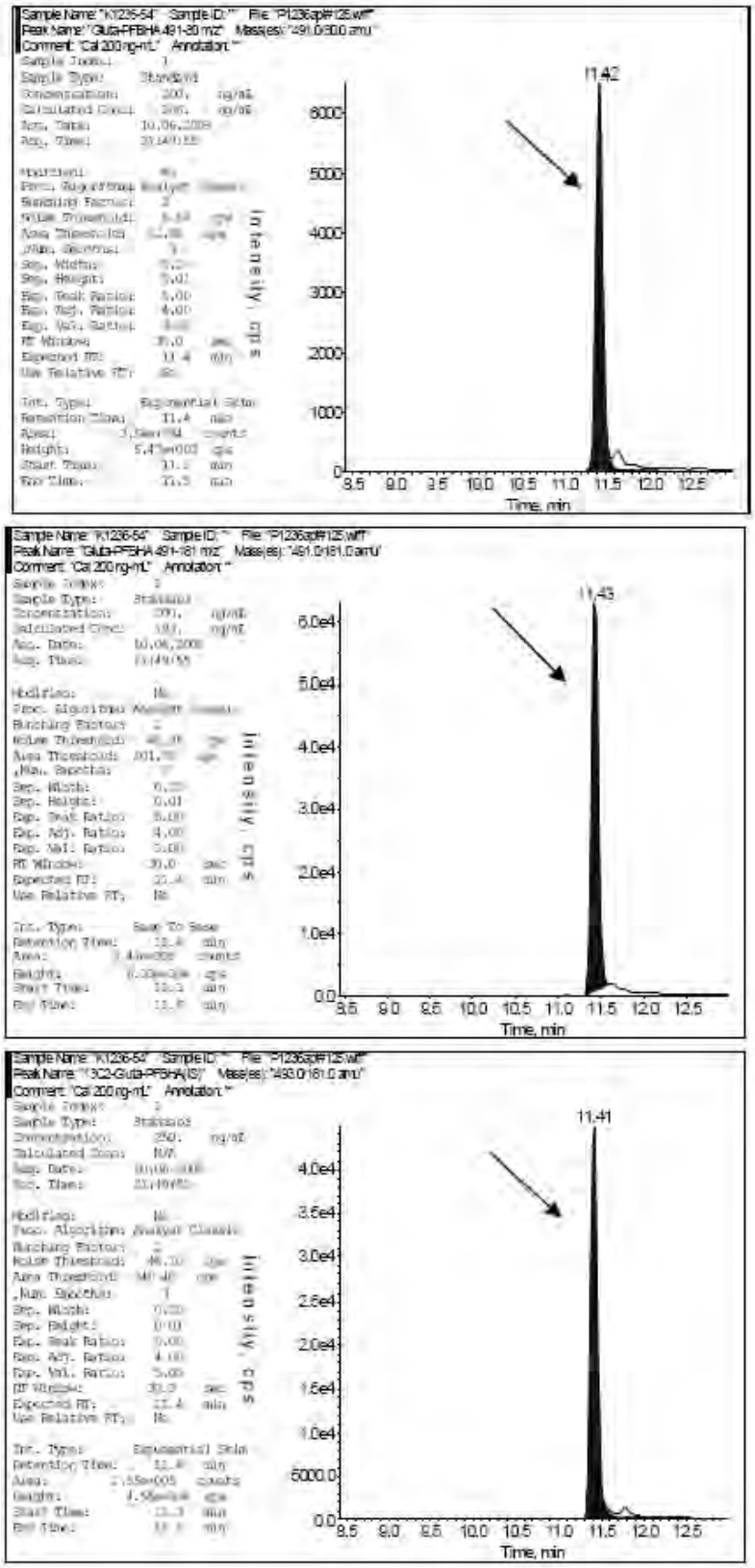


Figure A4.2[a]-2 Typical LC/MS/MS Chromatogram: Loamy Sand 2.2 Fortified at 0.50 mg/kg (10xLOQ)

Top: Glutaraldehyde-PFBHA (491 m/z -> 80 m/z) R: 0.433 mg/kg Recovery: 87 %
Middle: Glutaraldehyde-PFBHA (491 m/z -> 181 m/z) R: 0.418 mg/kg Recovery: 84 %
Bottom: $^{13}C_2$-Glutaraldehyde-PFBHA (493 m/z -> 181 m/z, internal standard)

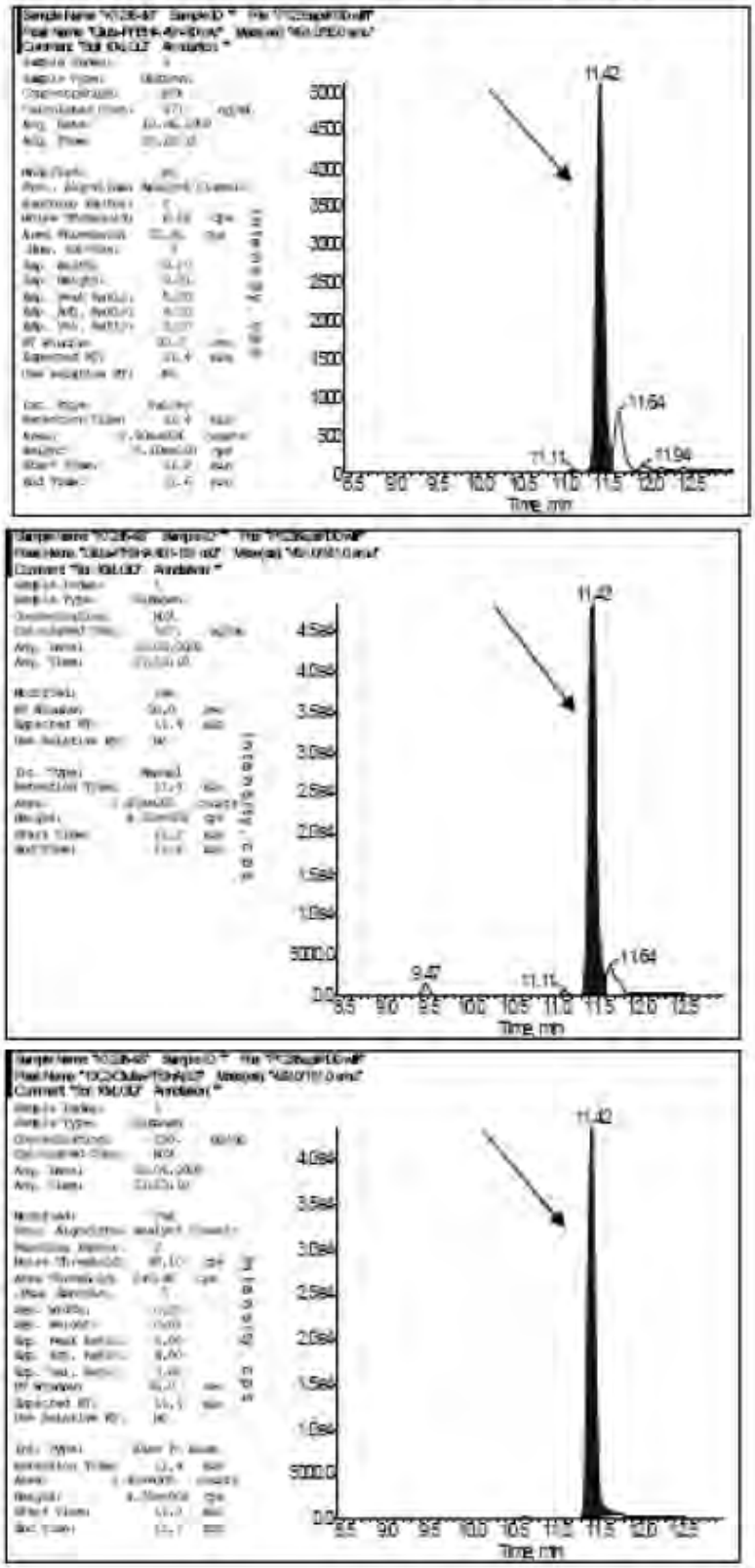
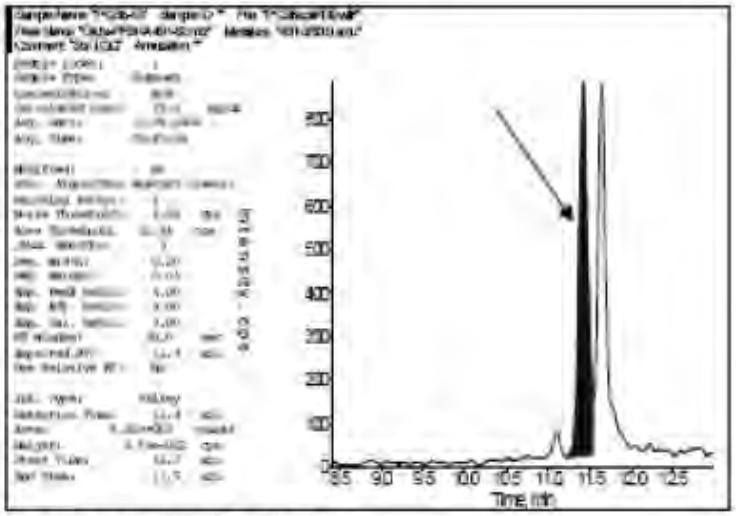
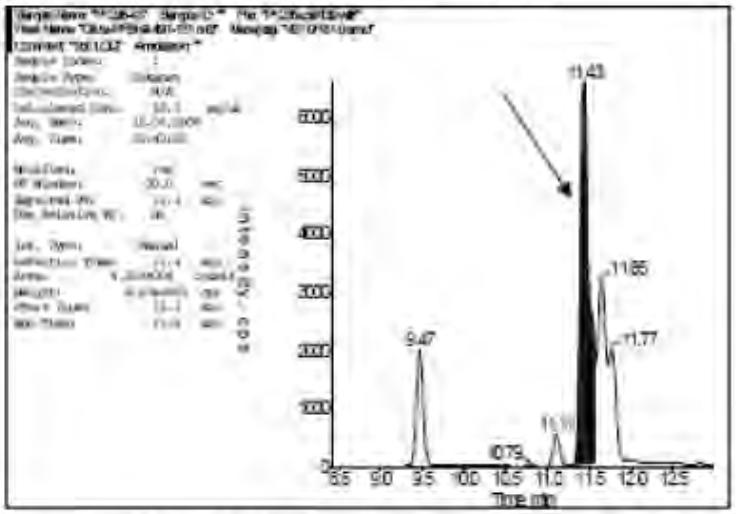


Figure A4.2[a]-3 Typical LC/MS/MS Chromatogram: Loamy Sand 2.2 Fortified at 0.05 mg/kg (LOQ)

Top: Glutaraldehyde-PFBHA (491 m/z -> 80 m/z) R: 0.0470 mg/kg Recovery: 94 %
Middle: Glutaraldehyde-PFBHA (491 m/z -> 181 m/z) R: 0.0498 mg/kg Recovery: 100 %
Bottom: $^{13}C_2$-Glutaraldehyde-PFBHA (493 m/z -> 181 m/z, internal standard)





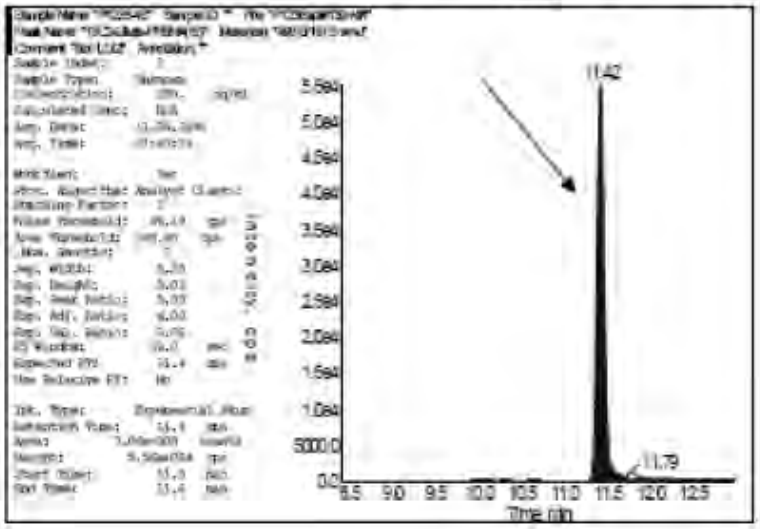


Figure A4.2[a]-4 Typical LC/MS/MS Chromatogram: Loamy Sand 2.2 Blank Control Specimen

Top: Glutaraldehyde-PFBHA (491 m/z -> 80 m/z) R: <0.01 mg/kg
Middle: Glutaraldehyde-PFBHA (491 m/z -> 181 m/z) R: <0.01 mg/kg
Bottom: $^{13}C_2$-Glutaraldehyde-PFBHA (493 m/z -> 181 m/z, internal standard)

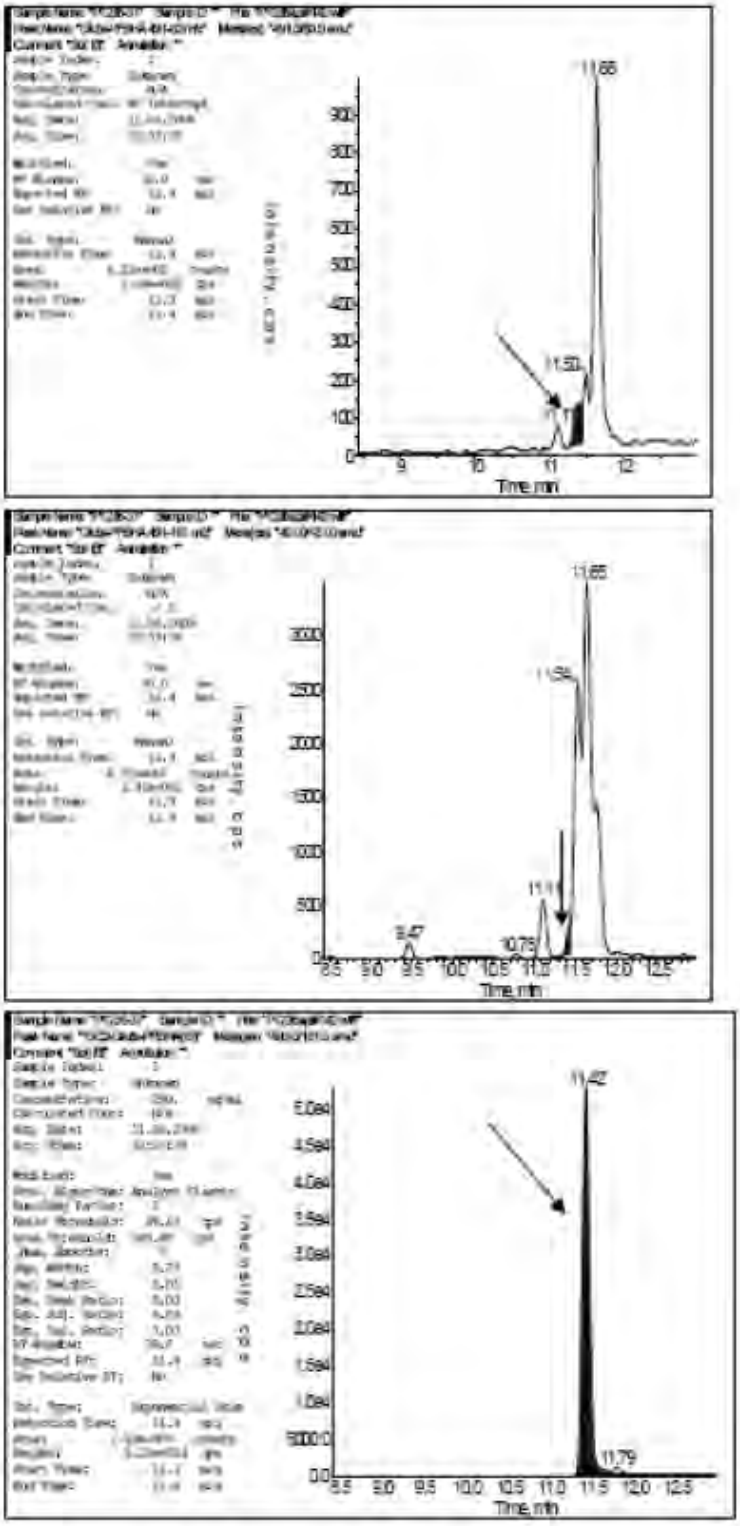
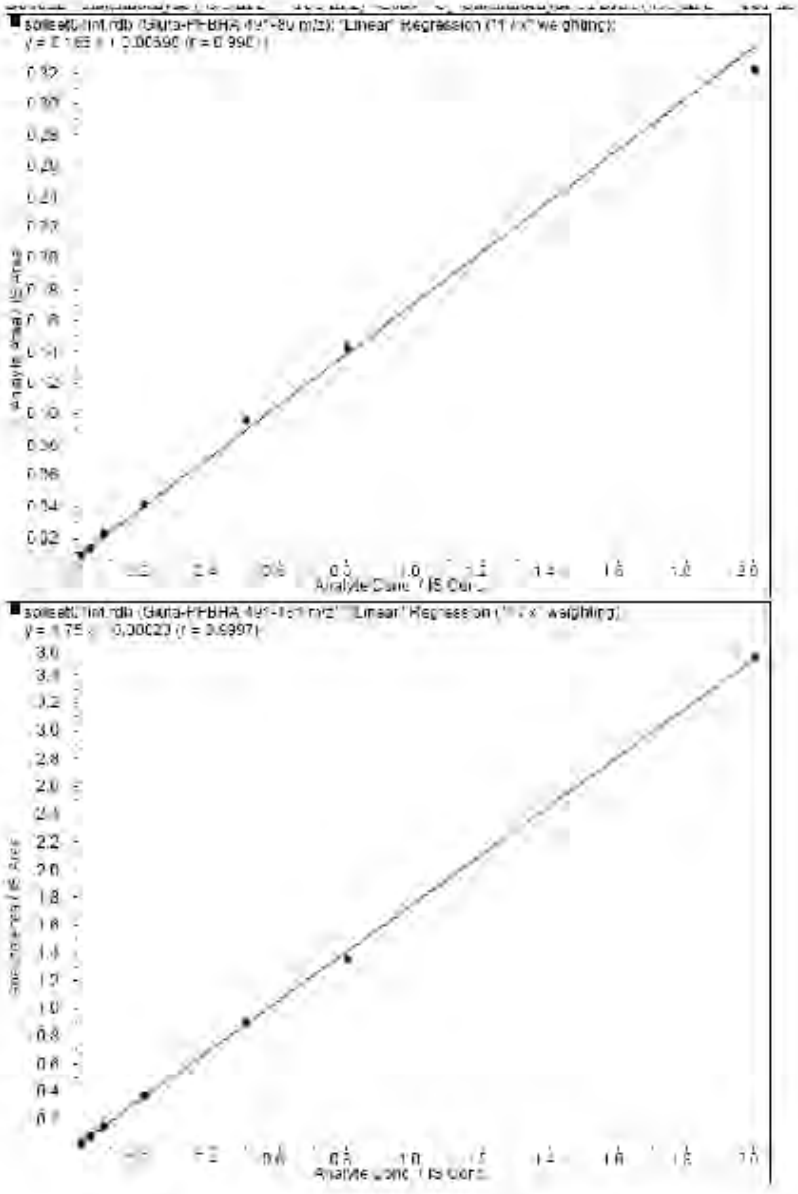


Figure A4.2[a]-5Typical LC/MS/MS Internal Standard Calibration Functions for Glutaraldehyde

Top: Glutaraldehyde (491 m/z -> 80 m/z) versus $^{13}C_2$-Glutaraldehyde-PFBHA (493 m/z -> 181 m/z)
Bottom: Glutaraldehyde (491 m/z -> 181 m/z) versus $^{13}C_2$-Glutaraldehyde-PFBHA (493 m/z -> 181 m/z)



File	Conc.	Solution	Glutaraldehyde-PFBHA		$^{13}C_2$-IS
Name	ng/mL	ID	491 > 80 m/z	491 > 181 m/z	493 > 181 m/z
P1236API#141.wiff	4.0	K1236-49	3.06E+03	1.16E+04	3.26E+05
P1236API#144.wiff	4.0	K1236-49	2.98E+03	1.20E+04	3.30E+05
P1236API#140.wiff	10	K1236-50	4.43E+03	2.40E+04	3.33E+05
P1238API#133.wiff	20	K1238-51	8.34E+03	4.28E+04	2.78E+05
P1238API#132.wiff	50	K1238-52	1.14E+04	1.00E+05	2.71E+05
P1238API#131.wiff	125	K1238-53	2.26E+04	2.13E+05	2.37E+05
P1238API#125.wiff	200	K1238-54	3.84E+04	3.47E+05	2.55E+05
P1238API#124.wiff	500	K1238-55	4.10E+04	5.04E+05	1.43E+05

Section IIIA4.2(c) **Annex Point IIA- IV.4.2**	**Analytical methods including recovery rates and the limits of determination for the active substance, and for residues thereof, and where relevant in/on the following: (c) Water and Natural Sediment**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [ ]** **Other justification [X]**	
Detailed justification:	Natural Sediment The method presented in TNG Summary IIIA4.2(a)(1) ([redacted] (2008)) for detection and quantification of Glutaraldehyde in soil could be adapted for sediment. Sediment is essentially formed from the finer particles of soil (<0.05 mm) and has the same range of textures (*e.g.* sandy, clay, silty) as soil. The organic matter content in sediment can also vary to a similar extent as soil. For the purposes of developing an analytical method, sediment can be considered to be a saturated soil containing very fine particle sizes. The extraction method used for soil would be acceptable for sediment. As sediment is not considered to be a compartment of concern it has not been considered necessary to develop a specific method for this matrix.	
Undertaking of intended data submission [X]	A study entitled 'Glutaraldehyde: Development and Validation of an Analytical Method for the Determination of Glutaraldehyde in Water', [redacted] will be completed in August 2007.	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	14 August 2008	
Evaluation of applicant's justification	Applicant's justification is correct.	
Conclusion	Applicant's 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		

Section A4.2(d) **Annex Point IIA, IIA-IV.4.2** **IUCLID 6.2/04**	**Analytical Methods for Detection and Identification** **Method for the determination of Glutaraldehyde in animal blood**	
	1 REFERENCE (REF. O6, A4.2/02)	**Official use only**
1.1 Reference	[redacted] 2004), Glutaraldehyde: Pharmacokinetics in [redacted] Rats Following Oral Gavage or Dermal Application, [redacted] Unpublished, 16 June 2004	
1.2 Data protection	Yes	
1.2.1 Data owner	The Dow Chemical Company[redacted]	
1.2.2 Companies with letter of access	[redacted]	
1.2.3 Criteria for data protection	Data on an existing active substance for first entry to Annex I	
	2 GUIDELINES AND QUALITY ASSURANCE	
2.1 Guideline study	Yes	
2.2 GLP	Yes	
2.3 Deviations	No	
	3 MATERIALS AND METHODS	
3.1 Preliminary treatment		
3.1.1 Enrichment	Aliquots (0.5 mL) of acidified water (0.5M HCl), containing 200 ng of $^{13}C_2$-glutaraldehyde internal standard were added to tared, glass vials and net weights of the aqueous layers determined. Aliquots (~ 0.2 mL) of sample blood were added to each vial, the vials briefly vortexed and then reweighed to obtain net sample weights. The glutaraldehye analyte and corresponding $^{13}C_2$-internal standard were converted to oxime derivatives by the addition of 0.5 mL pentafluorobenzylhydroxylamine (30 min at ambient temperature, followed by brief vortexing). Derivatized analyte was extracted into 0.5 mL toluene via 2-min vortexing. The toluene layer was separated by centrifugation (10 min x 2350g) and transferred to a clean Econovial glass GC vial. The toluene solvent was removed via evaporation (Savant SpeedVac) and the residue reconstituted in 0.040 mL toluene for GC/MS analysis.	
3.1.2 Cleanup	None	
3.2 Detection		
3.2.1 Separation method	The samples are chromatographed by gas chromatography using a J&W DB-5 fused silica capillary column: 30 m length, 0.25 mm inner diameter, 0.5 µm film thickness. GC temperature program: 150 °C (1 min hold), ramp to 300	

Section A4.2(d) Annex Point IIA, IIA-IV.4.2 IUCLID 6.2/04	Analytical Methods for Detection and Identification Method for the determination of Glutaraldehyde in animal blood	
	°C (10 °C/min). Injector and transfer line temperatures were 280 °C and 300 °C, respectively.	
3.2.2 Detector	Detection of glutaraldehyde residue derivative is performed by negative-ion chemical ionization mass spectrometry (NCI-GC/MS) monitoring the M-$(HF)_2^-$ fragment ions of m/z 450 for glutaraldehye and m/z 453 for the stable isotope labeled internal standard.	
3.2.3 Standard(s)	Quantitation of glutaraldehyde residues is performed using an internal standard technique employing a stable isotope labelled standard of glutaraldehyde. Quantitative standards were made in acidified water and derivatized as above.	
3.2.4 Interfering substance(s)	None observed	
3.3 Linearity		
3.3.1 Calibration range	20-26,500 ng glutaraldehyde per gram blood.	
3.3.2 Number of measurements	8 standard levels injected. Total number of injections = 28	
3.3.3 Linearity	Two calibration curves were used (0-15 ng and 15-250 ng/standard). The calibration curves yielded correlation coefficients (r^2) of 0.9999.	
3.4 Specifity: interfering substances	NCI-GC/MS affords a highly specific method for both quantitation and confirmation of residue identity by retention time matching in conjunction with monitoring the specific NCI-MS fragment ions of glutaraldehyde and the corresponding $^{13}C_2$-internal standard.	
3.5 Recovery rates & Standard deviations at different levels		

Approx. Conc. ng Glutaraldehyde/ g blood	No. of fortifications	Average Recovery (%)	Relative Standard Deviation
20	6	118	14.3
50	12	105	13.0
265	3	102	1.75
504	9	100	1.63
2650	3	101	0.309
26500	3	97.5	1.41

Mean Average recovery (%) = 104%

Mean RSD = 5.4%

3.5.1 Relative standard deviation	See Section 3.5	
3.6 Limit of	The limit of quantitation (LOQ) for the determination of glutaraldehyde in rat blood were set equal to the lowest	

Section A4.2(d) **Annex Point IIA, IIA-IV.4.2** **IUCLID 6.2/04**	**Analytical Methods for Detection and Identification** **Method for the determination of Glutaraldehyde in animal blood**	
determination	fortified "spike" prepared (20 ng/g blood) The chromatographic signal/noise (SN) for the analyte was approximately 30:1. No detectable peak was observed at a SN of 3:1 in the control blood matrix.	
3.7 Precision	See Section 3.5	
3.7.1 Repeatability	No specific repeatability data was generated.	
3.7.2 Independent laboratory validation	No independent validation was conducted.	
	4 APPLICANT'S SUMMARY AND CONCLUSION	
4.1 Materials and methods	The method described in "Glutaraldehyde: Pharmacokinetics in [redacted] Rats Following Oral Gavage or Dermal Application, [redacted] 2004" is valid for determination of glutaraldehyde in rat blood samples over the range of 20-26,500 ng/g. Aliquots (~ 0.2 mL) of sample blood were added to aliquots of acidified water containing $^{13}C_2$-internal standard and both compounds converted to oxime derivatives of pentafluorobenzylhydroxylamine. Derivatized analyte was extracted into toluene, concentrated approximately 10-fold prior to NCI-GC/MS analysis. NCI-GC/MS affords a highly specific method for both quantitation and confirmation of residue identity by retention time matching in conjunction with monitoring the specific NCI-MS fragment ions of glutaraldehyde and the corresponding $^{13}C_2$-internal standard. The method response was quite linear, with calibration curves (low and high) yielding correlation coefficients (r^2) of 0.999. Recovery of glutaraldehyde from fortified blood matrix ranged from 97.5-118% over the concentration range of 20-26,500 ng/g blood.	
4.2 Conclusion	The data summarized in Section 3.5 demonstrates the suitability of method for the analysis of glutaraldehyde in rat blood.	
4.2.1 Reliability	1	
4.2.2 Deficiencies	This method is validated for the analysis of glutaraldehyde in blood matrix only. No further validation work is planned for other biological matrices.	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	8 May 2008	

Section A4.2(d) Annex Point IIA, IIA-IV.4.2 IUCLID 6.2/04	**Analytical Methods for Detection and Identification** **Method for the determination of Glutaraldehyde in animal blood**	
Materials and methods	The applicant's version is acceptable.	
Conclusion	The submitted data demonstrates the suitability of method for the analysis of glutaraldehyde in rat blood.	
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		

Section A5 Effectiveness against target organisms and intended uses

Subsection (Annex Point)			Official use only
5.1	Function (IIA5.1)	Main Group 1 - Disinfectants and general biocidal products PT2 Private area and public health area disinfectants and other biocidal products: bactericide; fungicide; virucide PT3 Veterinary hygiene biocidal products: bactericide; fungicide; virucide PT4 Food and feed area disinfectants: bactericide; fungicide; virucide Main Group 2 - Preservatives PT6 In-can preservatives, drilling muds/fluids and cementing chemicals/fluids preservatives: bactericide; fungicide; virucide	x
5.2	Organism(s) to be controlled and products, organisms or objects to be protected (IIA5.2)		
5.2.1	Organism(s) to be controlled (IIA5.2)	Glutaraldehyde is potentially effective against a wide variety of micro-organisms including gram positive and negative bacteria, sulphate reducing bacteria, fungi, yeast and viruses. Examples of typical microbes to be controlled: • Gram negative bacteria: [redacted] • Gram positive bacteria: [redacted] • Fungi: [redacted] • Yeasts: [redacted] • Viruses: [redacted] These species are common in the whole area of the European Union. The species tested in the Rate of Kill (ROK) tests and Minimum Cidal Concentration (MCC) tests are present in most surface waters.	x x

Section A5 Effectiveness against target organisms and intended uses

5.2.2	**Products, organisms or objects to be protected (IIA5.2)**	[redacted] (50% glutaraldehyde) PT2: human health protection PT3: animal health protection PT4: human and animal health protection PT6: prevention of microbial spoilage in canned products	
5.3	**Effects on target organisms, and likely concentration at which the active substance will be used (IIA5.3)**		
5.3.1	**Effects on target organisms (IIA5.3)**	Glutaraldehyde kills the micro-organisms. The microbes are killed faster at higher concentrations, higher temperatures and higher pH. The Minimum Cidal Concentration (MCC) is [redacted] for bacteria with 24 h reaction time. The MCC for fungi is [redacted] with 48 h reaction time. The MCC for yeast is [redacted] with reaction time of 24 h.	
5.3.2	**Likely concentrations at which the A.S. will be used (IIA5.3)**		
	PT2	[redacted] **Note: Active substance (a.s.) refers to 100% glutaraldehyde**	x
	PT3	[redacted] **Note: Active substance (a.s.) refers to 100% glutaraldehyde**	x
	PT4	[redacted] **Note: Active substance (a.s.) refers to 100% glutaraldehyde**	x
	PT6	In-can preservative for detergents (e.g. laundry softeners, liquid detergent, wax emulsion, car polish): [redacted] Preservation of Paper Wet-End Additives and Paper Coatings: [redacted] Preservative for drilling muds/fluids, for cementing chemicals/fluids: [redacted] **Note: Active substance (a.s.) refers to 100% glutaraldehyde**	x
5.4	**Mode of action (including time delay) (IIA5.4)**		
5.4.1	**Mode of action**	Glutaraldehyde kills the micro-organisms by reacting with the free amino groups of some proteins that are located in the cell walls and membranes of the micro-organisms. The reaction is known as cross-linking. Cross-linked microbial cells cannot transport nutrients or	x

perform any critical metabolic functions. Glutaraldehyde also deactivates various membrane-bound enzymes. The kinetics of the cross-linking mechanism are influenced by the pH, the contact time, the glutaraldehyde concentration and the temperature.
In viruses, the main targets for glutaraldehyde are nucleic acid, proteins and envelope constituents. The established reactivity of glutaraldehyde with proteins suggests that the viral capsid or viral-specific enzymes are vulnerable to glutaraldehyde treatment.

5.4.2 Time delay

No time delay. The killing rate is faster at alkaline conditions, high temperatures and at higher glutaraldehyde concentrations. Under acidic conditions the free amino groups react more with H^+ ions (eq.1) and are less susceptible to react with Glutaraldehyde (eq.2):

pH< 6: $R\text{-}NH_2 + H^+ \Rightarrow RNH_3^+$ eq.1

pH >7: $R\text{-}NH_2 + GA \Rightarrow$ cross-linking eq.2

5.5 Field of use envisaged (IIA5.5)

MG01: Disinfectants, general biocidal products

PT2 Private area and public health area disinfectants and other biocidal products

- Hard surface disinfection in hospitals and industrial areas.

PT3 Veterinary hygiene biocidal products

- Disinfection of animal housing (poultry and pig farms).

PT4 Food and feed area disinfectants

- Food vessels/machinery disinfection.
- Food processing (e.g. slaughter house) surface disinfection.

MG02: Preservatives

PT6 In-can preservatives

- Preservatives for detergents (e.g. laundry softeners, liquid detergents, wax emulsions, car polishes).
- Other in-can preservatives (paper wet-end additives preservation, paper coatings preservation).
- Other in-can preservatives (preservatives for drilling muds/fluids).
- Other in-can preservatives (preservatives for cementing chemicals/fluids).

MG03: Pest control

Not supported

MG04: Other biocidal products

Not supported

Further specification

The product is a liquid formulation. It will be sold as a concentrate (SL). The concentrate is 50% water.

5.6 User (IIA5.6)

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	Industrial	[redacted] is sold to formulators for incorporation into products which may be for use by professionals or by the general public. These products will usually contain less than 50% glutaraldehyde. The use of [redacted] for formulation is not covered under this dossier.	
	Professional	[redacted] is used by professionals in PT3 and PT4. Other professional uses include PT2 and PT6.	
	General public	[redacted] is not sold to the general public. Products classified as PT6 (i.e. fabric conditioners, *etc.*) containing up to 0.5% glutaraldehyde are sold to the general public.	
5.7	**Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies (IIA5.7)**	.	
5.7.1	**Development of resistance**	It is a general practice in industry not to continuously use the same biocidal active substance to avoid the proliferation of tolerant or resistant strains. This, according to an expert review, is not a significant problem in industrial uses of glutaraldehyde, and is substantiated by several years of experience with the use of glutaraldehyde in water cooling systems at a Union Carbide plant. The following is a summary of Professor Russell's review:	x
		„On the basis of the mechanism of its lethal activity described above under Section 5.4.1 Mode of Action, it would not be expected that bacteria would develop resistance to the dialdehyde or that it would select resistant sub-populations of bacteria. Intrinsic insusceptibility to biocides is associated with cell wall or outer membrane, with efflux systems in MDR Gram-negative bacteria and possibly with biocide inactivation.	x
		A particular example is demonstrated by the physiological (phenotypic) adaptation to intrinsic resistance with bacteria and other micro-organisms found in biofilms. Acquired resistance to biocides may result from mutation, although the resistance may be stable or unstable, or from plasmid-mediated changes in outer membrane composition or plasmid-associated efflux systems.	
		Although resistance of non-sporulating bacteria to glutaraldehyde has been demonstrated, this generally is of a low level (with the notable exception of some glutaraldehyde-resistant strains of *M.chelonae*). Bacteria within a biofilm are less susceptible to the dialdehyde but there is no evidence that resistance has developed. There is also no evidence that glutaraldehyde selects for antibiotic-resistant bacteria. Experience over many years indicates that development of bacterial resistance to glutaraldehyde is not a significant problem in industrial usage" (Russell A.D. 2001).	
		The issue of resistance development to Glutaraldehyde, by the type of organisms one may encounter in applications that intend to use it, is not relevant. While it is likely that all microbiocides face potential	

resistance development, the only instances where such reports exist for resistant bacteria stem from applications where Glutaraldehyde is used for cleaning medical equipment (PT 02). In these cases improper uses of the disinfectant on dirty endoscopes (Duarte et al. 2009), use of non-sterile water to rinse disinfected equipment (Griffiths et al 1997) have been implicated.

Griffiths, P. A., J. R. Babb, et al. (1997). "Glutaraldehyde-resistant Mycobacterium chelonae from endoscope washer disinfectors." Journal of Applied Microbiology **82**(4): 519-526.

Glutaraldehyde is used to disinfect flexible and other heat-sensitive endoscopes often with the aid of automated systems. Mycobacterium chelonae is being isolated with increasing frequency from these washer disinfectors and processed endoscopes. This has, on occasions, led to misdiagnosis and iatrogenic infections. Recent reports suggest that disinfecting machines, on a sessional or regular basis, with 2% glutaraldehyde may have selected and therefore encouraged the growth of strains of Myco. chelonae, possibly in biofilm, with decreasing susceptibility to glutaraldehyde. In view of this, the resistance of three strains of Myco. chelonae var. chelonae (the type strain NCTC 916 and two machine isolates) was tested against 2% glutaraldehyde and a wide range of alternative disinfectants. Disinfectants tested were a chlorine releasing agent, sodium dichloroisocyanurate at 1000 ppm and 10 000 ppm av Cl, 0.35% peracetic acid (NuCidex, Johnson & Johnson), 70% industrial methylated spirit (IMS), 1% peroxygen compound ('Virkon', Antec International) and 10% succine dialdehyde ('Gigasept', Sanofi Winthrop). Suspension and carrier tests were carried out in the presence and absence of an organic load. Results showed the type strain, which had not been exposed to the selective pressure of disinfectant usage, to be very sensitive to most disinfectants with the exception of 1% Virkon. The washer disinfector isolates, on the other hand, were extremely resistant to 2% glutaraldehyde and showed greater resistance to 1% Virkon and 1000 ppm NaDCC. Purchasing machines in which the entire fluid pathways, including those for delivering rinse water, are disinfected With an appropriate agent during each cycle are preferred. If this is not possible then sessional cleaning and disinfection at the start of each day and regular maintenance should prevent biofilm formation and contamination with disinfectant-resistant strains of mycobacteria. In addition to machine disinfection, the use of sterile or bacteria-free (filtered <0.45 mu m) water is essential for bronchoscopes and all invasive endoscopes. If there is doubt over the effectiveness of the machine disinfection procedure or eater quality, the channels and surfaces of endoscopes may be rinsed with 70% IMS after automated processing. x

Duarte, R. S., M. C. S. Lourenco, et al. (2009). "Epidemic of Postsurgical Infections Caused by Mycobacterium massiliense." Journal of Clinical Microbiology **47**(7): 2149-2155.

An epidemic of infections after video-assisted surgery (1,051 possible cases) caused by rapidly growing mycobacteria (RGM) and involving 63 hospitals in the state of Rio de Janeiro,

Brazil, occurred between August 2006 and July 2007. One hundred ninety-seven cases were confirmed by positive acid-fast staining and/or culture techniques. Thirty-eight hospitals had cases confirmed by mycobacterial culture, with a total of 148 available isolates recovered from 146 patients. Most (n = 144; 97.2%) isolates presented a PRA-hsp65 restriction pattern suggestive of Mycobacterium bolletii or Mycobacterium massiliense. Seventy-four of these isolates were further identified by hsp65 or rpoB partial sequencing, confirming the species identification as M. massiliense. Epidemic isolates showed susceptibility to amikacin (MIC at which 90% of the tested isolates are inhibited [MIC(90)], 8 mu g/ml) and clarithromycin (MIC(90), 0.25 mu g/ml) but resistance to ciprofloxacin (MIC(90), > 32 mu g/ml), cefoxitin (MIC(90), 128 mu g/ml), and doxycycline (MIC(90), >= 64 mu g/ml). Representative epidemic M. massiliense isolates that were randomly selected, including at least one isolate from each hospital where confirmed cases were detected, belonged to a single clone, as indicated by the analysis of pulsed-field gel electrophoresis (PFGE) patterns. They also had the same PFGE pattern as that previously observed in two outbreaks that occurred in other Brazilian cities; we designated this clone BRA100. All five BRA100 M. massiliense isolates tested presented consistent tolerance to 2% glutaraldehyde. This is the largest epidemic of postsurgical infections caused by RGM reported in the literature to date in Brazil. | x

Gregory, A. W., G. B. Schaalje, et al. (1999). "The mycobactericidal efficacy of ortho-phthalaldehyde and the comparative resistances of Mycobacterium bovis, Mycobacterium terrae, and Mycobacterium chelonae." Infection Control and Hospital Epidemiology **20**(5): 324-330.

OBJECTIVES: To assess the mycobactericidal efficacy of an agent relatively new to disinfection, ortho-phthalaldehyde (OPA) and to compare the resistances of three Mycobacterium species. Mycobacterium bovis (strain BCG) was compared with Mycobacterium chelonae and Mycobacterium terrae to investigate the feasibility of using either of the latter two species in tuberculocidal testing. M chelonae (a rapid grower) and M terrae (an intermediate grower) both grow faster and are less virulent than M bovis (a slow grower). DESIGN: The quantitative suspension protocol specified by the Environmental Protection Agency (EPA), the Tuberculocidal Activity Test Method (EPA test), was used throughout this study. Standard suspensions of all three species were prepared in a similar manner. Two suspensions of M bovis, created in different laboratories, were used. These were tested against two concentrations of alkaline glutaraldehyde to provide reference data. Two concentrations of OPA were evaluated against all mycobacterial test suspensions. Four replicates of each organism-disinfectant combination were performed. RESULTS: Results were assessed by analysis of variance. M terrae was significantly more resistant to 0.05% OPA than either M bovis or M chelonae. At 0.21% OPA, M terrae was slightly more susceptible than one test suspension of M bovis, but not significantly different from the other. M chelonae was significantly less resistant than the other species at both OPA concentrations. At their respective minimum effective concentration OPA achieved a 6-log(10) reduction of M bovis in nearly one sixth the time required by glutaraldehyde (5.5 minutes vs 32 minutes). | x

Section A5		Effectiveness against target organisms and intended uses
		CONCLUSIONS: These data, along with other recent studies, lend support to the idea that M terrae may be a suitable test organism for use in the tuberculocidal efficacy testing of disinfectants. They also confirm the relatively rapid tuberculocidal activity of OPA.
5.7.2	**Management strategies**	Avoid continuous dosage to prevent the evolution of tolerant bacteria strains.
5.8	**Likely tonnage to be placed on the market per year (IIA5.8)**	Refer to confidential IIIA Section 5-Appendix 11

Section A5 Effectiveness against target organisms and intended uses

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
General comments	The general comments below summarize the comments of individual studies. Comments on the individual studies are provided more in detail in III B5 section.
Date	November 2012
Materials and methods	The efficacy testing methods applied in the studies summarised in the table of 5.3, were either based on EN, modified AOAC and EPA methods, or method modifications developed by the manufacturer. The method descriptions in the original study reports were not fully satisfactory in part of the studies. The RMS requested additional information of the methodology, and they were provided by the applicant. One key study was an information leaflet summarising many studies. When requested, the applicant provided the original studies summarised in the information leaflet. In addition, four new study summaries based on EN standard test were provided by the applicant at the late stage of the evaluation period.
Function Point 5.1	On the basis of the study reports the product family tested shows bactericidal and virucidal activity. However, nearly all the studies conducted were performed under unsoiled conditions. If no evidence is available from tests conducted under challenge of organic load, this should be clearly stated in the text. In particular, with reference to the products classified as biocidal veterinary hygiene products (PT3), the role of organic load should not be neglected in efficacy assessment.
Organisms to be controlled Point 5.2.1	No clear results were provided about sporicidal efficacy of glutaraldehyde. In some studies, [redacted] has been used as a target organism, but results are not reported for sporicidal efficacy. Some evidence on sporicidal activity has been provided by the applicant as a review type handbook reference (Scott and Gorman 2001). For claiming sporicidal activity the applicant should provide the original study describing the method and the result (preferably performed with an EN method) at product authorization stage. To the list of organisms to be controlled can be included also: • Sulphate reducing bacteria: [redacted]
Likely concentrations at which the a.s. will be used Point 5.3.2	Glutaraldehyde is suggested as an active ingredient applicable for four different product types. Ideally, the likely use concentrations should be the minimum effective concentration, taking into account all relevant parameters that impact the efficacy. The likely concentrations for different product types and applications given should be justified with reference to individual studies attached to the dossier. The applicant should cite an appropriate reference to the likely concentrations. For example in the EN tests the effective concentration for PT4 use was [redacted] against studied bacteria (in 5 min) and [redacted] against studied fungi (in 15 min), instead of [redacted] proposed by the applicant.
Mode of action Point 5.4.1	Scientific reference has been provided by the applicant, and it should be cited at this point.

Section A5	Effectiveness against target organisms and intended uses
Development of resistance Point 5.7.1	The reference cited ([redacted]: "Bacterial Resistance to Glutaraldehyde: is it a Problem ?") is not a scientific reference but rather a written expert opinion. Abstracts of three other references related to resistance are given in this document. The information of the abstracts should rather be summarised briefly than the whole abstract written in this document. The information of these abstracts will be given in Doc IIA.
Conclusion	Current key studies demonstrate that glutaraldehyde exhibits bactericidal and virucidal activity in conditions where organic load is not interfering. In contrast, sporicidal activity was not demonstrated by any acceptable key study. For product authorisation further studies are needed on bacteria and fungi for in-use concentration in order to demonstrate bactericidal and fungicidal efficacy. Glutaraldehyde is not effective against fungi at low concentrations and is often used in combination with other disinfectants.
Remarks	At product authorization stage evidence on sporicical activity should be demonstrated if this claim will be used. For products to be used in veterinary hygiene purposes (PT3), the efficacy in soiled conditions should be demonstrated.
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

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

Function	Field of use envisaged	Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference*)
Bactericide Fungicide against yeast	PT6	[redacted] (50% Glutar-aldehyde)	<u>Gram negative bacteria</u> [redacted] [redacted] [redacted] [redacted] [redacted] <u>Gram positive bacteria</u> [redacted]	Rate of kill test (suspension test in saline solution); Tests have involved planktonic micro-organisms, no slime or biofilm has been tested. The tests have been carried out in a saline phosphate buffer because the usual liquid nutrient media contain proteins that would react with and deactivate glutaraldehyde. This is reason for a flat pattern in the control curves; the bacteria cannot grow and their population remains constant in the absence of the killing agent. Industrial microbes are exposed to adverse conditions and their cell wall is thicker. Therefore the requested biocide killing concentration might be slightly higher than for culture strains which are used in the laboratory tests.	<u>Bacteria</u> T = 37°C pH 7.5 Conc. mg/l (ppm) Glutar-aldehyde: 0, 5, 10, 15, 20 Exposure time: 0, 1, 7, 24 hours Initial population: > 10^6 CFU/ml <u>Yeast</u> T = 30°C pH 7.0 Conc. mg/l (ppm) Glutaraldehyde: 0, 75, 100, 125, 150 Exposure time: 0, 1, 3, 5, 24 hours Initial population: > 10^6 CFU/ml	[redacted]	[redacted] B5.10/01

			Yeast				
Bactericide Fungicide against yeasts and moulds	PT2, PT6 PT2, PT6	(50% Glutar-aldehyde)	Bacteria: Yeasts:	The method [Minimum Cidal Concentration (MCC)], suspension test in saline Tubes containing cultured cells in 0.1 M buffered saline solution and the biocide to test are incubated. Plates containing a suitable nutrient medium are inoculated with the tube content, incubated and examined for growth (colony formation). The MCC is the smallest concentration of a biocide necessary to kill all the microorganisms within a given period	Contact time: 24 h Incubation time: 24 h Incubation T°C: 37 °C Initial population: $5 \cdot 10^6$ to 10^7 CFU/ml Contact time: 24 h Incubation time: 24-48 h Incubation T°C: 30°C Initial population: $5 \cdot 10^6$ to 10^7 CFU/ml		B5.10/02

			Fungi: [redacted]	of time, referred to as contact time.	Contact time: 48 h Incubation time: 8 days Incubation T°C: 30°C Initial population: $5 \cdot 10^6$ to 10^7 CFU/ml	[redacted]	
Bactericide against sulphate reducing bacteria	PT11	[redacted] (50% Glutar-aldehyde)	[redacted]	Suspension test in sterile anaerobic vials containing API RP38 media (10 ml) and an iron nail. Untreated control. Concentrations: 40 mg/l (ppm) Glutaraldehyde	T = 37 °C, pH not reported Contact time 3 and 7 hours.	[redacted]	[redacted] B5.10/03
Virucide	PT2, PT3	[redacted] (50% Glutar-aldehyde) [redacted] (14% Glutar-aldehyde [redacted] [redacted] [redacted] (20% Glutar-aldehyde)	Human Coronavirus	Surface test. Aliquots of 0.2mL of virus were dried on sterile glass Petri dishes at 23°C until visibly dry (approximately 30 min). The dried viral aliquots were treated with 3 disinfectants, each supplied in 2 distinct lots, after a 5 min exposure period, the virucide/virus mixture was scraped from the plates, neutralised by gel filtration, diluted and assayed for the presence of infectious virions.	Contact time: 5 min Incubation time: 5 min Incubation T°C: 33°C Initial population: Approximately ~~$10^{5.5}$~~ $10^{6.23}$ $CCID_{50}$/mL Concentration tested: 500 and 1000 mg/l (ppm) Glutaraldehyde	[redacted]	[redacted] B5.10/04g

Virucide, bactericide fungicide	PT2, PT3, PT4	**Study A:** preparation containing 20% glutaraldehyde. **Studies B, D:** [redacted] (14% Glutaraldehyde [redacted]). **Studies C1, E1a, E1b, E2, E3, E4, E6:** [redacted] (12.8% Glutaraldehyde). **Studies C2, E5:** [redacted] (25.6% Glutaraldehyde). **Study E6:** [redacted] (25% Glutaraldehyde)	**Study A:** [redacted] **Study B:** [redacted] **Study C1:** [redacted] **Study C2:** [redacted]	**Study A:** the test was performed following the procedures for AOAC Test Reference Number 4.023 as described in AOAC Methods, 11th Edition. **Studies B, C2, D:** US EPA DIS/TSS 10 guideline. **Study C1:** the test was performed in accordance with the ASTM Standard Test Method for Efficacy of Sanitizers Recommended for Inanimate Non-Food Contact Surfaces. **Studies E1a, E1b, E2, E3, E4, E6:** the test was conducted according to U.S. Environmental Protection Agency (EPA) guidelines for determining the virucidal efficacy of disinfectants intended for use on dry inanimate surfaces (U.S.E.P.A. Pesticide Assessment Guidelines, Subdivision G: Product Performance, 1982, Section 91-30, p. 72-76). **Study E5:** the test was conducted according to US EPA guidelines for determining the potential of the test agent to sanitize hard surfaces contaminated with viruses (US EPA DIS/TSS 7 guideline).	**Dosage rate (ppm or mg/L Glutaraldehyde):** Study A = 2000, 1000, 500, 400, 200, 100. Studies B, D = 509, 1018. Studies C1, C2, E1b, E3, E4, E5 = 1000. Studies E1a, E2 = 500. Study E6 = 1000, 2000. **Incubation temperature** (°C): Studies A, B, C2, D, E1a, E1b, E2, E3, E4, E5, E6 = 37. Study C1 = in accordance with the ASTM standard. **Contact time (min):** Study A = 0.5, 1. Studies B, C1, C2, E1b, E3, E4, E5 = 5. Study D = 5, 10 for the spore; 5 for the hyphae. Studies E1a, E2 = 10. Study E6: 5, 10. **Number of organisms tested:** **Study A:** [redacted] **Study B:** [redacted] **Study C1:** [redacted]	[redacted]	B5.10/04f


Study D:
Study E1a:
Study E1b:
Study E2:
Study E3:
Study E4:
Study E5:
Study E6:
Study C2:
Study D:
Study E1a:

					[redacted] **Study E1b:** [redacted] **Study E2:** [redacted] **Study E3:** [redacted] **Study E4:** [redacted] **Study E5:** [redacted] **Study E6:** [redacted]		
Bactericide	PT2, PT4	As given in Section 2 [redacted] (50% Glutar-aldehyde)	[redacted]	EN1040: 2005; Chemical disinfectants and antiseptics - Quantitative Suspension test for the evaluation of basic bactericidal activity of chemical disinfectants and antiseptics. This test is a Phase 1, Step 1 basic efficacy test to determine innate activity.	T = 20 °C Contact time 5 and 60 minutes.	[redacted]	[redacted] B5.10/12
Bactericide	PT2, PT4	As given in Section 2 [redacted]	[redacted]	EN1276: 1997; Chemical disinfectants and antiseptics - Quantitative suspension test for the	T = 20 °C Contact time 5 and 60 minutes.	[redacted]	[redacted] B5.10/13

		(50% Glutar-aldehyde)		evaluation of bactericidal activity of chemical disinfectants and antiseptics used in food, industrial, domestic, and institutional area.			
Bactericide	PT2, PT4	As given in Section 2 (50% Glutar-aldehyde)		EN13697: 2001; Chemical disinfectants and antiseptics - Quantitative non-porous test for the evaluation of bactericidal and/or fungicidal activity of chemical disinfectants and antiseptics used in food, industrial, domestic, and institutional area.	T = 20 °C Contact time 5 and 60 minutes.		B5.10/14
Fungicide	PT2, PT4	As given in Section 2 (50% Glutar-aldehyde)		EN13697: 2001; Chemical disinfectants and antiseptics - Quantitative non-porous test for the evaluation of bactericidal and/or fungicidal activity of chemical disinfectants and antiseptics used in food, industrial, domestic, and institutional area.	T = 20 °C Contact time 15 and 60 minutes.		B5.10/15

						[redacted]	

References:

B5.10/01: [redacted] (2004a), Data on products and processes. [redacted] Rate of kill tests. [redacted]

B5.10/02: [redacted] (2004b), Data on products and processes. Minimum cidal concentration tests with [redacted]

B5.10/03: **Henry, B.** (2004c), Data on products and processes, [redacted] Biocide efficacy vs. sulfate-reducing bacteria. [redacted]

B5.10/04g: [redacted] (2004); [redacted] Effective against a Human Coronavirus; [redacted], summarizing the following study:
"Virucidal Effectiveness Test Glutaraldehyde-Based Products – Test Agents: [redacted] (unpublished), 5 August 2003.

B5.10/04f: [redacted] CAS Reg. No. 111-30-8, [redacted] (published), 18 April 2002, gathering the following studies:

1. **Study A** – [redacted] "Test Number 1. AOAC Germicidal and Detergent Sanitizer Test", [redacted] (unpublished), 28 January 1975. See 1st "AOAC Germicidal and Detergent Sanitizer Test" on top of the page 3 of the [redacted].
2. **Study B** – [redacted] Sanitizer Test for Non-Food Contact Surfaces Using Various Strains of Pathogenic Bacteria", [redacted] (unpublished), 15 December 1999. See 2nd "AOAC Germicidal and Detergent Sanitizer Test" on the page 3 of the [redacted].
3. **Study C1** – [redacted], "Efficacy Testing of Sanitizer: Phase 1", [redacted] (unpublished). See "Modified EPA Sanitizer Test" on the page 3 of the [redacted].
4. **Study C2** – [redacted] Sanitizer Test for Non-Food Contact Surfaces", [redacted] (unpublished), 9 February 1998.See "Modified EPA Sanitizer Test" on the page 3 of the [redacted].
5. **Study D** – [redacted] Sanitizer Test for Non-Food Contact Surfaces Using [redacted] (unpublished), 15 December 1999. See "EPA Sanitizer Test for Non-Food Contact Surfaces Using [redacted] on the page 4 of the [redacted].
6. **Study E1a** – [redacted] "Amendment to [redacted] Virucidal Efficacy of [redacted] (unpublished), 7 April 2006. See "EPA Virucidal Tests" on the page 4 of the [redacted].
7. **Study E1b** – [redacted] "Virucidal Efficacy of [redacted] Against the [redacted]", [redacted] (unpublished), 1 March 1990. See "EPA Virucidal Tests" on the page 4 of the [redacted].
8. **Study E2** – [redacted] "Amended Report: Virucidal Efficacy of [redacted] (unpublished), 7 April 2006. See "EPA Virucidal Tests" on the page 4 of the [redacted].
9. **Study E3** – [redacted] "Report Amendment: Virucidal Efficacy of [redacted] (unpublished), 20 March 2006. See "EPA Virucidal Tests" on the page 4 of the [redacted].
10. **Study E4** – [redacted] "Report Amendment: Virucidal Efficacy of [redacted] (unpublished), 20 March 2006. See "EPA Virucidal Tests" on the page 4 of the [redacted].
11. **Study E5** – [redacted] "Amended Final Report: Virucidal Effectiveness Test for [redacted] (unpublished), 8 October 1997. See "EPA Virucidal Tests" on the page 4 of the [redacted].
12. **Study E6** – [redacted] "Amended Final Report: Virus Efficacy Test for [redacted] (12.8% glutaraldehyde) and [redacted] (25% glutaraldehyde) against [redacted] (unpublished), 22 September 1997. See "EPA Virucidal Tests" on the page 4 of the [redacted].

B5.10/12: [redacted] 2007, Determination of the Activity of [redacted] using the European Disinfection Test EN 1040, [redacted] 19 November 2007, unpublished.

B5.10/13: [redacted] 2007, Determination of the Activity of [redacted] using the European Disinfection Test EN 1276, [redacted] 25 October 2007, unpublished.

B5.10/14: [redacted] 2007, Determination of the Activity of [redacted] using the European Disinfection Test EN 13697, [redacted] 19 November 2007, unpublished.

B5.10/15: [redacted] 2007, Determination of the Activity of [redacted] using the European Disinfection Test EN 13697, [redacted] 19 November 2007, unpublished.

Section A5 Effectiveness against target organisms and intended uses

Subsection (Annex Point)			Official use only
5.1	Function (IIA5.1)	Main Group 2 - Preservatives PT11 Preservatives for liquid cooling and processing systems, oilfield injection water and hydrotesting water: bactericide; fungicide PT12 Slimicides: bactericide; fungicide	
5.2	Organism(s) to be controlled and products, organisms or objects to be protected (IIA5.2)		
5.2.1	Organism(s) to be controlled (IIA5.2)	Glutaraldehyde is potentially effective against a wide variety of micro-organisms including gram positive and negative bacteria including sulphate-reducing bacteria, fungi and yeast. Examples of typical microbes to be controlled: • Gram negative bacteria: [redacted] • Gram positive bacteria: [redacted] Fungi: [redacted] • Yeast: [redacted] These species are common in the whole area of the European Union. The species tested in the Rate of Kill (ROK) tests and Minimum Cidal Concentration (MCC) tests are present in most surface waters.	x x
5.2.2	Products, organisms or objects to be protected (IIA5.2)	[redacted] (50% glutaraldehyde) PT11: preservation of liquid cooling systems, preservative in oilfield injection water and hydrotesting water PT12: prevention of slime growth in the paper	
5.3	Effects on target organisms, and likely concentration at which the active substance will be used (IIA5.3)		
5.3.1	Effects on target organisms (IIA5.3)	Glutaraldehyde kills the micro-organisms. The microbes are killed faster at higher concentrations, higher temperatures and higher pH. The Minimum Cidal Concentration (MCC) is [redacted] Glutaraldehyde for bacteria with 24 h reaction time. The MCC for fungi is [redacted] Glutaraldehyde with 48 h reaction time. The MCC for yeast is [redacted] Glutaraldehyde with reaction time of 24 h.	
5.3.2	Likely concentrations at which the A.S. will be used (IIA5.3)		

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	PT11	Open and closed re-circulating cooling systems: [redacted] Oilfield injection water [redacted] Hydrotesting water [redacted] Note: **active substance (a.s.) refers to 100% glutaraldehyde**	x
	PT12	[redacted]	
5.4	**Mode of action (including time delay) (IIA5.4)**		
5.4.1	**Mode of action**	Glutaraldehyde kills the micro-organisms by reacting with the free amino groups of some proteins that are located in the cell walls and membranes of the micro-organisms. The reaction is known as cross-linking. Cross-linked microbial cells cannot transport nutrients or perform any critical metabolic functions. Glutaraldehyde also deactivates various membrane-bound enzymes. The kinetics of the cross-linking mechanism are influenced by the pH, the contact time, the glutaraldehyde concentration and the temperature. In viruses, the main targets for glutaraldehyde are nucleic acid, proteins and envelope constituents. The established reactivity of glutaraldehyde with proteins suggests that the viral capsid or viral-specific enzymes are vulnerable to glutaraldehyde treatment.	
5.4.2	**Time delay**	No time delay. The killing rate is faster at alkaline conditions, high temperatures and at higher glutaraldehyde concentrations. Under acidic conditions the free amino groups react more with H^+ ions (eq.1) and are less susceptible to react with Glutaraldehyde (eq.2): pH< 6: $R\text{-}NH_2 + H^+ \Rightarrow RNH_3^+$ eq.1 pH >7: $R\text{-}NH_2 + GA \Rightarrow$ cross-linking eq.2	
5.5	**Field of use envisaged (IIA5.5)**		
	MG01: Disinfectants, general biocidal products	Supported in List 3	
	MG02: Preservatives	PT11Preservatives for liquid cooling and processing systems • 11.02 – preservatives used in open recirculating systems • 11.03 – preservatives used in closed recirculating systems • 11 - preservative in oilfield injection water • 11 - preservative in hydrotesting water PT12 Slimicides • 12.01 - Slimicides for paper pulp: wet-end slimicide • 12.01 - Slimicides for paper pulp: paper de-inking	
	MG03: Pest control	Not supported	
	MG04: Other biocidal products	Not supported	
	Further specification	The product is a liquid formulation. It will be sold as a concentrate (SL). The concentrate is 50% water.	
5.6	**User**		

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(IIA5.6)

Industrial [redacted] is sold to formulators for incorporation into products which are for use by professionals. These products may contain less than 50% glutaraldehyde. The use of [redacted] for formulation is not covered under this dossier.

Professional [redacted] is used by professionals in PT11 and PT12

General public [redacted] is not sold to the general public.

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

5.7.1 Development of resistance

It is a general practice in industry not to continuously use the same biocidal active substance to avoid the proliferation of tolerant or resistant strains. This, according to an expert review, is not a significant problem in industrial uses of glutaraldehyde, and is substantiated by several years of experience with the use of glutaraldehyde in water cooling systems at a Union Carbide plant. The following is a summary of Professor Russell's review:

„On the basis of the mechanism of its lethal activity described above under Section 5.4.1 Mode of Action, it would not be expected that bacteria would develop resistance to the dialdehyde or that it would select resistant sub-populations of bacteria. Intrinsic insusceptibility to biocides is associated with cell wall or outer membrane, with efflux systems in MDR Gram-negative bacteria and possibly with biocide inactivation.

A particular example is demonstrated by the physiological (phenotypic) adaptation to intrinsic resistance with bacteria and other micro-organisms found in biofilms. Acquired resistance to biocides may result from mutation, although the resistance may be stable or unstable, or from plasmid-mediated changes in outer membrane composition or plasmid-associated efflux systems.

Although resistance of non-sporulating bacteria to glutaraldehyde has been demonstrated, this generally is of a low level (with the notable exception of some glutaraldehyde-resistant strains of *M.chelonae*). Bacteria within a biofilm are less susceptible to the dialdehyde but there is no evidence that resistance has developed. There is also no evidence that glutaraldehyde selects for antibiotic-resistant bacteria. Experience over many years indicates that development of bacterial resistance to glutaraldehyde is not a significant problem in industrial usage" (Russell A.D. 2001).

The issue of resistance development to Glutaraldehyde, by the type of organisms one may encounter in applications that intend to use it, is not relevant. While it is likely that all microbiocides face potential