Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

COMPETENT AUTHORITY REPORT

Document IIIA

Glyoxal

Product types PT2 – 3 – 4

Evaluating Competent Authority: France

April 2020

Substance Name: Glyoxal

EC Name: 1,2-Ethanedial

EC Number: 203-474-9

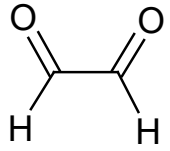
CAS Number: 107-22-2

Applicant: BASF SE

Section A1	**Applicant**
Annex Point IIA1	

1.1	**Applicant**	Name: BASF SE Address: D-67056 Ludwigshafen, Germany Telephone +49(0) 621 60-0 Applicant's representative: This information is confidential and presented in Document V
1.2	**Manufacturer of Active Substance** (if different)	This information is confidential and presented in Document V
1.3	**Manufacturer of Product(s)** (if different)	[redacted]

Section A2 Identity of Active Substance

Subsection (Annex Point)		
2.1	**Common name (IIA2.1)**	Glyoxal
2.2	**Chemical name (IIA2.2)**	1,2-Ethanedial
2.3	**Manufacturer´s development code number(s) (IIA2.3)**	Not applicable as the product has been marketed for many years
2.4	**CAS No and EC numbers (IIA2.4)**	
2.4.1	**CAS-No**	107-22-2
2.4.2	**EC-No**	203-474-9
2.4.3	**Other**	-
2.5	**Molecular and structural formula, molecular mass (IIA2.5)**	
2.5.1	**Molecular formula**	$C_2H_2O_2$
2.5.2	**Structural formula**	
2.5.3	**Molecular mass**	58.04 g mol^{-1}
2.6	**Method of manufacture of the active substance (IIA2.1)**	The method of manufacture is confidential and is presented in the confidential document V

2.7 Specification of the purity of the active substance, as appropriate (IIA2.7)

g/kg	g/l	% w/w	% v/v
388 - 406		nominal 40	

2.8	**Identity of impurities and additives, as appropriate (IIA2.8)**	The identity of impurities & additives are confidential and presented in the confidential document V. Also see report BPD ID A4.1_01, BPD ID A4.1_02 and BPD ID A4.1_03
2.8.1	**Isomeric composition**	There are no known isomers of Glyoxal
2.9	**The origin of the natural active substance or the precursor(s) of the active substance (IIA2.9)**	Glyoxal is manufactured from synthetic substances.

Doc III Section A2.10 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	
Subsection		**Official use only**
2.10.1 Human exposure towards active substance		
2.10.1.1 Production		
i) Description of processes	See confidential Doc V	
ii) Workplace description	[redacted]	
iii) Inhalation exposure	[redacted] The handling of glyoxal should only be carried out in sufficiently well ventilated areas, where this is not possible respirators with type A gas should be used.	
iv) Dermal exposure	Workers are expected to wear safety glasses and chemical protective gloves, made from neoprene and nitrile rubber. For maintenance or repair work with a higher risk, suitable chemical protective suits are additionally used. The combination of wearing PPE & the closed system of manufacture means direct contact with [redacted] can be kept very low or excluded.	
2.10.1.2 Intended use(s)	Glyoxal is used in products as the active substance for Product Types 2, 3 & 4 for application in medical areas, accommodation and industrial areas (PT2.1.2), animal housing including hatcheries and stables (PT 3.1) and disinfection of floors, walls, equipment in plant, production, preparation and consumption (PT4). No direct use on food is intended.	**X**
2.10.1.2.1 Professional Users		
i) Description of application process	[redacted] is used in PT2 application to industrial and institutional premises (floors, walls and infrastructure), machinery and bathroom surfaces, PT3 application to areas in which animals are housed, hatched, kept and transported and the utensils, pipes and surfaces contained within such areas and PT 4 application to industrial and institutional premises (floors, walls and infrastructure), machinery and kitchen. The product is applied directly to the surface requiring disinfection by mopping, wiping or low pressure spraying (for example with a finger operated trigger spray) or by use of immersion baths.	**X**
ii) Workplace description	Professional workers are expected to wear chemical resistant gloves, protective clothing & suitable respiratory protective devices so that inhalation exposure and dermal exposure can be excluded during the manufacture and use of biocidal products containing [redacted]	
iii) Inhalation exposure	A combination of engineering controls, workplace ventilation and the use of recommended respiratory equipment should be used to ensure that inhalation exposure is negligible. See Doc III A2.10.1.1(iii)	
iv) Dermal exposure	By using the recommended personal protective equipment (chemical resistant gloves, impermeable protective work-wear and footwear), direct contact with [redacted] can be kept very low or excluded.	
A2.10.1.2.2 Non-professional Users including the general public	[redacted] is not used by the general public and secondary exposure is not expected.	

Doc III Section A2.10 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
(i) via inhalational contact	Exposure is not expected
(ii) via skin contact	Exposure is not expected
(iii) via drinking water	Exposure is not expected
(iv) via food	Exposure is not expected
(v) indirect via environment	Exposure is not expected

2.10.2 Environmental exposure towards active substance

2.10.2.1 Production

(i) Releases into water	[redacted] Glyoxal is readily biodegradable according to OECD criteria and is therefore assumed to be removed from the water with high efficiency. Thus any exposure of the receiving waters to glyoxal is unlikely.
(ii) Releases into air	[redacted] Thus any atmospheric exposure to glyoxal is unlikely.
(iii) Waste disposal	Not relevant

2.10.2.2 Intended use(s)

Product Type 2 and 4

Affected compartment(s):	
water	Low
sediment	Excluded
air	Low
soil	Excluded

Predicted concentration in the affected compartment(s)

water	Very low concentrations could be discharged to the sewage treatment plants but release to the receiving water will be negligible due to the effects of dilution and ready biodegradability.
sediment	Release excluded
air	In PT 2 and PT4 Glyoxal is used indoors. Further the vapour pressure of Glyoxal is low, so a low exposure to air is expected.
soil	Release excluded

Product Type 3

Affected compartment(s):	
water	Excluded
sediment	Excluded
air	Low
soil	Low

Predicted concentration in the affected compartment(s)

water	Discharge to sewage treatment plants is not applicable for PT3 uses
sediment	Discharge to sewage treatment plants is not applicable for PT3 uses
air	Glyoxal has low Henry's Law Constant so only low exposure of the air is expected.
soil	Small quantities may be released with manure and slurry but will limited by extensive degradation in these media.

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	March 2019

Materials and methods	**2.10.1.2.1 Description of application process** 2.10.1.2 Intended use(s) Glyoxal is used in products as the active substance for Product Types 2, 3 & 4 for application in small areas in medical and industrial areas (PT2.1.2), animal clinics and animal shelters (PT 3.1) and small areas in plant, production, preparation and consumption and CIP (PT4). The disinfection of equipment by dipping is foreseen for all three PTs. No direct use on food is intended. PT 2: Disinfection of small, pre-cleaned areas and equipment, not frequently touched in the following areas and for the following purposes: - Disinfection of industrial and institutional areas - Disinfection for sanitary purposes (industrial/institutional, e.g. tiles) - Disinfection of instruments (pharmaceutical, cosmetic industry etc.), e.g. by immersion - Medical sector: Disinfection of rooms, furniture and objects - Medical sector: Disinfection of Instruments, e.g. by immersion PT 3: - Disinfection of small, pre-cleaned areas, not frequently touched, of animal housing in e.g. animal pensions, animal shelters, connected to a STP - Disinfection of tools, instruments etc. in e.g. animal pensions, animal shelters, connected to a STP, e.g. by immersion. PT 4: - Disinfection of small, pre-cleaned and not frequently touched areas of floors, walls, equipment in the food, drink and milk industries, in large scale catering kitchens and canteens and areas where food is handled or displayed - Disinfection of equipment by cleaning in place systems - Disinfection of tools, instruments etc, e.g. by immersion Comments on PT03 uses: There is no scenario for large scale animal housing (as farm) presented in this CAR. The assessed uses are in animal shelters, animal pensions or animal clinics. No releases to slurry/manure are foreseen in those cases and only releases to the STP have been evaluated. **.2.7 Specification of the purity of the active substance, as appropriate** See the confidential doc IIA for further details **2.8 Identity of impurities and additives, as appropriate (IIA2.8)** *The identity of impurities & additives are confidential and presented in the confidential document V.* *Also see report BPD ID A4.1_01, BPD ID A4.1_02 and BPD ID A4.1_03* Specification of the active substance is detailed in the confidential doc IIA.
Conclusion	Adopt applicant´s version with above amendments
Reliability	n.a.
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 A3 **Physical and Chemical Properties of Active Substance**

Additional physical and chemical data on the active substance (not available at the time of submission for the Part D dossier) is included in the table below. The data previously submitted in the Part D dossier is also included for reference purposes.

Subsection (Annex Point)	Method	Purity/ Specification	Results	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	OECD TG 102 92/69/EEC Part A.1 U.S. EPA OPPTS 830.7200	Test item: [redacted] glyoxal	**result:** -25 °C (extrapolated onset temperature; range: ca. -50 to -15 °C)	**Melting point** Differential Scanning Calorimetry (DSC)	Y	[redacted]	[redacted] (2002) BPD ID A3.01.1_01	
Melting pt. 2	ASTM designation D 1015-55	Glyoxal [redacted] aqueous solution	**result:** -14.98 ± 0.1 °C (solidification point) **pressure:** not specified	**Solidification point** measured by Cryoscopic Solidification Apparatus	N	[redacted]	[redacted] (1987) BPD ID A3.01.1_02 / BPD ID A3.01.1_03	
3.1.2 Boiling point								
Boiling pt.	OECD TG 103 & 104 92/69/EEC Part A.2 & Part A.4 U.S. EPA OPPTS 830.7220 & 830.7950	Test item: [redacted] glyoxal; [redacted]	**result:** 103.6 °C **pressure:** 1013.25 hPa	Obtained by interpolation from regression derived equation	Y	[redacted]	[redacted] (2002) BPD ID A3.01.2_01	
3.1.3 Bulk density/ relative density								
Relative density	OECD TG 109 92/69/EEC Part A.3 U.S. EPA OPPTS 830.7300	Test item: [redacted] Glyoxal [redacted] aqueous	**Mean relative density:** 1.2694 ± 0.0001 at 20 °C	Pycnometer method; relative to water at 4 °C	Y	[redacted]	[redacted] (2002) BPD ID A3.01.3_01	

	solution						
3.2 Vapour pressure (IIA3.2) Vapour pressure	OECD TG 104 92/69/EEC Part A.4 U.S. EPA OPPTS 830.7950	Test item: [redacted] glyoxal; [redacted]	**temperature:** 20.0/25.0/50.0 °C **result:** 20.2/27.4/106.7 hPa	Obtained by interpolation from regression derived equation	Y	[redacted]	[redacted] (2002) BPD ID A3.02_01
3.2.1 Henry´s Law Constant (Pt. I-A3.2)	Bubble-column technique	Glyoxal, [redacted] aqueous solution	**measured result:** ≤ 3.38E-04 Pa*m^3*mol^{-1} **temp.:** 15, 20, 25°C		N	[redacted]	[redacted] (1988) BPD ID A3.02.1_01
3.3 Appearance (IIA3.3)							
3.3.1 Physical state	Experience in use	Glyoxal [redacted] aqueous solution	Liquid		N	[redacted]	BASF (2006) BPD ID A3.03.1_01/ A3.03.2_01/ A3.03.3_01
3.3.2 Colour			Colourless to yellow		N	[redacted]	
3.3.3 Odour			Product specific		N	2	
3.3.1 Physical state	Visual inspection	Glyoxal [redacted] aqueous solution	Slightly viscous liquid, homogenous		Y	[redacted]	Also see [redacted] (2009) BPD ID 3.04_01
3.3.2 Colour			Clear, colourless		Y	[redacted]	
3.4 Absorption spectra (IIA3.4) **UV/VIS**	UV/VIS spectroscopy according to laboratory SOP IRL/015/current Version; UV/VIS spectrophotometer [redacted]	Glyoxal [redacted] aqueous solution	The UV/VIS spectrum of the test item shows an absorption maximum at approx. 265-266 nm. Specific absorbance ($A_{1cm1\%}$) and specific absorptivity (ε') at this wavelength: $A_{1cm1\%}$ = 0.016;		Y	[redacted]	[redacted] (2009) BPD ID 3.04_01

			ε' = 0.0016 L*g^{-1}* cm^{-1}.					
IR	IR spectroscopy according to laboratory SOP IRL/001/current version; IR spectrometer [redacted]	Glyoxal [redacted] aqueous solution	The IR spectrum of the test item shows the bands expected for the test item (glyoxal in water): approx. 3414 cm^{-1} (broad; ν_{O-H}, water); 2800-3000 cm^{-1} (ν_{CH}); 1643 cm^{-1} (predominantly δ_{O-H}, water); 1074 cm^{-1} (ν_{C-O}, assigned to C-O groups, e.g. in [redacted] glyoxal dimers/oligomers present in aqueous solutions of glyoxal). The IR spectrum of the test item shows the same bands as a reference spectrum (Aldrich® Library of Infrared Spectra).	The test item was measured neat and without pre-treatment between two KRS-5 windows. Preparation was performed at room temperature in a glove-box purged with dry nitrogen. Measurement at room temperature; 32 scans; resolution: 4 cm^{-1}	Y	[redacted]	[redacted] (2009) BPD ID 3.04_01	
NMR	^{1}H- and ^{13}C-NMR spectroscopy according to laboratory SOP NMR/001/current version; [redacted]	Glyoxal [redacted] aqueous solution	The ^{1}H- and ^{13}C- spectra of the test item show the same signal patterns present in reference spectra (Aldrich® Library of ^{13}C and ^{1}H FT-NMR Spectra).	The test item and reference item 3(TMSPS-Na) were dissolved in D_20. Measuring frequencies: 400 MHz (^{1}H-NMR) and 100 MHz (^{13}C-NMR) at 27°C.	Y	[redacted]	[redacted] (2009) BPD ID 3.04_01	
MS	Capillary GC/MS of positive ions after electron impact (EI, 70 eV) and chemical	Glyoxal [redacted] aqueous solution	The GC/MS analysis of the test item revealed free glyoxal (Mr = 58)	Direct injection; Reagents: Helium, Ammonia (for CI)	Y	[redacted]	[redacted] (2009) BPD ID 3.04_01	

		ionization (CI) with ammonia according to laboratory SOP MS/002/current version; [redacted]							
	UV/VIS	Fourier transform spectrometer	Glyoxal, [redacted] (purified)	**temperature:** 23 °C **pressure:** 1013 hPa **result:** 250 – 525 nm (major peaks at 299, 403, 413, 428, 440, 455 nm)	High-resolution absorption cross section	N	[redacted]	[redacted] (2005) BPD ID 3.04_02	
	IR	Fourier transform spectrometer	Glyoxal, [redacted] (purified)	**temperature:** 23 °C **pressure:** 0.2, 100, 300, 1013 hPa **result:** ca. 2730 – 2930 cm^{-1} (major peaks around 2835 cm^{-1})	High-resolution absorption cross section	N	[redacted]	[redacted] (2005) BPD ID 3.04_02	
3.5	**Solubility in water (IIA3.5)**								
	Water solubility	OECD TG 105 92/69/EEC Part A.6 U.S. EPA OPPTS 830.7840	Test item: [redacted] glyoxal; [redacted]	**result:** miscible at any ratio **temperature:** 20.2 ± 0.1 °C **pH:** 5 / 7 / 9	Complete miscibility in aqueous buffer solutions at pH 5, 7 and 9 at 20.2 ± 0.1 °C			[redacted] (2002) BPD ID A3.05_01	
3.6	**Dissociation constant (-)**	Calculation (SPARC)	Glyoxal, CAS 107-22-2	No dissociation (pH 0 – 14)		N	[redacted]	[redacted] (2007) BPD ID A3.06_01	X
3.7	**Solubility in organic solvents, including the effect of temperature on**	BASF SE, [redacted] chapter	Glyoxal [redacted]	The test item is miscible in any ratio with methanol and with 1,4dioxane at 20°C and	To apply the guideline method OECD 105, the preparation of a	Y	[redacted]	[redacted] (2009) BPD ID A3.7_01/ A3.14_01	

	solubility (IIIA3.1)	5 (visual method)		at 30°C. With 1-octanol, a phase separation was observed, because of the high amount of water in the test item. Due to this high amount of water, the determination of the solubility of the test item in solvents with low polarity is not feasible.	saturated solution of test item in the solvent is required. Since this was not possible for this test item, an in-house method was used.				
3.8	**Stability in organic solvents used in b.p. and identity of relevant breakdown products (IIIA3.2)**				Data not required since substance as manufactured does not include organic solvents. [redacted]			None as no data needed	
3.9	**Partition coefficient n-octanol/water (IIA3.6)** log K_{OW}	OECD TG 107 92/69/EEC Part A.8 U.S. EPA OPPTS 830.7550	Test item: [redacted] glyoxal; [redacted]	**log Kow:** -1.00 / -1.15 / -1.62 **temperature:** 23 ± 1 °C **pH:** 5 / 7 / 9		Y	[redacted]	[redacted] (2002) BPD ID A3.09_01	
3.10	**Thermal stability, identity of relevant breakdown products (IIA3.7)**	Dynamic Scanning Calorimetry (DSC)	Glyoxal [redacted] aqueous solution	1st measurement: **Onset temperature:** 140 °C **Peak temperature:** 195 °C	**Cup material:** V2A stainless steel **Heating rate:** 2 K/min	N	[redacted]	[redacted] (1992) BPD ID A3.10_01	

			Energy release: 480 J/g 2nd measurement: **Onset temperature:** 140 °C **Peak temperature:** 188 °C **Energy release:** 420 J/g 3rd measurement: **Onset temperature:** 110 °C **Peak temperature:** 158 °C **Energy release:** 370 J/g	**Temp. range:** 30 – 300 °C **Cup material:** Hastelloy C **Heating rate:** 2 K/min **Temp. range:** 35 – 300 °C **Cup material:** Hastelloy C **Heating rate:** 0.5 K/min **Temp. range:** 35 – 300 °C				
3.11 Flammability, including auto-flammability and identity of combustion products (IIA3.8)	German National Standard DIN 51 794	Glyoxal [redacted]	285 °C	Not flammable	N	[redacted]	[redacted] (1985) BPD ID A3.11_01/ A3.12_01	X
3.12 Flash-point (IIA3.9)								
Flash-point 1	German National Standard DIN 51 755	Glyoxal [redacted]	Not determinable up to 65 °C		N	[redacted]	[redacted] (1985) BPD ID A3.11_01/ A3.12_01	
Flash point 2	German National Standard DIN 51 758		Not determinable, the pilot light ceases at temp. ≥ 62 °C		N	[redacted]		
Flash point 3	German National Standard DIN ISO 2592		Not determinable, the pilot light ceases at temp. ≥ 86 °C		N	[redacted]		

3.13 Surface tension (IIA3.10)								
Surface tension	Expert judgement	Glyoxal, CAS 107-22-2	No surface activity	Molecule has no hydrophobic part	N	[redacted]	[redacted] (2008) BPD ID A3.13_01	
	Study according to OECD 115 resp. EU A.5	Glyoxal [redacted]	No surface activity		N	[redacted]	[redacted] (2017) BPD ID A3.13_02	
3.14 Viscosity (-)	OECD TG 114	Glyoxal [redacted]	Kinematic viscosity: v = 6.60 mm^2/s at 20.0°C v = 3.38 mm^2/s at 40.0°C Dynamic viscosity: η = 8.37 mPa*s at 20.0°C η =4.25 mPa*s at 40.0°C	The kinematic viscosity was measured by a capillary viscosimeter. The dynamic viscosity was calculated by the equation η = v*p (p is density).	Y	[redacted]	[redacted] (2009) BPD ID A3.7_01/ A3.14_01	
3.15 Explosive properties (IIA3.11)	Expert judgement	Glyoxal, CAS 107-22-2	Not explosive	No chemical groups indicating explosive properties	N	[redacted]	[redacted] (2000) BPD ID A3.15_01/ A3.16_01	
3.16 Oxidizing properties (IIA3.12)	Expert judgement	Glyoxal, CAS 107-22-2	Not oxidizing	No chemical groups indicating oxidizing properties	N	[redacted]	[redacted] (2000) BPD ID A3.15_01/ A3.16_01	
3.17 Reactivity towards container material (IIA3.13)	Expert judgement based on experience in packaging	Glyoxal ([redacted])	Compatible: - high density polyethylene - glass - stainless steel	During the many years of production, no interaction between the active ingredient and the container materials has been observed.	N	[redacted]	[redacted] (2008) BPD ID A3.17_01	

BPR 3.1.2. Aggregate state (at 20°C and 101.3 kPa)	Visual inspection	Glyoxal [redacted] aqueous solution	Other: the substance is a slightly viscous, clear, colorless and apparently homogeneous liquid.	-	Y	[redacted]	[redacted] (2009) BPD ID 3.04_01	
BPR 3.3. Acidity/Alkalinity	CIPAC Method MT 31; visual titration CIPAC Method MT 75, potentiometric measurement CIPAC Method MT 75, potentiometric measurement	[redacted] Ethanedial, [redacted] in water.	Acidity: 0.24g/100g Test item pH: 1.9 (25°C) 1% solution test item in water pH: 4.2 (20°C)	Because the shelf life of the test item was already expired, the test item from the storage stability test was used for the determination of the acidity and the pH value of the undiluted test item. The storage stability test had verified that the test item stored at 20°C was still unchanged at the time when these determinations were carried out.	Y Y Y	[redacted]	[redacted] (2009) BPD ID A3.7_01-[redacted] 09 BPD ID A3.07_01 and A3.14_01. [redacted]1	
BPR 3.14. Granulometry	Waiving argument (see BPR Guidance Vol. 1, Part A (2014, v1.1): Section3.14	-	Not applicable	This endpoint must be determined and reported for active substances such as powders and granules. The active substance Glyoxal [redacted] is a liquid, it is not in powder or granular form	-	-	-	
BPR 4.1. Explosives	Expert judgement	Not specified	Not explosive	No chemical groups indicating	N	[redacted]	[redacted] (2000) BPD ID A3.15_01	

				explosive properties			and A3.16_01.ox-explo_RL2	
BPR 4.2. Flammable gas	Waiving argument (see CLP Guidance (2015, v4.1): 2.3.3. Annex I, 2.3.2.1.: Note 2 Decision logic for flammable gases)	Glyoxal [redacted] aqueous solution	Not applicable.	The active substance is a liquid at ambient conditions 20 °C, 101.3 kPa); it is not a gaseous substance or mixture of gases.	-	-	-	
BPR 4.3. Flammable aerosol	Waiving argument	-	Not applicable.	The parameter flammable aerosols must be determined for active substances that are supplied as aerosols. Since the active substance is not an aerosol, this test does not need to be performed.	-	-	-	
BPR 4.4. Oxidising gases	Waiving argument (see CLP Guidance (2015, v4.1): Fig. 2.4.4-a: Decision logic for oxidising gases)	-	Not applicable.	The active substance is a liquid at ambient conditions 20 °C, 101.3 kPa); it is not a gaseous substance or mixture of gases.	-	-	-	
BPR. 4.5. Gases under pressure	Waiving argument (see CLP Guidance (2015, v4.1): Section 2.5	-	Not applicable.	The active substance is a liquid at ambient conditions 20 °C, 101.3 kPa); it is not a gaseous substance or mixture of gases.	-	-	-	

BPR 4.6. Flammable liquids	CLP criteria (Annex I, 2.6.1)	Glyoxal ca. [redacted]	Not subject of hazard class "flammable liquid".	CLP Guidance, Figure 2.6.4-a Amended GHS decision logic for flammable liquids: - Flash point ≤ 60 °C: No - Gas oil, diesel, light heating oil with flash point up to 75 °C: No - Halogenated substance, mixture containing halogenated, volatile or non volatile flammable substances: No Conclusion: Active substance not to be classified as flammable liquid.	N	[redacted]	[redacted] (1985) BPD ID A3.11_01/ A3.12_01	
BPR 4.7. Flammable solids	Waiving argument (see CLP Guidance (2015, v4.1): Section 2.7	-	Not applicable.	The active substance is a liquid at ambient conditions 20 °C, 101.3 kPa); it is neither a powdered, granular nor pasty substance or mixture.	-	-	-	
BPR 4.8. Self-reactive substances and mixtures	Waiving argument: UN Manual of Tests and Criteria (2010): Appendix 6, Section 5.1		Not a self-reactive substance or mixture	According to the criteria given in the MTC, 40% Glyoxal in water has no chemical	-	-	-	

				groups associated with explosive or self-reactive properties like those described in tables A6.1.and A6.2. of the MTC (e.g. no C-C unsaturation, C-metal or N-metal bonds, peroxides, azides etc.). Hence, glyoxal [redacted]n water is not considered a self-reactive substance of mixture.				
BPR 4.9. Pyrophoric liquids	Waiving argument (see CLP Guidance (2015, v4.1): Section 2.9	-	Not pyrophoric liquid based on auto-ignition temperature and experience in manufacture and handling.	According to CLP guidance, substances showing pyrophoricity, are characterized by an auto-ignition temperature lower than room (ambient) temperature. The auto-ignition temperature of the active substance Glyoxal [redacted] is 285°C. Therefore it is not a pyrophoric liquid. According to the additional	N	[redacted]	[redacted] (1985) BPD ID A3.11_01/ A3.12_01	

				classification considerations in CLP Annex I, 2.9.4, the classification procedure for pyrophoric liquids need not be applied when experience in manufacture or handling shows that the liquid does not ignite spontaneously on coming into contact with air at normal temperatures (i.e. the liquid is known to be stable at room temperature for prolonged periods of time (days)). This is the case for glyoxal [redacted]				
BPR 4.10. Pyrophoric solids	Waiving argument (see CLP Guidance (2015, v4.1): Section 2.10	-	Not applicable.	Glyoxal [redacted] in water is a liquid at ambient conditions 20 °C, 101.3 kPa); it is not a solid.	-	-	-	
BPR 4.11. Self-heating substances and mixtures	Waiving argument (see CLP Guidance (2015, v4.1): Section 2.11	-	Not applicable.	Glyoxal [redacted] is a liquid with melting point of -25°C. According to CLP Guidance	-	-	-	

				document (2015, v4.1), substances or mixtures with a low melting point (< 160 °C) should not be considered for classification in this class since the melting process is endothermic and the substance-air surface is drastically reduced.				
BPR 4.12. Substances and mixtures which in contact with water emit flammable gases	Waiving argument (see CLP Guidance (2015, v4.1): Section 2.12	-	Not applicable.	The active substance as manufactured contains ca. [redacted] water. Therefore an emission of flammable gases is not expected when the substance comes in contact with water.	-	-	-	
BPR 4.13 Oxidising liquids	Expert judgement	Glyoxal, CAS 107-22-2	Not oxidizing	No chemical groups indicating oxidizing properties	N	[redacted]	[redacted] (2000) BPD ID A3.15_01/ A3.16_01	
BPR 4.14 Oxidising solids	Waiving argument (see CLP Guidance (2015, v4.1): Section 2.14	-	Not applicable.	Glyoxal [redacted]% is a liquid at ambient conditions 20 °C, 101.3 kPa); it is not a solid.	-	-	-	
BPR 4.15 Organic peroxides	Expert judgement (see CLP Guidance (2015,	-	Not applicable	Glyoxal is not an organic peroxide	-	-	-	

	v4.1): Section 2.15; Definition according to CLP Regulation Annex I: 2.15.1.			as it does not contain the bivalent -O-O structure.				
BPR 4.16. Corrosive to metals	Annex A of ADR/Class 8; IATA-DGR 3.8.2.4; IMDG-Code, Class 8, 2.1.4.3; 49 CFR § 173; GHS-Regulation (EU) No. 1272/2008 and UN Recommendations on the Transport of Dangerous Goods; ASTM G31-72	Glyoxal [redacted]%	Non-corrosive		N	[redacted]	[redacted] (2012) BPR A4.16	
BPR 4.17. Additional physical indicators for hazards	-	-	-	-	-	-	-	
BPR 4.17.1. Auto ignition temperature (liquids and gases)	German National Standard DIN 51 794	Glyoxal ca. [redacted]	285 °C	Not flammable	N	[redacted]	[redacted] (1985) BPD ID A3.11_01/ A3.12_01	
BPR 4.17.2. Relative self-ignition temperature for solids	Waiving argument (see CLP Guidance (2015, v4.1): Section 2.11	-	Not applicable.	[redacted]% Glyoxal in water is a liquid at ambient conditions 20 °C, 101.3 kPa); it is not a solid.	-	-	-	
BPR 4.17.3. Dust explosion hazard	Waiving argument (see BPR Guidance (2014, v1.1): Section 4.17.3	-	Not applicable.	Glyoxal [redacted]% is a liquid at ambient conditions (20 °C, 101.3 kPa). Dust explosion hazard is only applicable to powders and products containing or able to produce, dust.	-	-	-	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	March 2018
Evaluation of applicant's justification	**Dissociation constant** QSAR data is not acceptable. No further data is required as based on the chemical structure, no dissociation is expected at environmental pH **Flammability, including auto-flammability and identity of combustion products** Not a CLP criteria. Data have been provided on self-heating substances and mixtures. See in the table above (BPR 4.11).
Conclusion	Agree with applicant's version with above amendments. For the other endpoints see table reported in the doc IIA
Reliability	As reported in the table, except for dissociation constant where reliability index is [redacted]
Acceptability	Acceptable.
Remark	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A3.1.1/3.1.2/3.1.3/ 3.2/ 3.	**Glyoxal anhydrous, Physical chemical parameters**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [X]	**Technically not feasible [ ]** **Scientifically unjustified [X]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification:	[redacted]	

Section A3.1.1/3.1.2/3.1.3/ 3.2/ 3.	Glyoxal anhydrous, Physical chemical parameters

Glyoxal anhydrous, PC data, OECD SIDS (2003)

CAS-NO.: 107-22-2			PROTOCOL	RESULTS
PHYSICAL CHEMICAL				
2.1	Melting Point	40% aq. sol.	NA	-14°C
		Anhydrous *	NA	15°C
2.2	Boiling Point	40% aq. sol.	NA	104° C (at 101.3 kPa)
		Anhydrous *	NA	50.4°C (at 101.3 kPa)
2.3	Density	40% aq. sol.	NA	1270 kg/m^3
		Anhydrous *	NA	1140 kg/m^3
2.4	Vapour Pressure	Anhydrous *	NA	< 0.01Pa at 20°C
		40% aq.sol	NA	1800 Pa at 20°C
2.5	Partition Coefficient (Log Pow)	Anhydrous *	calculated	- 1.65
2.6 A	Water solubility		NA	miscible at 20°C

Glyoxal anhydrous, PC data, CICAD (2004)

Property	Value	Reference
Glyoxal		
Relative molecular mass	58.04	
Density (g/cm^3)	1.14 (20 °C)	Lide (1995)
Refractive index	1.3826 (20 °C)	Lide (1995)
Melting point (°C)	15	Brabec (1993)
Boiling point (°C)	50.4 (101.3 kPa)	Lide (1995)
Vapour pressure (kPa)	29.33 (~20 °C)	Brabec (1993)
n-Octanol/water partition coefficient (log K_{ow})	–1.65 (calculated)	This report[a]
	–0.85 (measured)	BASF AG (1988)
Water solubility (g/litre)	600 (25 °C)	Hoechst AG (1994)
Henry's law constant		Betterton & Hoffmann (1988)
(Pa·m^3/mol)	≤3.38 × 10^{-4} (25 °C, measured)	
(dimensionless)	≤1.36 × 10^{-7}	

Section A3.1.1/3.1.2/3.1.3/ 3.2/ 3.	Glyoxal anhydrous, Physical chemical parameters

Glyoxal anhydrous, PC data, SCCP (2004)	
Boiling point:	50.4 °C at 1013 hPa (pure substance)
	approximately 105 °C (40% solution)
Vapor pressure:	293.3 hPa at 20 °C (pure substance)
	$<10^{-4}$ hPa (40% solution)
Density:	1.14 g/cm² at 20 °C (pure substance)
	1.27 g/cm² at 20 °C (40% solution)
Log P_{ow}:	-2.54 (calculated)
	-0.85 (experimental)
pH value	2.1 – 2.7 (at 400 g/l, 20 °C)

Glyoxal anhydrous, PC data, BUA (1996)

Section A3.1.1/3.1.2/3.1.3/ 3.2/ 3.	Glyoxal anhydrous, Physical chemical parameters

2.1 Pure Substance

Solidification Point (°C):	15	(Anonymous, 1987; Mattioda & Blanc, 1989; Weast, 1988)
Boiling Point (°C):		
at 1,013 hPa	50.4	(Lösch, 1976; Mattioda & Blanc, 1989; Weast, 1988)
at 1,035 hPa	51	(Anonymous, 1987; Budavari et al., 1989)
Flash Point (°C):	220	(Anonymous, 1987)
Explosion Limit:	Mixtures with air are explosive.	(Budavari et al., 1983)
Density (g/cm^3):		
at 20 °C	1.14	(Hommel, 1983; Lösch, 1976; Mattioda & Blanc, 1989; Budavari et al., 1989)
Gas Density (air = 1):	2.00	(Fassett, 1962)
Vapour Pressure (hPa):		
at 15 °C	208.1	(DIPPR, 1990)
at 20 °C	293.3	(Fassett, 1962)
at 25 °C	345.4	(DIPPR; 1990)
Solubility Glyoxal in Water:	very soluble	(Fassett, 1962)
600 g/l	(80 % glyoxal, powder, in which mostly trimeric hydrates exist)	(Hoechst AG, 1994)

Section A3.1.1/3.1.2/3.1.3/ 3.2/ 3.	Glyoxal anhydrous, Physical chemical parameters

Solubility

Glyoxal in Organic Sovents:	soluble in ethanol and diethyl ether	(Weast, 1988)
pH Value:		
at 20 °C	ca. 4 (at 500 g/l)	(Hoechst AG, 1994)
at 25 °C	ca. 2 (pK_a ~ 3.6)	(OECD, 1992)
Refractive Index:		
$n_D^{20.5}$	1.3826	(Lösch, 1976; Mattioda & Blanc, 1989; Budavari et al., 1989)
Henry's Law Constant (Pa • m^3 • mol^{-1})		
(at 15-25 °C)	≤ 3.38 • 10^{-4} (experimental)	(Betterton & Hoffmann, 1988; see Sect. 6.3.1)
Partition Coefficient (see Sect. 6.3.2):		
n-Octanol/water		
(log P_{ow})	-3.88 (calculated accord. to CLOG 3.42 for the dihydrate)	(OECD, 1992)
	-2.54 (calculated)	(Hoechst AG, 1994)
	-0.85 (experimental)	(BASF AG, 1988)
UV/VIS-Absorption Spectrum:		
Absorption bands (ranges)	480/460-340 nm	(Calvert & Pitts, 1966; Parmenter, 1964)
	320-230 nm	
(no further details)		

Conversion Factor for the Concentration by Volume in the Gaseous Phase into the Concentration by Weight and vice versa:

at 20 °C	1 ppm	Δ	2.41 mg/m^3
	1 mg/m^3	Δ	0.14 ppm
at 25 °C	1 ppm	Δ	2.37 mg/m^3
(1,013 hPa)	1 mg/m^3	Δ	0.42 ppm

References:

1. German Chemical Society Advisory Committee on Existing Chemicals of Environmental Relevance (1996) **BUA** Report 187: Glyoxal (Ethanedial). Stuttgart, S. Hirzel, Wissenschaftliche Verlagsgesellschaft, pp: 1–64, ISBN 3-7776-0824-6, Stuttgart, BPD ID A4_01

Section A3.1.1/3.1.2/3.1.3/ 3.2/ 3.	**Glyoxal anhydrous, Physical chemical parameters**
	2. Schilling K (2004) The Toxicological Dossier of Glyoxal. The European Federation for Cosmetic Ingredients, **SCCP**, BPD ID A6.02_04 3. WHO (2004) The Concise International Chemical Assessment Document **CICAD** 57. The International Program of Chemical Safety of the WHO, IPCS, BPD ID A4_02 4. **INRS** Fiche Toxicologique No 229, Glyoxal et solutions aqueuses, 1995 5. **OECD SIDS** (2001) Glyoxal. SIAM 11
Undertaking of intended data submission [ ]	The available data on Glyoxal anhydrous have been reported in several acknowledged reviews, thus, these data are acceptable and sufficient, and they justify the non-submission of experimental data.
	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	March 2018
Evaluation of applicant's justification	
Conclusion	Agree with applicant’s version
Acceptability	Acceptable
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A3.6	Dissociation constant	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible [ ]** **Scientifically unjustified [X]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]		
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	March 2018	
Evaluation of applicant's justification	QSAR data is not acceptable. No further data is required as based on the chemical structure, no dissociation is expected at environmental pH	
Conclusion	Acceptable	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A3.8 **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**Stability in organic solvents used in b.p. and identity of relevant breakdown products**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]	Not relevant	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	March 2018	
Evaluation of applicant's justification		
Conclusion	Agree with applicant's version	
Acceptability	Acceptable	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section A3.11 **Ann IIA3.8**	**Flammability including auto-flammability and identity of combustion products**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]		
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	March 2018	
Evaluation of applicant's justification	Not a CLP criteria. Data have been provided on self-heating substances and mixtures. See in the table above (BPR 4.11).	
Conclusion	No further data required	
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 IIIB 4 METHODS OF IDENTIFICATION AND ANALYSIS

Section A4.1 **Analytical methods for the determination of pure active substance and where appropriate for relevant degradation products, isomers and impurities of active substance and their additives**

Official use only

Information provided in the confidential information section.

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	March 2019
Materials and methods	
Conclusion	See confidential part
Reliability	
Acceptability	n. a.
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant´s summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A4.2a **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**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:** **a) Soil**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible [ ]** **Scientifically unjustified [X]**	
Limited exposure [X]	**Other justification [ ]**	
Detailed justification:	[redacted]	

Section A4.2a **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**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:** **a) Soil**
	[redacted]
Undertaking of intended data submission [ ]	Not relevant
	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	01/03/2019, 08/01/2020
Evaluation of applicant's justification	[redacted]
Conclusion	A fully validated analytical method for the determination of glyoxal in soil with adequate LOQ will be required at the product authorisation stage if exposure of soil is expected.
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 A4.2b **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**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:** **b) Air**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [X] **Limited exposure [X]**	**Technically not feasible [ ]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification:	[redacted]	

Section A4.2b **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**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:** **b) Air**

[redacted]

Sample Type	Sample Preparation	Detection Method	Detection Limit	Recovery Rate (%)	Literature
Air	derivatization with DNSH, catalysis of the derivatization reaction with acid, extraction of the derivative with CH_2Cl_2 and accumulation in a nitrogen stream	RP-HPLC-FD	37 pg (without specification of the relative volume)	ca. 93 ± 3	Bächmann et al., 1989
Air/room air	sampling with a pump in DNPH-coated C_{18}-cartridges, derivatization, elution of the hydrazone derivative with acetonitrile, direct injection	HPLC-UV (λ_{max} = 437 nm)	n.s. (0.34-2.99 µg/l) (60 l sample)	n.s.	Druzik et al., 1990
Air (workplace air)	reaction with phenylhydrazine-hydro-chloride	photometry λ = 380 nm	0.2 µg/ml prepared sample	n.s.	Yeremian, 1987

Sample Type	Sample Preparation	Detection Method	Detection Limit	Recovery Rate (%)	Literature
Ambient air	sampling in a microimpinger, mixing with aqueous and acidified (HCl) DNPH, alternatively, in a cartridge packed with glass beads coated with acidified (H_3PO_4) DNPH, extraction of the DNPH-derivative in a shaker with a solution of methylene chloride and n-hexane for 15 minutes, washing of the extract with deionized water in order to remove acid and excess DNPH, tranfer of the organic phase into test tubes and concentration until dryness at 60 °C in a vacuum exsiccator, taking up in methanol and injection	RP-HPLC-UV	n.s.	n.s.	Fung & Grosjean, 1981
Marine air	sampling on DNPH-coated C_{18}-cartridges (derivatization with DNPH), elution of the hydrazone derivative with acetonitrile, direct injection	HPLC-UV	0.024 µg based on a 100 l sample	> 95	Zhou & Mopper, 1990b

Section A4.2b

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

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:

b) Air

Sample Type	Sample Preparation	Detection Method	Detection Limit	Recovery Rate (%)	Literature
Cigarette smoke	sampling, trapping of the smoke and filtration through glass-fibre filters, blowing of the water-soluble fraction of the gaseous phase into an aqueous solution of o-phenylenediamine, derivatization, direct injection of the quinoxaline	HPLC-UV photometric detection	n.s.	n.s.	Moree-Testa & Saint-Jalm, 1981
	sampling, trapping of the smoke and filtration through glass-fibre filters, blowing of the water-soluble fraction of the gaseous phase into an aqueous solution of o-phenylenediamine, derivatization, extraction of the filtered samples with chloroform, direct injection	capillary-GC-FID or GC-MS	n.s.	n.s.	Moree-Testa & Saint-Jalm, 1981
Urban air („simulated smog")	derivatization of the sample in an acidic solution with 4-chlorophenylenediamine, heating to 90 °C for 30 minutes, cooling to room temperture, shaking 1-2 minutes with benzene/distilled water, allowing to stand for 10-20 minutes, addition of anhydrous sodium	GC-ECD	n.s.	n.s.	Nojima et al., 1974

Sample Type	Sample Preparation	Detection Method	Detection Limit	Recovery Rate (%)	Literature
Cont. from p. 12	sulfate to the benzene phase (drying), filtration, injection of the filtrate into the GC				
Air („simulated smog")	NO_x-treated, aromatic-containing, UV-illuminated air sample, no further details, direct measurement	FT-IR spectrometer/DOAS	ca. 29 µg/m^3	n.s.	Plum et al., 1983; Tuazon et al., 1984

DNPH 2,4-Dinitrophenylhydrazine
DNSH Dansylhydrazine
DOAS Differential optical absorption
ECD Electron capture detector
FD Fluorescence detector
FID Flame ionization detector
FT-IR Fourier transformation infrared spectroscopy
GC Gas chromatography
HPLC High-pressure liquid chromatography
MS Mass spectrometry
n.s. Not specified
RP Reversed phase
UV Ultraviolet irradiation

[redacted]

Section A4.2b **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**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:** **b) Air**
	[redacted]
Undertaking of intended data submission [ ]	[redacted]

Section A4.2b **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**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:** **b) Air**
	[redacted]
	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*Give date of action*
Evaluation of applicant's justification	*Discuss applicant's justification and, if applicable, deviating view*
Conclusion	*Indicate whether applicant's justification is acceptable or not. If unacceptable because of the reasons discussed above, indicate which action will be required, e.g. submission of specific test/study data*
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	March 2018
Evaluation of applicant's justification	[redacted]
Conclusion	A fully validated analytical method for the determination of glyoxal in air with adequate LOQ should be provided.
Remarks	

Section A4.2b _ 01 Aldehydes 6045; BGIA Workbook, 39th suppl., XI/07

Annex Point IIA, IV.4.1

Official use only

1 REFERENCE

1.1	**Reference**	Assenmacher-Maiworm H and Hahn J-U (2007) Final Report - Aldehydes 6045; BGIA Workbook, 39th suppl., XI/07.
1.2	**Data protection**	Yes
1.2.1	Data owner	[redacted]
1.2.2	Companies with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	The method validated in this report is suitable for measurements performed according to TRGS 402 and meets the requirements if DIN EN 482.
2.2	**GLP**	No
2.3	**Deviations**	Not applicable

3 MATERIALS, METHODS AND RESULTS

3.1	**Preliminary treatment**	
3.1.1	Extraction	Samples of air are collected using a suitable pump to draw ambient air through a Sep-Pak cartridge of silica gel impregnated with 2,4-dinitrophenylhydrazine. The aldehydes, in this case glyoxal and glutaraldehyde, react with the 2,4-dinitrophenylhydrazine to form the corresponding hydrazine. After elution with acetonitrile, the aldehydes are determined qualitatively and quantitatively by HPLC. Residues of the aldehyde are quantified using and external standard method.
3.1.2	Cleanup	Not applicable
3.2	**Detection**	
3.2.1	Separation method	**a) HIGH PERFORMANCE LIQUID CHROMATOGRAPHY: GLYOXAL** REAGENTS Acetonitrile HPLC, UGG or hypergrade. Methanol HPLC, GG or hypergrade. H_3PO_4 80% AR. Glyoxal 40% AR Supelco Carbonyl DNPH mix, Order No. 47649. Supelco Custom Standard 110, Lot No. 1837. Supelco glutaraldehyde DNPH solution, Order No. DE 281.

Section A4.2b _ 01 **Aldehydes 6045; BGIA Workbook, 39th suppl., XI/07**

Annex Point IIA, IV.4.1

APPARATUS

High performance liquid chromatograph equipped with a binary pump, diode array detector and evaluation unit.

CALIBRATION

Glyoxal solution 1: Approximately 30 mg of glyoxal 40% AR was added to a 25 mL volumetric flask and made to volume with water.

Glyoxal solution 2: Approximately 60 mg of glyoxal 40% AR was added to a 25 mL volumetric flask and made to volume with water.

Standard solution: Aliquots of glyoxal solution 1 (200 µL), carbonyl DNPH mix (500 µL) and glutaraldehyde DNPH solution (1000 µL) were transferred to a 2 mL volumetric flask and made to volume with acetonitrile.

Ten different calibration solutions were prepared over the range 0.10 to 1.0 mg/L by applying between 20 and 200 µL of standard solution to a Sep-Pak cartridge before pumping purified laboratory air through the cartridge at a flow rate of 20 L/hour for 1 hour. The cartridges were then stored refrigerated for 48 hours prior to elution with acetonitrile (approximately 9.5 mL) into a 10 mL volumetric flask. After the addition of H_3PO_4 (50 µL), the solution is made to volume with acetonitrile. After storing the flask refrigerated for 48 hours, the solution was passed through a syringe filter.

TEST SOLUTION

Determination of precision: An aliquot of the standard solution (100 µL) was applied to a Sep Pak cartridge before pumping purified laboratory air through the cartridge at a flow rate of 20 L/hour for 1 hour. The cartridge was then stored refrigerated for 48 hours prior to elution with acetonitrile (approximately 9.5 mL) into a 10 mL volumetric flask. After the addition of H_3PO_4 (50 µL), the solution is made to volume with acetonitrile. After storing the flask refrigerated for 48 hours, the solution was passed through a syringe filter. The resulting solution was then analysed by HPLC/DAD under the conditions described below.

Determination of accuracy: Aliquots of the glyoxal solution 2 (50 µL) and the Supelco custom standard 110 (500 µL) were added to a 1 mL volumetric flask and made to volume with acetonitrile. An aliquot of the solution (200 µL) was applied to a Sep Pak cartridge before pumping purified laboratory air through the cartridge at a flow rate of 20 L/hour for 1 hour. The cartridge was then stored refrigerated for 48 hours prior to elution with acetonitrile (approximately 9.5 mL) into a 10 mL volumetric flask. After the addition of H_3PO_4 (50 µL), the solution is made to volume with acetonitrile. After storing the flask refrigerated for 48 hours, the solution was passed through a syringe filter. The resulting solution was then analysed by HPLC/DAD under the conditions described below.

Section A4.2b _ 01 **Aldehydes 6045; BGIA Workbook, 39th suppl., XI/07**

Annex Point IIA, IV.4.1

CONDITIONS

Column:	Prontosil 120-5-C18 ACE-EPS, 5 µm, 250 x 4 mm
Column temperature:	23°C
Flow:	1.0 mL/min
Eluent A:	Acetonitrile/water/methanol, 32:40:40, v/v/v
Eluent B:	Acetonitrile

Gradient:

0-3 mins	100% A
3-10 mins	>12% B
10-17 mins	12% B
17-30 mins	>30% B
30-34 mins	30% B
34 mins	>100% B
34-36 mins	100% B
36 mins	>100% A

DAD settings: 365/8 nm, Ref. 550/80 nm

3.2.2	Detector	Diode array detector (DAD)
3.2.3	Standard(s)	Glyoxal 40% AR; Supelco Glutaraldehyde DNPH solution.
3.2.4	Interfering substance(s)	See 3.4
3.3	**Linearity**	
3.3.1	Calibration range	0.10 to 1.0 mg/L.
3.3.2	Number of measurements	Ten different calibration solutions were prepared over the range 0.10 to 1.0 mg/L.
3.3.3	Linearity	No data provided for glyoxal or glutaraldehyde.
3.4	**Specificity: interfering substances**	No data provided for glyoxal or glutaraldehyde.
3.5	**Recovery rates at different levels**	
3.5.1	Relative standard deviation	For the determination of glyoxal, the coefficient of variation is 1.3. For the determination of glutaraldehyde, the coefficient of variation is 1.1.

Section A4.2b _ 01 **Aldehydes 6045; BGIA Workbook, 39th suppl., XI/07**

Annex Point IIA, IV.4.1

3.6 Limit of determination

For the determination of glyoxal, the limit of determination coefficient of variation is 0.039 mg/m^3.

For the determination of glyoxal, the limit of determination coefficient of variation is 0.035 mg/m^3.

3.7 Precision

3.7.1 Repeatability

In every analysis, six cartridges were exposed in order to assess recovery rate and the precision values were as follows:

Substance	Concentration (mg/m^3)	Precision (%)	Expanded measurement uncertainty (%)
Glyoxal	0.10 1.0 2.0	4.23 1.94 2.42	15.83 16.23 16.87
Glutaraldehyde	0.060 0.60 1.2	2.24 3.74 2.92	19.02 20.40 15.48

The expanded measurement uncertainty was calculated according to DIN EN 482.

Recovery:

For the determination of glyoxal over the range 0.039 to 2.0 mg/m^3, the mean recovery was 96%.

For the determination of glutaraldehyde over the range 0.039 to 2.0 mg/m^3, the mean recovery was 97%.

3.7.2 Independent laboratory validation

Not required for this study.

Section A4.2b _ 01 **Aldehydes 6045; BGIA Workbook, 39th suppl., XI/07**

Annex Point IIA, IV.4.1

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods

The method was successfully validated for the determination of glyoxal and glutaraldehyde in air incorporating qualitative and quantitative determination by HPLC with DAD detection.

Characteristics of the method are as follows:

Substance	Validation range (mg/m^3)	Average recovery (%)	Quantitation limit for 20L air (mg/m^3)	Coefficient of variation of the method
Glyoxal	0.039 - 2.0	96	0.039	1.3
Glutaralde-hyde	0.035 - 1.2	97	0.035	1.1

4.2 Conclusion

A method has been successfully validated in this study for the determination of residues of glyoxal and glutaraldehyde in air over the concentration ranges 0.039 to 2.0 mg/m^3 and 0.035 to 1.2 mg/m^3, respectively.

4.2.1 Reliability [redacted]

4.2.2 Deficiencies [redacted]

Section A4.2b _ 01 **Aldehydes 6045; BGIA Workbook, 39th suppl., XI/07**

Annex Point IIA, IV.4.1

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	March 2018
Materials and methods	The provided analytical method is not considered sufficiently validated based on the data provided. Data on linearity and specificity are missing. Moreover regarding recovery data there is only a mean of different levels (0.039-2 mg/m^3). No data is provided on recovery rates at each level. It is not clear how has been determined the LOQ of the method. Indeed, recovery rates seem to be determined at 0.1; 1 and 2 mg/m^3 and the lowest calibration point is 0.1 mg/m^3. Therefore the value of 0.039 mg/m3 is outside the calibration range and is not the lowest recovery rate.
Conclusion	Agree with applicant's version however the provided analytical method is not sufficiently validated. It remains uncertainties. A fully validated analytical method for the determination of glyoxal in air with adequate LOQ should be provided.
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant´s summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A4.2c **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**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**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [X] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [ ]** **Other justification [ ]**	

Detailed justification:

Several methods for detection of glyoxal in water, including drinking water, surface water and sediment, have been published between 1980 and 2000. Reviews of these methods are available from the BUA report 187 [1] and from the CICAD 57 [2]. These reviews are summarised here.

Preparation	**Detection Method and Limit**	**Recovery rate (%)**	**Suitable / tested for / with**	**Ref.**
Aqueous-phase PFBHA derivatization followed by hexane extraction	GC-ECD 0.13-0.39 µg/L	no data	Water in general	[3]
Derivatization with o-phenylenediamine to quinoxaline	HPLC/UV no data	no data	Water in general; alcoholic beverages	[4]
Addition of $Na_2S_2O_3$, derivatization with PFBOA, pH adjustments, heating	GC-MS/UV 26 µg/L	82–99	Water in general	[5]

Section A4.2c Annex Point IIA4.1/4.2 & IIIA-IV.1	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				
	to 80°C, cooling, addition of H_2SO_4, hexane extraction, mixing with Na_2SO_4				
	Dissolution in n-hexane/ethyl acetate, separation on silica gel, derivatization with DMB, dissolution in water, heating to 70°C, extraction with chloroform, drying, taking up in methanol	RP-HPLC-FD 4.64 pg/µL injected sample	no data	Water in general	[6]
	2,4-DNPH derivatization followed by dichloromethane extraction	a) HPLC b) GC-MS c) MS no data	no data	Water in general; rain, fog, mist	[7]
	Aqueous-phase PFBHA derivatization to pentafluorobenzyl oxime, acidification with H_2SO_4, extraction with n-hexane	a) GC-ECD 5.1 µg/L b) GC-MS/SIM 7.7 µg/L	no data	Drinking water	[8,9]
	Addition of	GC-ECD	91–99	Distilled	[10]

Section A4.2c Annex Point IIA4.1/4.2 & IIIA-IV.1	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				
	NH_3OHCl and HCl, washing with benzene, separation of aqueous phase, derivatization with 4-chlor-o-phylenediamine, heating to 90°C, cooling, extraction with benzene, washing with dest. H_2O, drying with Na_2SO_4, filtration	1 µg/L		tap water, surface water, industrial waste water	
	Filtration, fixation with $HgCl_2$, acidification with HCl, derivatization with 2,4-DNPH, taking up in acetonitrile	RP-HPLC-UV 0.295 µg/L	no data	Seawater, brackish water	[11]
	Derivatization with DNPH	RP-HPLC-UV 0.058-0.116 µg/L	94–102	Seawater	[12]
	Derivatization with PFBOA, saturation with NaCl, acidification with H_2SO_4, extraction	GC-MS 0.3 µg/L	no data	Surface water (ozonized), waste	[9]

Section A4.2c Annex Point IIA4.1/4.2 & IIIA-IV.1	**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**

with n-hexane, drying with Na_2SO_4			water	
Shaking with NH_3OHCl and dest. H_2O, filtration, addition of HCl, washing with benzene, derivatization with 4-chlor-o-phylenediamine, heating to 90°C, cooling, extraction with benzene, washing with dest. H_2O, drying with Na_2SO_4, filtration	GC-ECD 0.02 mg/kg	89	Sediment	[10]

References

[1] BUA Report 187: Glyoxal (Ethanedial), GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance (BUA), Feb 1996; Publisher: S. Hirzel Wissenschaftliche Verlagsgesellschaft, ISBN 3-7776-0824-6, Stuttgart (1998), BPD ID A4_01

[2] CICAD 57: Glyoxal, Concise International Chemical Assessment Document, 1st draft prepared by Kiehlhorn J, Pohlenz-Michel C, Schmidt S and Mangelsdorf I, Fraunhofer Institute for Experimental Medicine, Hanover, Germany, published by WHO, Geneva (2004), BPD ID A4_02

[3] US EPA (1999) Determination of carbonyl compounds in drinking water by fast gas chromatography. Washington, DC, US Environmental Protection Agency, Office of Research and Development, September 1999, pp. 1–38 (Method 556.1)

[4] Barros A, Rodrigues JA, Almeida PJ, Oliva-Teles MT (1999) Determination of glyoxal, methylglyoxal, and diacetyl in selected beer and wine, by HPLC with UV spectrophotometric detection, after

Section A4.2c **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**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**	
	derivatization with o-phenylenediamine. Journal of Liquid Chromatography and Related Technology 22(13), 2061–2069 [5] Cancilla DA, Chou C-C, Barthel R, Que Hee SS (1992) Characterization of the O-(2,3,4,5 ,6-pentafluorobenzyl)-hydroxylamine hydrochloride (PFBOA) derivatives of some aliphatic mono- and dialdehydes and quantitative water analysis of these aldehydes. J. AOAC Int. 75, 842–853 [6] Hara S, Yamaguchi M, Takemori Y, Yoshitake T, Nakamura M (1988) 1,2-diamino-4,5-methylenedioxybenzene as a highly sensitive fluorogenic reagent for a-dicarbonyl compounds. Anal. Chim. Acta 215, 267–276 [7] Steinberg S, Kaplan I (1984) The determination of low molecular weight aldehydes in rain, fog and mist by reversed phase liquid chromatography of the 2,4-dinitrophenylhydrazone derivatives. International Journal of Environmental and Analytical Chemistry 18, 253–266 [8] Glaze WH, Koga M, Cancilla D (1989) Ozonation byproducts. 2. Improvement of an aqueous-phase derivatization method for the detection of formaldehyde and other carbonyl compounds formed by the ozonation of drinking water. Environ. Sci. Res. 23, 838–847 [9] Le Lacheur RM, Singer PC, Charles MJ (1991) Disinfection by-products in New Jersey drinking waters. Proc. Ann. Conf., Am. Water Works Assoc. 61-5, 791–805 [10] Kawata K, Ozaki K, Mukai H (1980) Gas chromatographic determination of micro amount of glyoxal in water and sediment. Bunseki Kagaku 29, 517–522 [11] Edelkraut F, Brockmann U (1990) Simultaneous determination of carboxylic acids and carbonyl compounds in estuaries by HPLC. Chromatographia 30, 432–435 [12] Mopper K, Stahovec WL (1986) Sources and sinks of low molecular weight organic carbonyl compounds in seawater. Mar. Chem. 19, 305–321	
Undertaking of intended data submission [X]	[redacted]	

Section A4.2c **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**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**
	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	March 2018
Evaluation of applicant's justification	Only bibliographical data have been provided with limited or absent validation data which is not sufficient.
Conclusion	A fully validated analytical method with adequate LOQ should be provided. In addition, sufficient information should be submitted to determine the background concentration in water.
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 A4.2c_01
Annex Point IIA, IV.4.2

Method Validation for the Determination of Glyoxal in Water

Official use only

1 REFERENCE

1.1	**Reference**	[redacted] BPD ID A4.2c_01.
1.2	**Data protection**	Yes
1.2.1	Data owner	[redacted]
1.2.2	Companies with letter of access	[redacted]
1.2.3	Criteria for data protection	[redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	No guideline mentioned; the analytical methods were prepared and validated [redacted] Method: Oximation of glyoxal, GC/MS, quantification with standard addition
2.2	**GLP**	Yes
2.3	**Deviations**	Not applicable

3 MATERIALS, METHODS AND RESULTS

3.1	**Preliminary treatment**	
3.1.1	Extraction	Not applicable
3.1.2	Cleanup	Not applicable
3.2	Detection	
3.2.1	Separation method	Oximation of glyoxal, GC/MS, quantification with standard addition CAPILLARY GAS CHROMATOGRAPHY EQUIPPED WITH SPLIT/SPLITLESS INJECTOR AND MASS SPECTROMETER DETECTOR (MSD) REAGENTS - Drinking water: Sampling point: [redacted] total hardness 12 °dH, TOC 5 mg/L, pH = 7.9 - Surface water [redacted] total hardness 10 °dH, TOC 2 mg/L, pH = 7.1, residue after filtration < 50 mg/L

Section A4.2c_01
Annex Point IIA, IV.4.2

Method Validation for the Determination of Glyoxal in Water

[redacted] glyoxal in water:
Chemical identity: Oxaldehyde, glyoxal, [redacted] solution in water
Batch identification: [redacted]
Date of production: [redacted]

- Glutaraldehyde, solution in water, [redacted] standard
- O-(2,3,4,5,6-Pentafluorobenzyl)-hydroxylamine hydrochloride (PFBHA)
- n-Hexane
- Hydrochloric acid, c(HCl) = 0.1 mol//ptp
- Sodium sulfate, anhydrous
- Water, for liquid chromatography, "[redacted]"
- Methane 4.5, reactand gas for chemical ionization

APPARATUS

Capillary gas chromatograph equipped with split/splitless injector and mass spectrometer detector (MSD)

CALIBRATION SOLUTIONS

Six different solutions were prepared out of three dilutions from two stock solutions containing six different quantities of gyloxal in the range of 5.76 to 92.0 µg/L. Calibration solutions were prepared by adding an aliquot of a diluted stock solution, 100 µL of the solution of the internal standard (glutaraldehyde, 651.8 ng/100 µL) and 1 mL of reagent solution to 50 mL of drinking water or surface water.

TEST SOLUTIONS

Drinking water:

500 mL of drinking water were spiked with the test item. The mixture was homogenized Then aliquots of 50 mL each were taken. Two test solutions were prepared:

Drinking test solution 1: β (glyoxal) = 4.60 µg/L

Drinking test solution 2: β (glyoxal) = 43.2 µg/L

Surface water:

500 mL of surface water were spiked with the test item. The mixture was homogenized Then aliquots of 50 mL each were taken.

Two test solutions were prepared:

Surface water sample 1: β (glyoxal) = 4.60 µg/L

Surface water sample 2: β (glyoxal) = 43.2 µg/L

SAMPLE PREPARATION

100 µL of the solution of the internal standard and 1 mL of reagent solution were added to 50 mL of a test solution. The mixture was heated at 70 °C for 2 h. Then it was allowed to cool down. Subsequently it was extracted twice with 2 mL of n-hexane each. The hexane phases were collected, washed 3 times with 1 mL of hydrochloric acid each and dried over sodium

sulfate.

Calibration solutions and test solutions were treated similarily: In order to determine reagent blanks 1 mL of the reagent solution was added either to 50.1 mL of water (blank without internal standard) or to a mixture of 50 mL of water and 100 µL of the solution of the internal standard.

CONDITIONS

GC:	Fused silica capillary:	[redacted]
	Length:	30 m
	Internal diameter:	0.25 mm
	Film thickness:	0.25 µm
Carrier gas:	Helium	
	Constant flow:	1.2 mL/min
	Injection:	Splitless, duration 0.5 min
Temperatures:		
	Oven:	50 °C isothermal for 1 min
		50 °C → 280 °C, 10 K/min
		280 °C, isothermal for 10 min
	Injector:	250 °C

Injection volume: 1 µL

3.2.2 Detector

Mass spectrometer detector (MSD)

Negative chemical ionization with methane as reactand gas

Individual masses were monitored in selected ion mode (SIM) as follows:

Glyoxal: m/z = 267, m/z = 196, m/z = 167

Glutaraldehyde: m/z = 450, m/z = 470, m/z = 178

3.2.3 Standard(s)

Glutaraldehyde

3.2.4 Interfering substance(s)

See 3.4

Section A4.2c_01
Annex Point IIA, IV.4.2

Method Validation for the Determination of Glyoxal in Water

3.3	**Linearity**		
3.3.1	Calibration range	a) Matrix: Drinking water: 5.76 to 46.0 µg/L b) Matrix: Surface water: 5.76 to 92.0 µg/L	
3.3.2	Number of measurements	Six concentration levels	X
3.3.3	Linearity	a) Matrix: Drinking water: a. Slope: 1.080 b. Intercept: -1.592 c. Coefficient of correlation: 0.9877 b) Matrix: Surface water: a. Slope: 0.797 b. Intercept: -2.036 c. Coefficient of correlation: 0.9939	

Section A4.2c_01
Annex Point IIA, IV.4.2

Method Validation for the Determination of Glyoxal in Water

3.4 Specifity: interfering substances

Peaks in the gas chromatogram are assigned to the analyte glyoxal by comparison of retention times and by the selection of characteristic ions in MS-detection. Constituents of the sample which coelute with the analyte and which yield the same ions as selected for glyoxal give rise to excessively high mass fractions. Constituents in the sample having the same retention time as the internal standard and the same ions as selected for glutaraldehyde give rise to underestimates.

Retention times are listed below:

Glyoxal: 18.0 min

Glutaraldehyde: 20.4 min

3.5 Recovery rates at different levels

Two test solutions each of glyoxal in drinking water and surface water were prepared in order to determine accuracy and precision of the method. These solutions were analysed 6 times each. X

Matrix: Drinking water:

Spiked with 43.2 µg/L glyoxal:

Determination No.	Analytical value [µg/L]	Recovery [%]	Arithmetic mean of recoveries [%]
1	21.60	50	46
2	20.20	47	
3	23.90	55	
4	18.80	44	
5	18.50	43	
6	16.60	38	

It cannot be accounted for the low mean recovery of the 6-fold analysis which is only 46 %, especially since the recoveries which were calculated for the calibration are satisfactory with an arithmetic mean of 104 %.

Calibration No.	Concentration level of calibration [µg/L]	Analytical value [µg/L]	Recovery [%]	Arithmetic mean of recoveries [%]
1	5.76	6.62	115	104
2	14.4	11.7	81	
3	23.0	25.8	112	
4	28.8	29.9	104	
5	46.0	50.8	110	
6	92.0	~~66.0~~	~~72~~	

Calibration no. 6 was regarded as an outlier and hence not considered for the calculation.

Section A4.2c_01
Annex Point IIA, IV.4.2

Method Validation for the Determination of Glyoxal in Water

Matrix: Surface water:

Spiked with 4.60 µg/L glyoxal:

Determination No.	Analytical value [µg/L]	Recovery [%]	Arithmetic mean of recoveries [%]
1	5.86	127	128
2	6.09	132	
3	6.55	142	
4	6.45	140	
5	4.92	107	
6	5.47	119	

Spiked with 43.2 µg/L glyoxal:

Determination No.	Analytical value [µg/L]	Recovery [%]	Arithmetic mean of recoveries [%]
1	58.2	135	132
2	63.6	147	
3	51.9	120	
4	57.5	133	
5	55.5	128	
6	54.5	126	

As in the case of drinking water recoveries which were calculated for the calibration are satisfactory with an arithmetic mean of 103 %.

Calibration No.	Concentration level of calibration [µg/L]	Analytical value [µg/L]	Recovery [%]	Arithmetic mean of recoveries [%]
1	5.76	6.51	113	103
2	14.4	11.9	83	
3	23.0	23.8	103	
4	28.8	30.0	104	
5	46.0	45.0	98	
6	92.0	105	114	

Section A4.2c_01
Annex Point IIA, IV.4.2

Method Validation for the Determination of Glyoxal in Water

3.5.1	Relative standard deviation	**Matrix: Drinking water:** Relative standard deviation: 43.2 µg/L glyoxal: 13% **Matrix: Surface water:** Relative standard deviation: 4.60 µg/L glyoxal: 11% Relative standard deviation: 43.2 µg/L glyoxal: 7.0%	
3.6	**Limit of determination**	The limits of quantification (LOQ) were estimated based on the calibrations at the lowest concentration levels. It was taken into account that the LOQ should exceed the blank at least by a factor of 5. The limits of detection (LOD) were calculated as follows: LOD = 0.3 * LOQ Drinking water: LOQ: 5 µg/L LOD: 1.5 µg/L Surface water: LOQ: 3 µg/L LOD: 1 µg/L	X
3.7	**Precision**		
3.7.1	Repeatability	The measurement uncertainties of the test method are estimated. They are calculated by multiplication of the standard deviations by a factor of 3. a) Drinking water, spiked with 43.2 µg/L glyoxal Analytical values: 21.6, 20.2, 23.9, 18.8, 18.5, 16.6 µg/L Arithmetic mean: 19.9 µg/L Std. dev.: 2.57 µg/L Rel. std. dev.: 13% Measurement uncertainty: 7.71 µg/L Rel. measurement uncertainty: 39% b) Surface water, spiked with 4.60 µg/L glyoxal Analytical values: 5.86, 6.09, 6.55, 6.45, 4.92, 5.47 µg/L Arithmetic mean: 5.9 µg/L Std. dev.: 0.62 µg/L Rel. std. dev.: 11% Measurement uncertainty: 1.86 µg/L Rel. measurement uncertainty: 33% c) Surface water, spiked with 43.2 µg/L glyoxal Analytical values: 58.2, 63.6, 51.9, 57.5, 55.5, 54.5 µg/L Arithmetic mean: 56.9 µg/L Std. dev.: 3.99 µg/L Rel. std. dev.: 7.0% Measurement uncertainty: 12.0 µg/L Rel. measurement uncertainty: 21%	
3.7.2	Independent laboratory validation	Not in this study.	

Section A4.2c_01

Annex Point IIA, IV.4.2

Method Validation for the Determination of Glyoxal in Water

C) APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods

This study presents the validation of a method for the determination of glyoxal in water. The method is the oximation of glyoxal and the quantification via GC/MS with standard addition.

4.2 Conclusion

[redacted]

[redacted]

The mean recovery of glyoxal in drinking water spiked with glyoxal was low (46%), although the mean recovery for the calibration was satisfactory (104%).

The mean recovery for the calibration with surface water was satisfactory as well (103%). In contrast to this, the mean recoveries for surface water spiked with glyoxal were too high (4.60 µg/L: 128%; 43.2 µg/L: 132%).

4.2.1 Reliability [redacted]

4.2.2 Deficiencies [redacted]

Section A4.2c_01
Annex Point IIA, IV.4.2

Method Validation for the Determination of Glyoxal in 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	March 2018
Materials and methods	**3.3.2 Number of measurements** *6 concentration levels*, but the last concentration is an outlier for drinking water **3.5 Recovery rates at different levels** The recovery rates for drinking and surface water are not acceptable. Indeed, according to the provided acceptable recoveries calculated with the calibration there is a discrepancy but there is no fully satisfactory explanation for the observed discrepancy. **3.6 Limit of determination** *The limits of quantification (LOQ) were estimated based on the calibrations at the lowest concentration levels. It was taken into account that the LOQ should exceed the blank at least by a factor of 5.* This is not acceptable, the LOQ should be the lowest fortification level with acceptable mean recovery.
Conclusion	Agree with applicant's version with above amendments. The provided method is not acceptable. A fully validated analytical method for the determination of glyoxal in water with LOQ below 0.1µg/L for drinking water and below the PNEC water for surface water should be provided.
Reliability	[redacted]
Acceptability	Not acceptable. Recovery and LOQ are not 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 A4.2c_02

Annex Point IIA, IV.4.2

Analytical Method for the Determination of Glyoxal in Water

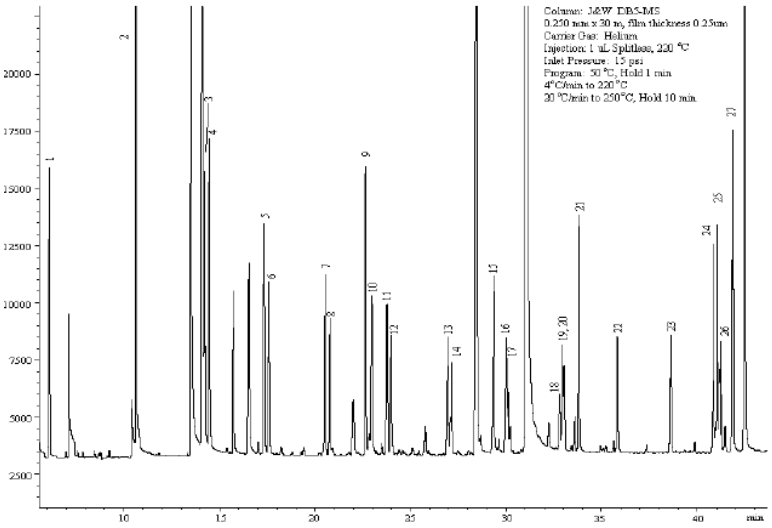
			Official use only
		1 REFERENCE	
1.1	**Reference**	Munch, J.W., Munch D.J. and Winslow, S.D. (1998) EPA Method 556: Determination of carbonyl compounds in drinking water by pentafluorobenzylhydroxylamine derivatization and capillary gas chromatography with electron capture detection, Cincinnati, published, BPD ID A4.2c_02.	
1.2	**Data protection**	No	
1.2.1	Data owner	Published study in the open domain	
1.2.2	Companies with letter of access	Not applicable (N/A)	
1.2.3	Criteria for data protection	N/A	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	No guideline mentioned.	
2.2	**GLP**	No	
2.3	**Deviations**	N/A	
		3 MATERIALS, METHODS AND RESULTS	
3.1	**Preliminary treatment**		
3.1.1	Extraction	Water samples are pH adjusted to pH 4 with potassium hydrogen phthalate; then the derivatization reagent Pentafluorobenzylhydroxylamine (PFBHA) is added and the reaction is allowed to complete within 2 h at 35°C. The oxime is extracted from the water with hexane. An acidic wash step is used to minimize unreacted PFBHA in the hexane.	
3.1.2	Cleanup	N/A	
3.2	Detection		
3.2.1	Separation method	Capillary GC equipped with split/splitless injector. Column: 30 m x 0.25 mm J&W DB-5ms, 0.25 µm film thickness. Carrier gas helium. Injector temp. 220°C; head pressure 15 psi; detector temperature 300°C; splitless injector; 1 min split delay; temp Program: 50°C for 1 min, program at 4°C/min to 220°C; program at 20°C/min to 250°C and hold at 250°C for 10 min.	
3.2.2	Detector	Electron capture detector (ECD). Detector gas P5 Argon/Methane	
3.2.3	Standard(s)	An internal standard is used: 1,2-dibromopropane. For the calibration, standard solutions of glyoxal from a reputable commercial source should be used.	

Section A4.2c_02 Annex Point IIA, IV.4.2	Analytical Method for the Determination of Glyoxal in Water

3.2.4	Interfering substance(s)	The method as described for glyoxal does not show interferences with signals from other aldehydes or ketones in the water sample. Chlorine in the water sample or microorganisms may interfere, but according to the method addition of ammonium compounds and copper sulfate, respectively, can minimize interfering effects. Contamination of the reagent water with aldehydes can be reduced by exposing the reagent water to UV light or by distillation with permanganate. Aldehyde contaminations on equipment can be minimized by using non-Latex gloves and by minimizing exposure of reagent and sample to air (formaldehyde source), and by the use of polypropylene (not phenolic resin) caps.
3.3	**Linearity**	
3.3.1	Calibration range	2 – 40 µg/L
3.3.2	Number of measurements	5
3.3.3	Linearity	Not reported: The method prescribes the analyst to measure a calibration curve before start of analysis. As this is an official standard method from the US-EPA (i.e. a specific method with an official status). It is assumed that the method is validated and the linearity is satisfactory.

Section A4.2c_02 **Annex Point IIA, IV.4.2**	**Analytical Method for the Determination of Glyoxal in Water**

3.4 Specifity: interfering substances	The method is specific for glyoxal via the retention time in the chromatogram. On the column and conditions as described, the two peaks of glyoxal after derivatization (2 oxime isomers) are at 40.87 min and 41.09 min, respectively. In the chromatogram below the 2 peaks due to glyoxal are nr. 24 and 25. The other peaks are due to other carbonyl compounds that can be analyzed by the same method.



Interfering substances: see comment at 3.2.4

3.5 Recovery rates at different levels	In reagent water, for a fortified concentration of 20 µg/L (8 determinations; n=8) a mean accuracy of 92% was found. In chlorinated tap water and 20 µg/L fortification level the mean accuracy was 112% (n=4), In untreated surfaces water at 20 µg/L the mean accuracy (n=4) was 102%.
3.5.1 Relative standard deviation	In reagent water, for a fortified concentration of 20 µg/L (8 determinations; n=8) the RSD was 3.1%. In chlorinated tap water and 20 µg/L fortification level the RSD was 3.5% (n=4), In untreated surfaces water at 20 µg/L the RSD was 5.4% (n=4).
3.6 Limit of determination	The method detection limit is reported to be 0.59 µg/L. The limits of quantification (LOQ) can be calculated following LOD = 0.3 * LOQ. LOQ = 2 µg/L, also in accordance with the lowest end of the calibration range.
3.7 Precision	
3.7.1 Repeatability	In reagent water, for a fortified concentration of 20 µg/L (8 determinations; n=8) the RSD was 3.1%. In chlorinated tap water and 20 µg/L fortification level the RSD was 3.5% (n=4), In untreated surfaces water at 20 µg/L the RSD was 5.4% (n=4).
3.7.2 Independent laboratory validation	Several method performance parameters have been assessed in a separate laboratory. Method performance in both laboratories was similar.

Section A4.2c_02

Annex Point IIA, IV.4.2

Analytical Method for the Determination of Glyoxal in Water

4 APPLICANT'S SUMMARY AND CONCLUSION

4.1 Materials and methods

Using this official EPA method traces of glyoxal in water down to 2 µg/L can be determined. The method is based on a derivatization of the aldehyde with pentafluorobenzylhydroxylamine in water followed by extraction with hexane. The sample is then analyzed by GC with electron capture detection. Recovery rate of 92% in reagent water is acceptable with respect to the requirements 70-110%. RSD are all <20%.

4.2 Conclusion

4.2.1 Reliability **2**

4.2.2 Deficiencies Not all validation parameters and raw data are reported in this document. However, this method is a standard method of the US-EPA authority (i.e. a specific method with official status) and can be assumed to be fully validated and suitable, in accordance with the BPR guidance *Guidance on the BPR: Volume I. Part A Chapter II: Requirements for Active Substances Version 1.1 November 2014, Page 71, section 5.2.*

Section A4.2c_02 Annex Point IIA, IV.4.2	Analytical Method for the Determination of Glyoxal in 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	March 2018
Materials and methods	**3.6 Limit of determination** The LOQ of the method is too high for drinking water. The LOQ should be lower than 0.1µg/L.
Conclusion	Agree with applicant's version with above amendments. The provided analytical method is not sufficient. A fully validated analytical method for the determination of glyoxal in water with adequate LOQ should be provided. In addition, sufficient information should be submitted to determine the background concentration in water.
Reliability	3
Acceptability	Not acceptable as the LOQ is too high for drinking water
Remarks	
	COMMENTS FROM ...
Date	*Give date of comments submitted*
Results and discussion	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant´s summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section A4.2d Annex Point IIA4.1/4.2 & IIIA-IV.1	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: **(d) Animal and human body fluids and tissues**

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only

Section A4.2d **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**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:** **(d) Animal and human body fluids and tissues**	
Other existing data [ ] **Limited exposure [X]**	**Technically not feasible [ ]** **Scientifically unjustified [ ]** **Other justification [ ]**	
Detailed justification:	Some data about glyoxal in body fluid and tissues are available from literature. In the CICAD review (2004) it was reported that glyoxal is produced endogenously and is commonly present in blood plasma of healthy subjects, with one study giving values of about 67 ng/ml (corresponding to about 1.16 µmol/litre); other data were mentioned in the review reporting values of 0.23 µmol/L and 0.3 µmol/L. Referring to analytical methods, a recent study was published by Neng and coworkers (2007), who had developed a method for the determination of glyoxal (Gly) in different matrices including urine samples. The method is based on Stir bar sorptive extraction with *in-situ* derivatization using 2,3-diaminonaphthalene (DAN) followed by liquid desorption and high performance liquid chromatography with diode array detection (SBSE(DAN)*in-situ*-LD-HPLC-DAD). The authors found out that the analytical performance showed good accuracy, suitable precision (<12.0%), low detection limits (15 ng/L for glyoxal) and excellent linear dynamic ranges ($r2 > 0.99$) from 0.1 to 120.0 µg/L; they reported that by using the standard addition method, the application of the present method to tap and swimming-pool water, beer, yeast cells suspension and urine samples allowed very good performance at the trace level. Zardari and corworkers (2009) used capillary gas chromatography analysis for detecting glyoxal and methylglyoxal in the serum and urine of diabetic patients after use of 2,3-Diamino-2,3-dimethylbutane as derivatizing reagent. Following values were reported:	

Section A4.2d Annex Point IIA4.1/4.2 & IIIA-IV.1	**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:** **(d) Animal and human body fluids and tissues**

Table 2. Results from GC analysis of glyoxal and methylglyoxal in urine from diabetic patients

No.	Age (sex)	Blood glucose level (mg dL^{-1})	Average amount of glyoxal, μg mL^{-1} (RSD, %, $n = 3$)	Average amount of methylglyoxal, μg mL^{-1} (RSD, %, $n = 3$)
1	41 (Male)	405	0.24 (1.0)	0.25 (0.9)
2	55 (Male)	481	0.40 (1.1)	0.30 (0.8)
3	32 (Male)	480	0.32 (1.2)	0.36 (1.2)
4	35 (Male)	370	0.18 (1.0)	0.28 (1.0)
5	45 (Female)	410	0.23 (1.0)	0.35 (1.2)
6	33 (Male)	390	0.21 (1.1)	0.29 (1.0)
7[a]	50 (Male)	350	0.19 (1.0) 0.17 (1.2)[a]	0.21(1.1) 0.23 (1.0)[a]
8	45 (Male)	370	0.18 (1.0)	0.19 (0.8)

[a] Internal standard

Table 3. Results from GC analysis of glyoxal and methylglyoxal in serum from a healthy volunteer

No.	Age (sex)	Blood glucose level (mg dL^{-1})	Average amount of glyoxal, μg mL^{-1} (RSD, %, $n = 3$)	Average amount of methylglyoxal, μg mL^{-1} (RSD, %, $n = 3$)
1	29 (Male)	125	0.05 (1.0)	0.04 (1.2)
2	33 (Male)	135	0.06 (0.9)	0.04 (1.1)
3	30 (Female)	155	0.06 (1.0)	0.05 (1.0)
4	29 (Male)	158	0.08 (1.2)	0.05 (1.0)
5	35 (Male)	160	0.08 (1.0)	0.10 (1.1)
6	35 (Female)	170	0.07 (1.1)	0.09 (1.0)
7	28 (Male)	168	0.08 (1.0)	0.10 (1.0)

The method was described by the authors as a simple and sensitive gas chromatography(GC) method for analysis of glyoxal and methylglyoxal as markers for diabetic patients. Dimethylglyoxal was used as internal standard. The linear calibration range and LOD of 0.06– 1.33 μg/mL and 10–20 ng/mL, respectively, were found suitable for analysis of the compounds in biological fluids. The detection limit for glyoxal was reported to be 20 ng/mL, and amounts of glyoxal in serum from healthy volunteers were 0.05–0.08 μg/mL

Because of the scheduled use patterns of glyoxal, it is unlikely that the chemical reaches animal or human body fluids and tissues in relevant amounts. Moreover, in the kinetic and metabolism studies BPD ID A6.02_01 and BPD ID A6.02_02 it was found that Glyoxal is extensively metabolized in rats and was not detected in any excreta and tissue samples. This is due to the highly reactive nature of Glyoxal, e.g. with regard to proteins.

References

[1] WHO (2004) The Concise International Chemical Assessment Document CICAD 57. The International Program of Chemical Safety of the WHO, IPCS, BPD ID A4_02

[2] German Chemical Society Advisory Committee on Existing Chemicals of Environmental Relevance (1996) BUA Report 187:

Section A4.2d **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**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:** **(d) Animal and human body fluids and tissues**	
	Glyoxal (Ethanedial). Stuttgart, S. Hirzel, Wissenschaftliche Verlagsgesellschaft, pp: 1–64, ISBN 3-7776-0824-6, Stuttgart, BPD ID A4_01 [5] Neng, Cordeireo, Freire, Nogueira (2007) Determination of glyoxal and methylglyoxal in environmental and biological matrices by stir bar sorptive extraction with in-situ derivatization. J Chromatogr A 1169(1-2): 47-52 [6] Zardari, Khuhawar, Laghari (2009) Capillary GC Analysis of Glyoxal and Methylglyoxal in the serum and urine of diabetic patients after use of 2,3-Diamino-2,3-dimethylbutane as derivatizing Reagent. Chromatographia 70 (5/6): 891-897	
Undertaking of intended data submission [ ]	Because of the scheduled use patterns of glyoxal, it is unlikely that the chemical reaches animal or human body fluids and tissues in relevant amounts. Moreover, in the kinetic and metabolism studies BPD ID A6.02_01 and BPD ID A6.02_02 it was found that Glyoxal is extensively metabolized in rats and was not detected in any excreta and tissue samples. This is due to the highly reactive nature of Glyoxal, e.g. with regard to proteins.	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	March 2019	
Evaluation of applicant's justification	As the substance is not classified as toxic or very toxic, analytical method in body fluids and tissues is not necessary.	
Conclusion	Acceptable with above amendments	
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*	

Section A4.2d **Annex Point IIA4.1/4.2 & IIIA-IV.1**	**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:** **(d) Animal and human body fluids and tissues**
Remarks	

Section A4.3 **Ann. IIIA, IV.1.**	**Analytical methods including recovery rates and the limits of determination for the active substance, and for residues thereof, in/on food or feedstuffs and other products where relevant**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification:	Referring to the presence of residual glyoxal in food and feedstuffs, the BUA [1] reported glyoxal contents ranging between 0.02 and 4.9 mg/L in liquids (tea, soysauce, some alcoholic beverages), and between 0.3 and 127 mg/kg in solids (bread, toast, soyabean paste, caffein-containing and decaffeinated instant and ground coffees) which had been detectable/extractable. Furthermore glyoxal was also detectable in cooked pork muscle meat, defatted and minced afterwards, as well as in foodstuff samples of beef, lamb, chicken and whale. Reviewed data of glyoxal in food/feedstuff are also reported in CICAD [2]. Glyoxal is described as being frequently detected in fermented food and beverages. This is mainly due to microbial activity as well as non-enzymatic browning reactions such as caramelization and Maillard reactions of saccharides (Hollnagel & Kroh, 1998; Glomb & Tschirnich, 2001; Hollnagel & Kroh, 2002; all cited in CICAD). Accordingly, Barros et al. (1999; cited in CICAD) found glyoxal present in different brands of beer and wine on sale in Portugal. Sampling three different brands of white wine, they detected glyoxal at concentrations of 6.2, 8.7, and 26 µmol/litre (about 360, 464, and 1509 µg/litre). De Revel & Bertrand (1993; cited in CICAD) evaluated a range of French wines and detected glyoxal in one white wine (mean of 125 µg/litre), red wines (151–368 µg/litre), and five sherry wines (lowest level of glyoxal in a Seco with 435 µg/litre and highest level in an Olorosso with 1556 µg/litre). Palamand et al. (1970; cited in CICAD) detected glyoxal levels ranging from about 230 to 1000 µg/litre in eight different beers. Nagao et al. (1986; cited in CICAD) detected glyoxal in Bourbon whiskey (390 µg/litre), wine (970 µg/litre), and apple brandy (33 µg/litre), as well as in black tea (20 µg/litre) and instant (340 µg/litre) and brewed coffee (870 µg/litre). Yamaguchi et al. (1994; cited in CICAD) detected glyoxal in beverages such as beer (20–40 µg/litre) as well as white (510 µg/litre) and red wine (740 µg/litre). Nagao et al. (1986; cited in CICAD) found glyoxal in soybean paste (4.2 mg/kg), soy sauce (4.9 mg/litre), toast (0.5 mg/kg), and bread (0.3 mg/kg). Markianova et al. (1971; cited in CICAD) reported glyoxal levels in bread ranging from 0.07 to 0.31 mg/kg, depending on the yeast type employed. However, Roiter & Borovikova (1972; cited in CICAD) showed that using amylase in the baking process led to glyoxal levels of up to 1.4 mg/kg in the bread crust and of up to 1.6 mg/kg in the bread crumbs. Plant materials used for brewing (rice — about 14 mg/kg; barley — about 3 mg/kg; malt — about 7 mg/kg) might contain glyoxal as well (Palamand et al., 1970). Yamaguchi et al. (1994) detected glyoxal in fermented food such as yoghurt (about 0.63–0.92 mg/kg). Due to heat-induced autoxidation, edible oils might contain glyoxal, as was shown for sardine oil, containing up to 6.5 mg/kg (Hirayama et al., 1984).	

Section A4.3 Ann. IIIA, IV.1.	Analytical methods including recovery rates and the limits of determination for the active substance, and for residues thereof, in/on food or feedstuffs and other products where relevant

Referring to the detection of glyoxal in food, a highly sensitive and rapid high-performance liquid chromatographic method for the determination of glyoxal in fermented foods was developed and described by Yamaguchi and coworkers (1994) with detection limits of 11.6-13.8 fmol per 10-µL injection at a signal to noise ratio of 3.

Gas chromatography-mass spectrometry or gas chromatography with an electron-capture detector have been described as suitable methods for the evaluation of the levels of glyoxal formed during fermentation and present in wine by de Revel (1993); according to the author, reproducibility and linearity studies gave satisfying results. More recently, Neng and coworkers (2007) developed a method for the determination of glyoxal (Gly) in different matrices including food, which was based on Stir bar sorptive extraction with *in-situ* derivatization using 2,3-diaminonaphthalene (DAN) followed by liquid desorption and high performance liquid chromatography with diode array detection (SBSE(DAN)*in-situ*-LD-HPLC-DAD). The authors found out that the analytical performance showed good accuracy, suitable precision (<12.0%), low detection limits (15 ng/L for glyoxal) and excellent linear dynamic ranges ($r2 > 0.99$) from 0.1 to 120.0 µg/L. They reported that by using the standard addition method, the application of the present method to tap and swimming-pool water, beer, yeast cells suspension and urine samples allowed very good performance at the trace level.

Glyoxal as biocidal product is not intended to be added to food and feedstuffs, only traces may be expected in food and feed indirectly, from surfaces treated before with Glyoxal. Due to the high reactivity of Glyoxal, any remains will react with proteins contained in the food and feedstuffs in a matter of minutes to hours. Photodegradation of glyoxal, which takes place with a half-live of about 11.2 h, will additionally deplete the substance (see section Doc IIIA7.3.1). Moreover, since Glyoxal is contained naturally (see above) in many (fermented) foodstuffs, there will in many cases be no direct link between Glyoxal detected in foodstuffs and Glyoxal used for disinfecting surfaces in the food industry. Therefore and since sufficient data on glyoxal and glyoxal detection in food/feedstuffs are available from acknowledged reviews and scientifically acceptable literature, there is no need in provided further data here.

References

[1] WHO (2004) The Concise International Chemical Assessment Document CICAD 57. The International Program of Chemical Safety of the WHO, IPCS, BPD ID A4_02

[2] German Chemical Society Advisory Committee on Existing Chemicals of Environmental Relevance (1996) BUA Report 187: Glyoxal (Ethanedial). Stuttgart, S. Hirzel, Wissenschaftliche Verlagsgesellschaft, pp: 1–64, ISBN 3-7776-0824-6, Stuttgart, BPD ID A4_01

[3] Yamaguchi, Ishida, Xuan, Nakamura, Yoshitake (1994) Determination of Glyoxal, Methylglyoxal, Diacethyl, and 2, 3-Pentanedione in Fermented Foods by High-Performance Liquid Chromatography with Fluorescence Detection. Journal of Liquid

Section A4.3 **Ann. IIIA, IV.1.**	**Analytical methods including recovery rates and the limits of determination for the active substance, and for residues thereof, in/on food or feedstuffs and other products where relevant**
	Chromatography & Related Technologies 17(1): 203 – 211 [4] de Revel, Bertrand (1993) A method for the detection of carbonyl compounds in wine: Glyoxal and methylglyoxal. J Sci Food Agriculture 61(2): 267-272 [5] Neng, Cordeireo, Freire, Nogueira (2007) Fetermination of glyoxal and methylglyoxal in environmental and biological matrices by stir bar sorptive extraction with in-situ derivatization. J Chromatogr A 1169(1-2): 47-52
Undertaking of intended data submission [ ]	
	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	March 2018, January 2020
Evaluation of applicant's justification	Only bibliographical data have been provided with limited or absent validation data which is not acceptable. As the exposure of food and/or feedstuffs cannot be excluded, an analytical method for the determination of glyoxal in food and feedstuff is necessary with LOQ as low as possible.
Conclusion	An analytical method for the determination of glyoxal in food and feedstuff is necessary with LOQ as low as possible. In addition, sufficient information should be submitted to determine the background concentration in food and/or feedstuff.
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	