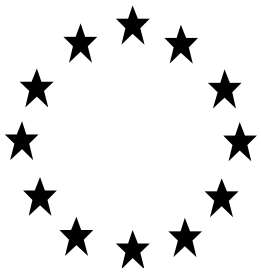
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

***Evaluation of active substances***

Assessment Report



# Glutaraldehyde

# Product-type 2, 3, 4, 6, 11, 12

(Private area and public health area disinfectants and other biocidal products; Veterinary hygiene biocidal products; Food and feed area disinfectants; In-can preservatives; Preservatives for liquid-cooling and processing systems; Slimicides)

30.9.2014

eCA Finland

# CONTENTS

# 1. STATEMENT OF SUBJECT MATTER AND PURPOSE

## 1.1. Procedure followed

This assessment report has been established as a result of the evaluation of the active substance glutaraldehyde as product-type 2 (Private area and public health area disinfectants and other biocidal products), 3 (Veterinary hygiene biocidal products), 4 (Food and feed area disinfectants), 6 (In-can preservatives), 11 (Preservatives for liquid-cooling and processing systems) and 12 (Slimicides), carried out in the context of the work programme for the review of existing active substances provided for in Article 89 of Regulation (EU) No 528/2012, with a view to the possible approval of this substance.

Glutaraldehyde (CAS no. 111-30-8) was notified as an existing active substance, by Dow Benelux B.V. and BASF SE, hereafter referred to as the applicants or by their short names Dow and BASF, in product-types 2, 3, 4, 6, 11 and 12.

Commission Regulation (EC) No 1451/2007 of 4 December 2007[1] lays down the detailed rules for the evaluation of dossiers and for the decision-making process.

In accordance with the provisions of Article 7(1) of that Regulation, Finland was designated as Rapporteur Member State to carry out the assessment on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for glutaraldehyde as an active substance in Product Types 2, 3, 4 and 6 was 31 July 2007 and in Product Types 11 and 12 31 October 2008 in accordance with Annex V of Regulation (EC) No 1451/2007.

Finland's competent authorities received a dossier for PT 2, 3, 4, 6 from BASF on 23 July 2007 and from Dow on 27 July 2007. The Rapporteur Member State accepted the dossier of BASF as complete for the purpose of the evaluation on 23 October 2007 and the dossier of Dow as complete for the purpose of the evaluation on 26 October 2007. Finland's competent authorities received a dossier for PT 11 and 12 from BASF on 27 October 2008 and from Dow on 30 October 2008. The Rapporteur Member State accepted the dossiers as complete for the purpose of the evaluation on 30 April 2009.

On 30 March 2011, the Rapporteur Member State submitted to the Commission and the applicant a copy of the first part of the evaluation report (documents IIA and IIIA), hereafter referred to as the competent authority report. On 31 January 2013 the second part of the competent authority report (Documents I, IIB, IIC, IIIB) was submitted to the Commission and the applicants. The Commission made the report available to all Member States by electronic means on 31 January 2013.

In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by

[1] Commission Regulation (EC) No 1451/2007 of 4 December 2007 on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. OJ L 325, 11.12.2007, p. 3

the Agency. Revisions agreed upon were presented at the Biocidal Products Committee and its Working Groups meetings and the competent authority report was amended accordingly.

## 1.2. Purpose of the assessment report

The aim of the assessment report is to support the opinion of the Biocidal Products Committee and a decision on the approval of glutaraldehyde for product-types 2, 3, 4, 6, 11, 12, and, should it be approved, to facilitate the authorisation of individual biocidal products. In the evaluation of applications for product-authorisation, the provisions of Regulation (EU) No 528/2012 shall be applied, in particular the provisions of Chapter IV, as well as the common principles laid down in Annex VI.

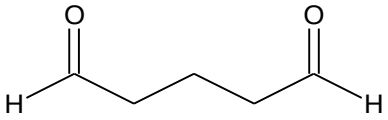
For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report, which is available from the Agency web-site shall be taken into account.

However, where conclusions of this assessment report are based on data protected under the provisions of Regulation (EU) No 528/2012, such conclusions may not be used to the benefit of another applicant, unless access to these data for that purpose has been granted to that applicant.

# 2. OVERALL SUMMARY AND CONCLUSIONS

## 2.1. Presentation of the Active Substance

### *2.1.1. Identity, Physico-Chemical Properties & Methods of Analysis*

| | |
|---|---|
| CAS-No. | 111-30-8 |
| EINECS-No. | 203-856-5 |
| Other No. (CIPAC, ELINCS) | None |
| IUPAC Name | 1,5-Pentanedial |
| Common name, synonym | Glutaraldehyde<br>Glutaral<br>Glutardialdehyde<br>Glutaric dialdehyde |
| Molecular formula | $C_5H_8O_2$ |
| Structural formula |  |
| Molecular weight (g/mol) | 100.11 |

For other information on identity of the substance, see Doc IIA and the List of Endpoints.

Physical chemical properties are detailed in Appendix 1 (List of Endpoints).

Methods of analysis have been developed and validated for the active substance and the active substance in water, soil and blood. Analytical methods for the determination of residues in food and feedstuffs are not deemed necessary, because residues are not expected due to chemical nature of glutaraldehyde, which reacts rapidly with proteins and other organic matter contained in the food and feed stuffs. For a method of determination in air, it has been agreed that a modern method will be submitted at product authorization. Furthermore, method(s) of determination of glutaraldehyde and impurities in the active substance as manufactured need to be updated. Furthermore, confirmatory methods will be required, see the Document IIA.

### *2.1.2. Intended Uses and Efficacy*

The assessment of the biocidal activity of the active substance demonstrates that it has a sufficient level of efficacy against the target organism(s) and the evaluation of the summary data provided in support of the efficacy of the accompanying product, establishes that the product may be expected to be efficacious. The fungicidal, sporicidal mycobactericidal, and algicidal efficacy and efficacy against biofilms were not demonstrated for the intended use concentrations.

**Target organisms specified for product Types (PT). The specific species are given in App. II.**

| PT | Intended use | Target organisms |
|---|---|---|
| PT02 | Hard Surface Disinfection in Hospitals<br>Hard Surface Disinfection in Industrial Areas | Bacteria, mycobacteria, bacterial spores, fungi (yeasts and moulds), virus, algae, biofilms |
| PT03 | Poultry Farm Disinfection<br>Pig Farm Disinfection | Bacteria, mycobacteria, bacterial spores, fungi (yeasts and moulds), virus |
| PT04 | Food vessel/Machinery Disinfection<br>Food Processing Surface Disinfection | Bacteria, mycobacteria, bacterial spores, fungi (yeasts and moulds), virus, biofilms |
| PT06 | Preservatives for Detergents (*e.g.* Laundry Softeners; Liquid detergent; Wax Emulsion; Car Polish)<br>Paper Wet-End Additives Preservation and Paper Coatings Preservation | Bacteria, mycobacteria, bacterial spores, fungi (yeasts and moulds), algae |
| PT11 | Closed Recirculating Cooling Systems<br>Open Recirculating Cooling Systems | Bacteria, fungi (yeasts and moulds), algae, biofilms |
| PT12 | Slimicide for paper pulp: wet-end slimicides<br>Slimicide for paper pulp: paper de-inking | Bacteria, fungi (yeasts and moulds), algae |
| **Oilfield applications** | | |
| PT11 | Preservative for oilfield injection water | Bacteria, fungi (yeasts and moulds), algae, biofilms |
| PT06 | Preservative for drilling muds/fluids | Bacteria, fungi (yeasts and moulds), algae |
| PT06 | Preservative for cementing fluids | Bacteria, fungi (yeasts and moulds), algae |
| PT11 | Preservative for hydrotesting water | Bacteria, fungi (yeasts and moulds), algae, biofilms |

Resistance to glutaraldehyde in certain mycobacteria strains has been reported in hospitals. Resistant strains have grown in surgical equipment, e.g. endoscopes. Resistance against glutaraldehyde has been associated with improper uses of the disinfectant on dirty endoscopes and use of non-sterile water to rinse disinfected equipment. At industry, resistance has not been a significant problem according to the applicants. The RMS is of the opinion that the development of resistant strains in industry cannot be ruled out. The recommended resistance management strategy is to

vary the products used, to use more than one product simultaneously, or to alternate treatment regimes and monitor occurrence of resistance.

Glutaraldehyde has been evaluated for several uses in PT 2, 3, 4, 6, 11 and 12. The intended uses and use concentrations are the same for both applicants.

**Intended uses and use concentrations based on data provided by BASF and Dow. The efficacy concentrations are obtained from Table 7.3.a and 7.3.b in Doc IIB and include data from both applicants. The minimum concentrations are partially based on MIC tests, which are not suitable to prove the efficacy of disinfectants and preservatives and are only given for information. Tests showing sufficient efficacy for a.s. approval were provided for the intended in-use concentrations.**

| PT | Intended use | Likely conc. g/l | Proved efficacy at conc. g/l |
|---|---|---|---|
| PT02 | Hard Surface Disinfection in Hospitals<br>Hard Surface Disinfection in Industrial Areas | 1.4[1]<br>3[2] | [redacted] |
| PT03 | Poultry Farm Disinfection<br>Pig Farm Disinfection | 1[1,2] (spraying)<br>20[1] (fogging) | [redacted] |
| PT04 | Food vessel/Machinery Disinfection<br>Food Processing Surface Disinfection | 1[1,2] | [redacted] |
| PT06 | Preservatives for Detergents<br>(*e.g.* Laundry Softeners; Liquid detergent; Wax Emulsion; Car Polish) | 1[1,2] | [redacted] |
| | Paper Wet-End Additives Preservation and Paper Coatings Preservation | 0.5[1,2] | [redacted] |
| PT11 | Closed Recirculating Cooling Systems | 0.1[1]<br>0.025-0.1[2] | [redacted] |
| | Open Recirculating Cooling Systems | 0.1[1]<br>0.05-0.1[2] | [redacted] |
| PT12 | Slimicide for paper pulp: wet-end slimicides | 0.075[1]<br>0.0375-0.075[2] | [redacted] |
| | Slimicide for paper pulp: paper de-inking | 0.2[1] | [redacted] |
| **Oilfield applications** | | | |
| PT11 | Preservative for oilfield injection water | 3[1]<br>0.24-0.5[2] | [redacted] |
| PT06 | Preservative for drilling muds/fluids | 3[1]<br>0.0004-0.3[2] | [redacted] |
| PT06 | Preservative for cementing fluids | 5[1]<br>0.004-0.5[2] | [redacted] |
| PT11 | Preservative for hydrotesting water | 0.3[1]<br>$4.9x10^{-5}$-$5x10^{-3}$ [2] | [redacted] |

[1] Human exposure scenario
[2] Environment exposure scenario

In addition, in order to facilitate the work of Member States in granting or reviewing authorisations, the intended uses of the substance, as identified during the evaluation process, are listed in Appendix II.

### *2.1.3. Classification and Labelling*

**Current classification of a.s.[1] according to Directive 67/548/EEC**

| Class of danger | R phrases | S phrases |
|---|---|---|
| T<br>C<br>N | R23/25<br>R34<br>R42/43<br>R50 | S(1/2)<br>S26<br>S36/37/39<br>S45 - 61 |
| Specific Concentration Limits: | | |
| T<br>Xn<br>T<br>Xn<br>C<br>Xi<br>Xi | R25<br>R22<br>R23<br>R20<br>R34<br>R37/38-41<br>R36/37/38<br>R43 | C ≥ 50 %<br>2 % ≤ C < 50 %<br>C ≥ 25 %<br>2 % ≤ C < 25 %<br>C ≥ 10 %<br>2 % ≤ C < 10 %<br>0,5 % ≤ C < 2 %<br>C ≥ 0.5 % |

[1] Note: Annex I of Council Directive 67/548/EEC lists glutaraldehyde as the pure (100%) substance.

**Current classification of a.s.[1] according to Regulation 1272/2008**

| Hazard Class and Category codes | Hazard Statement codes |
|---|---|
| Acute Tox. 3 *<br>Acute Tox. 3 *<br>Skin Corr. 1B<br>Resp. Sens. 1<br>Skin Sens. 1<br>Aquatic Acute 1 | H331: Toxic if inhaled<br>H301: Toxic if swallowed<br>H314: Causes severe skin burns and eye damage<br>H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled<br>H317: May cause an allergic skin reaction<br>H400: Very toxic to aquatic life |
| Specific Concentration Limits and M Factors: | |
| C ≥ 10 %<br>0,5 % ≤ C < 10 %<br>2 % ≤ C < 10 %<br>0,5 % ≤ C < 2 %<br>C ≥ 0,5 %<br>C ≥ 0,5 % | Skin Corr. 1B; H314<br>Skin Irrit. 2; H315<br>Eye Dam. ; H318<br>Eye Irrit. 2; H319<br>STOT SE; H335<br>Skin Sens. 1; H317 |

[1] Note: Annex VI of Regulation 1272/2008 lists glutaraldehyde as the pure (100%) substance.

## Proposed classification of a.s.

The applicants have proposed to classify the 50 % glutaraldehyde aqueous solution. The existing harmonised classification concerns 100 % (pure) glutaraldehyde, which does not exist in commerce because of its instability. The RMS is of the opinion that there should be only one classification, and has submitted a Proposal for Harmonised Classification and Labelling to ECHA in June 2012. The Risk Assessment Committee (RAC 29) formed an opinion on 2-6 June 2014 that is presented below.

**RAC 29 opinion on the classification of a.s. according to Regulation 1272/2008. The classification is based on 100% glutaraldehyde.**

| **Classification according to the CLP Regulation** | |
|---|---|
| Hazard Class and Category Codes | Acute Tox. 3; H301<br>Acute Tox. 2; H330<br>Skin Corr. 1B; H314<br>Resp. Sens. 1; H334<br>Skin Sens. 1A; H317<br>STOT SE 3; H335<br>Aquatic Acute 1 H400<br>Aquatic Chronic 2 H411 |
| **Labelling** | |
| Pictograms | GHS06, GHS05, GHS08, GHS09 |
| Signal Word | Danger |
| Hazard Statement Codes | H301: Toxic if swallowed<br>H330: Fatal if inhaled<br>H314: Causes severe skin burns and eye damage<br>H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled<br>H317: May cause an allergic skin reaction<br>H335: May cause respiratory irritation<br>H410: Very toxic to aquatic life with long lasting effects |
| Supplementary Hazard Statement Code(s) | EUH071 |
| Specific Concentration Limits, M Factors | STOT SE 3; H335: C ≥ 0,5%<br>M = 1 for aquatic acute |

## 2.2. Summary of the Human Health Risk Assessment

### 2.2.1. *Hazard identification and effects assessment*

- Toxicokinetics

**Oral absorption.** The test substance was rapidly but incompletely absorbed from the gastrointestinal tract, with no remarkable differences between sexes. Oral absorption of 40 % is proposed for estimating the systemic dose. Glutaraldehyde is rapidly transformed following absorption, as the highest glutaraldehyde concentration measured in the rat blood corresponded to 1.6 % of the dosed amount.

**Distribution.** Free glutaraldehyde is rapidly removed from circulation, presumably through macromolecular binding or metabolism. When using radioactive labelling, the label was distributed in all organs and tissues, while free glutaraldehyde is mostly assumed to be rapidly metabolised.

**Metabolism.** It has been demonstrated that glutaraldehyde is largely metabolised either before or soon after absorption, but no detailed metabolic pathways have been suggested. Furthermore, the only metabolite identified is glutaric acid. The scheme presented in Doc IIA is poorly substantiated with regard to the pathway from glutaraldehyde to glutaryl CoA. The results obtained in the QSAR analysis did not suggest any metabolites with effects other than those already attributed to glutaraldehyde, and the additional structural alert for simple aldehydes as possible genotoxic carcinogens (which is the same for the parent compound glutaraldehyde). Due to very fast metabolism, the relevant metabolites can be assumed to have been involved in the toxicological studies.

**Excretion.** The excretion of radioactivity was rapid and occurred mainly via the faeces, followed by exhaled air and urine. There was no indication of bioaccumulation in any of the tissues.

- Dermal penetration

None of the studies gave sufficient information for establishing a value for dermal absorption due to methodological problems. Most of the glutaraldehyde that was found to absorb in the skin will react immediately, leaving little free glutaraldehyde for absorption. Nevertheless, the absorption of metabolites needs to be considered as well, and furthermore it was shown that small amounts of free glutaraldehyde can also be detected from the blood after dermal dosing. In the study using human skin, the total combined radioactivity in the receptor fluid and in the full combusted skin sample was up to 6.6 %. A conservative value of 10 % for dermal absorption is assumed unless further information is provided.

- Acute toxicity

**Oral route.** Glutaraldehyde was toxic when administered by the oral route. The toxic effects were caused by the corrosive effect on the mucosal surfaces of the GI tract. The oral $LD_{50}$ of pure (100% w/w) glutaraldehyde is 77 mg/kg bw (154 mg/kg bw for the 50 % test substance). This is based on local effects and the $LD_{50}$ value given is valid for 50

% (w/w) glutaraldehyde, while lower concentrations would presumably have a higher $LD_{50}$ value.

Glutaraldehyde is classified as acute toxic by oral route Category 3 and is assigned the hazard statement H301 ' Toxic if swallowed'.

**Dermal route.** 50% (w/w) Glutaraldehyde caused local effects when administered by the dermal route. Due to the direct corrosive effect there is a danger of irreversible damage to the skin upon exposure to the undiluted solution. Toxicity is secondary to the local tissue damage rather than a result of percutaneously absorbed material. The dermal $LD_{50}$ of the active substance (50 % glutaraldehyde) is above 2000 mg/kg bw. For 100% glutaraldehyde the $LD_{50}$ value is 1000 mg/kg bw. The toxicity is based on local effects and is dependent on the concentration of the substance.

**Inhalation route.** Glutaraldehyde was very toxic when administered by inhalation. Taking the most critical study, the inhalation $LC_{50}$ of pure (100 %) glutaraldehyde was 0.35 mg/L in male rats and 0.28 mg/L in female rats. Glutarladehyde is classified acute toxic by inhalation route Category 2 and is assigned the hazard statement H330 'Fatal if inhaled'.

**Skin sensitisation.** Human data confirms the skin sensitizing potential seen in animal experiments which are not reported (see p. 16).

**Skin irritation.** Glutaraldehyde is irritating to the skin according to the human data (see p. 16) and thus no animal data is reported.

- Repeat-dose toxicity

**Oral route**

Oral repeat dose toxicity studies have been conducted in the mouse, rat and dog. There is no conclusive evidence of systemic toxicity upon repeated oral exposure to glutaraldehyde in the drinking water, and rather the effects are most likely secondary to local effects at the site of contact.

In the subchronic studies, all effects were relatively mild and not clearly indicative of systemic toxicity, still allowing the establishment of NOAELs. The effects included increased kidney weight (without necropsy findings), increase in urea nitrogen, lesions in the glandular stomach and mild mucus gland hyperplasia. Dose dependent decrease in water consumption was noted in all studies, indicating unpalatability of the test substance. There was no conclusive evidence of systemic toxicity in the subchronic studies in rats, dogs or mice when administering doses up to 2000, 250 and 1000 ppm glutaraldehyde, respectively. The overall NOAELs in these experiments were as follows:

- Rat: 50 ppm (2.9 and 3.6 mg/kg bw/day for ♂ and ♀, respectively)
- Dog: 50 ppm (3.3 and 3.2 mg/kg bw/day for ♂ and ♀, respectively)
- Mouse: 250 ppm (61 and 74 mg/kg bw/day for ♂ and ♀, respectively)

In the chronic studies, the main findings were found in gross pathology and histopathology of the stomach and the kidneys. There was also large granular lymphocyte

leukaemia [LGLL], which is discussed in Chapter 2.2.1.1.6 Carcinogenicity. There were no significant differences in survival times between the dose groups and the control group. In the stomach, there was a somewhat increased incidence in several types of findings that together allow the conclusion that the effects were secondary to local irritation in the stomach. There was diffuse degeneration of the testes which is considered as an adverse effect and is discussed more thoroughly in Chapter 2.2.1.1.6. Other effects included increased kidney weights, tubular basophilia and tubular pigmentation, red colour in the urine, reduced water and food consumption, and decreased body weight. Altogether, the effects indicate a local irritant effect in the stomach. LGLL was observed in all dose levels in both sexes. However, it is not considered to be a toxicologically relevant end point to humans and so, it has not been used as the basis for setting the NOAEL in this study, It should be noted that at 1.8 and 2.8 mg/kg bw/day for males and females respectively, LGL leukaemia was the only effect. Overall, **t**he most evident effects occur in the GI tract, and especially in the glandular stomach. These effects are concluded to result from irritation. All oral chronic studies were performed with glutaraldehyde administered in the drinking water. The unpalatability of the drinking water resulted in reduced water consumption and urine volume, increased urine osmolality and specific gravity, and was in some cases linked to reduced food consumption. Effects in the kidneys may have been secondary to leukaemia and/or resulting from reduced water consumption. Other mechanisms cannot be excluded, and effects in the kidney are considered as relevant. The lowest overall NOAEL for the rat is 100 ppm (3.2 and 4.8 mg GA/kg bw/day for ♂ and ♀, respectively).

**Dermal route**

In a 90-day rat study the test concentrations of up to 7.5 % caused effects on the skin but no signs of systemic toxicity. The skin effects consisted of scabs and erythema of increasing incidence and severity with increasing concentration. There were skin effects at all dose levels, but the systemic NOAEL was the highest tested dose, 150 mg GA/kg bw/day that was obtained using the 7.5 % solution. There was no site of contact genotoxicity following dermal exposure. Irritation was observed at all dose levels, down to 1.25 % glutaraldehyde. Higher concentrations of glutaraldehyde will cause more severe skin effects, allowing more glutaraldehyde to be also systemically available.

**Inhalation route**

**Subchronic.** There was no mortality in the rats with concentrations up to 1000 ppb, and the clinical signs dyspnea, ruffled fur and emaciation were only seen in this highest dose group. In contrast, all mice in the high dose group and two females of the 500 ppb group died. The lesions observed in rats and mice were similar, and the deaths of mice were concluded to have resulted from blocking of the airways by nasal congestion. Gross and histopathology of rats and mice indicated changes in the respiratory tract indicating an irritant effect. Histoautoradiographic evaluation revealed an increase in cell replication in the squamous epithelium of the nasal vestibule. All these lesions concerned the upper respiratory tract, and no effects were seen in the lower respiratory tract (trachea, bronchi and lungs). Haematology and clinical chemistry findings were concluded to be either incidental or indicative of irritant effects. The systemic NOAEC for rats is 125 ppb (0.51 mg GA/$m^3$) based on histopathological lesions in the nasal passages and turbinates seen

at 250 ppb. In mice, effects were seen at all dose levels and NOAEC could not be set. The LOAEC is 62.5 ppb (0.26 mg/ $m^3$) based on nasal lesions and increased cell replication rates in the nasal vestibule. These NOAEC and LOAEC values are based on adverse effects that are considered to be secondary to irritation, and are therefore not truly systemic.

**Chronic.** No valid studies were provided for chronic inhalation toxicity, but scientifically valid information was available from the NTP (National Toxicology Program, USA). The effects seen in rats and mice were qualitatively similar and were mainly seen in the nose of both rats and mice, decreasing in severity and in frequency towards the inner portions of the nasal passage. This pattern is common with other aldehydes and irritant chemicals in inhalation studies. The findings are compatible with glutaraldehyde causing a local irritant effect which over chronic exposure resulted in lesions in the nasal passages. There were effects at all dose levels in both rats and mice, and therefore no NOAEC is established and is below 250 ppb (1.02 mg/$m^3$) for rats and below 62.5 ppb (0.255 mg/$m^3$) for mice.

- Genotoxicity

***In vitro***

Glutaraldehyde is genotoxic *in vitro*. Positive results were obtained in Ames test, sister chromatid exchange assay, *in vitro* chromosomal aberration assay, and a forward mutation assay.

***In vivo***

Intraperitoneal dosing resulted in an inconsistent pattern of slight increases in micronucleated polychromatic erythrocytes (PCE) in an *in vivo* micronucleus test. The result is interpreted as indicative of moderate genotoxicity. Negative results were obtained in a bone marrow chromosomal aberration assays or an unscheduled DNA synthesis assay, but definitive conclusions on *in vivo* genotoxicity should not be made based on these studies because it is not clear whether the test substance reached the blood circulation or the target organs (bone marrow and liver). Overall, the *in vivo* genotoxicity studies gave inconclusive results. Due to the reactivity of the substance, the *in vivo* tests might not have demonstrated an existing *in vivo* genotoxic potential of glutaraldehyde. The slightly positive result in an intraperitoneal test demonstrates the possibility for *in vivo* genotoxicity in tissues that are accessible to glutaraldehyde. *In vivo* genotoxicity has not been studiedby the inhalational route, which is the most relevant human exposure route and could ideally be covered by a site of contact genotoxicity study. It was however considered that for the purpose of human risk assessment, inhalation exposure is sufficiently covered by chronic and oncogenicity studies and the data gap is therefore acceptable. Classification for genotoxicity is not proposed.

- Carcinogenicity

### Oral route

A 2-year drinking water study was performed in two different rat strains (Fischer 344 and Wistar).

The main finding in Fischer 344 rats was a significant increase in the number of large granular lymphocyte leukaemia (LGLL) in the liver and spleen of females. There were no other carcinogenic effects In Wistar rats, there was the possibility of a treatment-related increase in testis Leydig cell adenomas. The incidence of Leydig cell adenomas was slightly but clearly increased in all dose groups and it was coupled with an increased incidence of Leydig cell hyperplasia. Leydig cell adenomas occurred at similar incidence as in the historical control data, but this is nevertheless considered as treatment related because there is a continuum from hyperplasia to adenoma, and Leydig cell hyperplasia was increased in a dose dependent manner. No treatment-related increase could be detected in the total number of neoplasms, and other studies failed to identify Leydig cell adenomas. Due to the lack of other carcinogenicity findings, the most probable cause of the Leydig cell changes is damage to the seminiferous epithelium and/or the Leydig cells themselves. Risk Assessment Committee (RAC) did not consider the appearance of LGLL and Leydig cell tumours as being relevant to humans and classification for carcinogenicity was not proposed.

NOAEL for carcinogenicity was 100 ppm corresponding to 3.5 and 5.3 mg GA/kg bw/day for males and females, respectively.

### Inhalation route

No valid studies were provided for carcinogenicity by inhalation, but scientifically valid information was available from the NTP (National Toxicology Program, USA). The effects seen were consistent with local irritant effects in the most rostral portions of the nasal passages, decreasing in severity and in frequency towards the inner portions of the nasal passage. There was no evidence of carcinogenicity in rats or mice when tested for two years at glutaraldehyde concentrations up to 750 ppb (rats) and 250 ppb (mice).

- Reproductive toxicity

Teratogenicity of glutaraldehyde has been studied in rabbits and rats, and both indicate no teratogenic or embryotoxic potential at doses below maternal toxicity. There was slight (statistically non-significant) increase of skeletal variations. Due to the nature and incidence of the findings, the RMS concludes that there is no ground for classification for teratogenicity.

Effects on fertility have been studied in a one year study with rats. There were very few signs of any effects on reproduction parameters, and those revealed are considered to result from maternal/overall toxicity and/or to be incidental in nature. In conclusion, glutaraldehyde had little effect on any reproduction parameters even at maternally toxic doses and there is no ground for classification for fertility effects.

NOAEL for reproductive toxicity was set to 3.2 and 4.8 mg GA/kg bw/day for males and females, respectively.

- Neurotoxicity

Studies are not available and none are required. Systemic exposure to glutaraldehyde is very limited because of chemical reactivity of the active substance. There were no indications of possible neurotoxicity in the human data or any of the long-term studies available.

Classification for neurotoxicity is not warranted.

- Human data

**Skin sensitisation**

Human data confirms the skin sensitizing potential seen in animal experiments. Glutaraldehyde is classified as skin sensitizer of Category 1, and is assigned the hazard statement H317 "*May cause an allergic skin reaction*" (or according to the criteria set in the 2nd ATP of the CLP regulation, as Skin Sens. 1A, and is assigned the hazard statements H317 "*May cause an allergic skin reaction*").

**Respiratory sensitisation**

There is mounting evidence of occupational asthma among health care workers, and this is often connected with glutaraldehyde exposure. The studies show that a number of health care workers that have been exposed to glutaraldehyde become asthmatic and the symptoms are triggered by glutaraldehyde. Molecular diagnosis of asthma due to glutaraldehyde cannot easily be based on specific IgE measurements due to poor correlation with clinical symptoms. There are however studies showing clearly elevated cellular and molecular indicators for asthma as a response to glutaraldehyde challenge. Overall there is strong evidence that glutaraldehyde is a moderately potent respiratory sensitizer.

Glutaraldehyde is classified as respiratory sensitizer of Category 1, and is assigned the hazard statement H334 "May cause allergy or asthma symptoms or breathing difficulties if inhaled".

**Skin irritation**

Glutaraldehyde is irritating to the skin. Skin irritation is minimal at concentrations below 0.5 %. Similar results obtained in other studies confirm that non-recurring dermal exposure to glutaraldehyde concentrations below 0.5 % are unlikely to cause any adverse health effects apart from mild, reversible skin irritation. Exposure at workplace or otherwise repeated exposure may however cause sensitization.

**Other health effects**

Apart from irritant and sensitising properties, glutaraldehyde has not been connected with any considerable health effects except in cases of accidental spillage causing severe damage at the site of contact during endoscopy and surgery.

Glutaraldehyde has been reported to cause various effects on the skin (rash and contact dermatitis), eyes (itching, irritation, conjunctivitis), nose (sinus discomfort, irritation,

inflammation, bleeding) and throat (itching, tingling, soreness, unpleasant taste). These effects can mostly be attributed to irritant properties. Additional effects sometimes reported include headache and lethargy. There is no evidence of carcinogenicity or effects in mortality or longevity.

Glutaraldehyde has a discernible green apple odour that is detectable to humans at a concentration of around 0.3 ppb.

- Establishment of reference values

There were very few effects that could be considered as systemic, but AEL values have been derived based on the studies where systemic effects cannot be excluded. The systemic NOAEL values are corrected by the oral absorption value of 40 % obtained in the toxicokinetic studies in the rat. In addition, external reference values are derived for acute and long-term inhalation exposure.

**$AEL_{acute}$**

An acute AEL is not derived because all signs of acute toxicity are based on local rather than systemic effects. The effects were dependent on the route of exposure.

**$AEL_{medium\text{-}term}$**

$AEL_{medium\text{-}term}$ is based on the NOAEL of 3.5 mg/kg bw/day of a rat carcinogenicity study. Below this dose level there were no effects in any of the repeated dose studies. An AF of 10 for intraspecies variation and an AF of 10 for interspecies variation are applied because truly systemic effects cannot be excluded. The correction for oral absorption is 40 %.

– $AEL_{medium\text{-}term}$ = [3.5 mg/kg bw/day / (10 × 10)] × 40 % = 14 µg/kg bw/day

**$AEL_{long\text{-}term}$**

The same NOAEL is applied as for $AEL_{medium\text{-}term}$. Below this dose level there were no effects in any of the repeated dose studies. The same AFs and rationale are used as for deriving the $AEL_{medium\text{-}term}$.

– $AEL_{long\text{-}term}$ = [3.5 mg/kg bw/day / (10 × 10)] × 40 % = 14 µg/kg bw/day

**$AEC_{inhalation}$**

The lowest relevant LOAEC of 0.255 mg/m$^3$ was obtained in a 2-year inhalation study in the mouse and in a 90-day inhalation study in the mouse. The toxicodynamic component of 2.5 of the interspecies AF is applied, while the toxicokinetic component of 4 is disregarded due to the mode of action being direct chemical reactivity. The intraspecies toxicodynamic component of 3.2 is applied while the toxicokinetic component of 3.2 is disregarded because 1) the mechanism is direct chemical reactivity without involvement of local metabolism; 2) there is abundant data on humans exposed to low levels of glutaraldehyde without adverse health effects (see Doc IIA, 3.10.5 Considerations of respiratory sensitisation) and 3) no large differences were seen in the human response to irritant effects of glutaraldehyde in a group of volunteers. An additional AF of 3 is applied because the reference value is derived from a LOAEC instead of a NOAEC.

$AEC_{inhalation}$ = 0.255 mg/m$^3$ / ($2.5_{interspecies}$ × $3.2_{intraspecies}$ × $3_{LOAEC\text{-}to\text{-}NOAEC}$) = 0.0106 mg/m$^3$

= 10.6 µg/$m^3$ = 2.6 ppb

Currently there are no validated, internationally accepted animal models available to adequately characterize the thresholds of induction and elicitation of respiratory sensitizers. The evidence does however support the general principle that sensitization occurs in workplaces where high exposure rates take place either regularly or as high peak concentrations. The available data seem to suggest that where sensitization has occurred, exposure has occurred to at least 20-30 ppb, and often much higher. This should however not be understood as a proposal for a threshold value. Nevertheless, as the data indicate that sensitization has occurred at significantly higher concentrations than the $AEC_{inhalation}$, this is considered as a reference value that is likely to be protective for sensitization effects as well.

**$AEC_{acute\ inhalation}$**

The derivation of $AEC_{acute\ inhalation}$ is based on the assumption that in inhalational exposure, the mode of action of glutaraldehyde is direct chemical reactivity. In short exposure durations, effects would only be expected at concentrations that produce irritation. The threshold of nasal chemesthetic detection in humans was determined to be 390 ppb, corresponding to 1.60 mg/$m^3$. An AF of 3.2 is applied to cover human variation and uncertainties in the experimental setup.

$AEC_{acute\ inhalation}$ = 1.60 mg/$m^3$ / 3.2 = 0.5 mg/$m^3$ = 122 ppb

Repiratory sensitization has been linked with high peak exposure concentrations, and therefore $AEC_{acute\ inahalation}$ (122 ppb) should be regarded as a ceiling value that should never be exceeded.

**$AEC_{dermal}$**

Not derived due to lack of suitable data. The "indicative" values presented in Doc IIA are not considered suitable for risk characterisation.

**ADI**

Glutaraldehyde is very reactive with for example proteins, as has been demonstrated in the metabolism studies and no residues remain. Therefore, glutaraldehyde is not expected to be present in food, and an ADI is not derived.

### 2.2.2. *Exposure assessment*

#### 2.2.2.1. Product Type 2

The control of nosocomial diseases in hospitals requires, among others, thorough disinfection of inanimate hard surfaces such as floors, walls, tables, etc.

A solution containing glutaraldehyde is usually applied by mopping. Rinsing is sometimes performed but most of the time the treated surfaces are left to dry naturally. The applied glutaraldehyde evaporates with the water. Ventilation is compulsory. For floor disinfection, specific cleaning machines can be used.

Summary table: Professional exposure (PT2).

| **Exposure scenario** | **PPE** | **Inhalation uptake** | | **Systemic exposure** |
|---|---|---|---|---|
| | | Mean event concentration - acute ($mg/m^3$) | TWA (8-h) concentration - chronic ($mg/m^3$) | (mg/kg bw/day) |
| Scenario 1 -Hard Surface Disinfection - Mixing and Loading | None | 0.022 | 0.0005 | 0.021 |
| Scenario 1 -Hard Surface Disinfection - Mixing and Loading | Gloves | 0.022 | 0.0005 | 0.0021 |
| Scenario 2 - Hard Surface Disinfection – Application , 330 min | None | 0.027 | 0.0186 | 0.028 |
| Scenario 2 - Hard Surface Disinfection – Application ,180 min | None | 0.027 | 0.0101 | - |
| Scenario 2 - Hard Surface Disinfection – Application | Gloves | 0.027 | 0.0186 | 0.011 |
| Scenario 3 - Disposal | None | 0.0017 | 0.00006 | 6.97E-5 |
| Scenario 3 - Disposal | Gloves | 0.0017 | 0.00006 | 1.57E-5 |

Total systemic exposure hard surface disinfection - mixing and loading and application

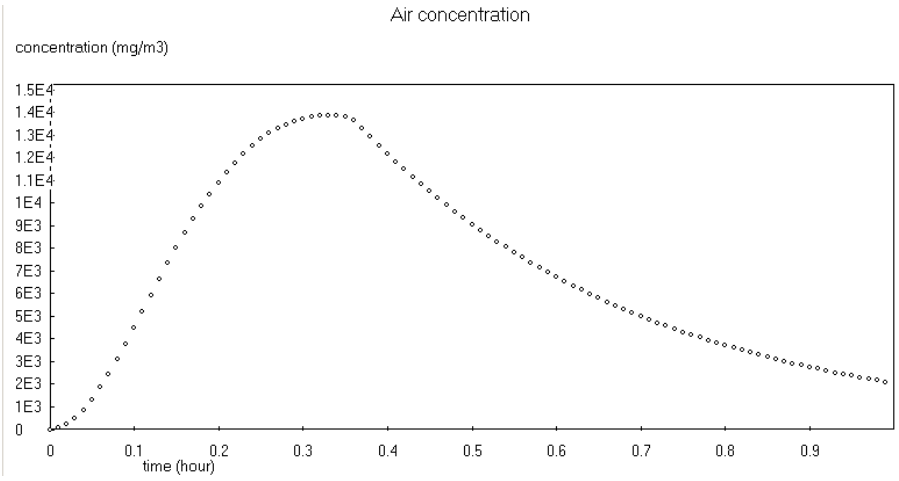
| **Exposure scenario** | | **Mixing and loading (mg/kg bw/day)** | **Application (mg/kg bw/day)** | **Post application (mg/kg bw/day)** | **Total systemic exposure (mg/kg bw/day)** |
|---|---|---|---|---|---|
| Scenarios 1 , 2 and 3: Hard Surface Disinfection | No PPE | 0.021 | 0.028 | 0.000070 | 0.049 |
| | PPE | 0.0021 | 0.011 | 0.000016 | 0.013 |

Summary table secondary exposure (Hard surface disinfection - PT2)

| Exposure scenario | Inhalation uptake | Inhalation exposure | Dermal exposure | Oral uptake | Systemic exposure |
|---|---|---|---|---|---|
| | Mean event concentration ($mg/m^3$) | (mg/kg) | (mg/kg) | (mg/kg) | (mg/kg bw/day) |
| Scenario 4 -Exposure to a child following inhalation and dermal contact with wet residues following Hard Surface Disinfection - **Child** | 0.027 | 3.1E-04 | 0.17 | 0.067 | 0.24 |
| Scenario 4 -Exposure to a child following inhalation and dermal contact with wet residues following Hard Surface Disinfection - **Infant** | 0.027 | 4.6E-04 | - | - | 4.6E-04 |

Re-entry time for a child was calculated using the ConsExpo model and scenario 2 assumptions. The water has evaporated from the mopped floor after 20 minutes (20 minutes after task started, task duration is 15 minutes in one room, so 5 minutes for last mopped area to dry). Thus, the re-entry time to allow surfaces to dry is 20 minutes, which protects the child from possible skin sensitisation due to dermal contact with wet residues.

The predicted peak water concentration occurs at 0.33 hour; then the vapor concentration decreases because water evaporation has ceased.



2.2.2.2. Product Type 3

Poultry/pig Farm Disinfection

Poultry farms are disinfected approximately 6 times per year and pig farms approximately twice a year either by spraying with a 0.1 % glutaraldehyde 50% aqueous solution solution or by fogging with a 2 % glutaraldehyde 50% aqueous solution solution. Prior to application of the disinfectant the following steps must be carried out:

- Evacuate the animals (to the abattoir)
- Clean out manure and other waste matter
- Carry out a high pressure water washing
- Close doors, windows, fans *etc*.

Summary table professional exposure (PT3)

| **Exposure scenario** | **PPE** | **Inhalation uptake** | | **Systemic exposure** (mg/kg bw/day) |
|---|---|---|---|---|
| | | Mean event concentration ($mg/m^3$) | TWA (8-h) concentration - chronic ($mg/m^3$) | |
| Scenario 5 - Mixing and loading disinfectant for application by spraying or fogging - Tier 1 | None | 0.12 | - | 0.0024 |
| Scenario 5 - Mixing and loading disinfectant for application by spraying or fogging - Tier 2 | Gloves, coated coveralls, RPE (10%) | 0.012 | - | 0.00024 |
| Scenario 6 - Disinfection of a Poultry Farm by Spraying - Tier 1 | None | 0.076 | 0.019 | 0.204 |
| Scenario 6 - Disinfection of a Poultry Farm by Spraying - Tier 2 | Gloves, double coveralls, RPE (10 %) | 0.0076 | 0.0019 | 0.0104 |
| Scenario 7 - Disinfection of a Poultry Farm by Fogging | None | None | None | None |

Total systemic exposure Poultry farm disinfection - mixing and loading and application

| **Exposure scenario** | | **Mixing and loading** (mg/kg bw/day) | **Application** (mg/kg bw/day) | **Total systemic exposure** (mg/kg bw/day) |
|---|---|---|---|---|
| Scenarios 5 and 6: poultry farm Disinfection | No PPE | 0.0024 | 0.204 | 0.206 |
| | PPE | 0.00024 | 0.0104 | 0.0106 |

Summary table secondary exposure (Veterinary Hygiene Biocidal Products - PT3)

| Exposure scenario | Inhalation uptake | Inhalation exposure/ Re-entry time | Dermal exposure | Oral uptake | Systemic exposure |
|---|---|---|---|---|---|
| | Mean event concentration ($mg/m^3$) | | (mg/kg) | (mg/kg) | (mg/kg bw/day) |
| Scenario 8 -Child enters a barn following disinfection | 180 | 2 h (ventilation rate 3.5 1/h) | 0.55 | 0.22 | 0.77 |

2.2.2.3. Product Type 4

Glutaraldehyde is used for disinfecting glass bottles, cold food processing vessels and walls of slaughter houses and other rooms where food is processed/stored.

Secondary exposure was not assessed because the potential for secondary exposure was very low since the application of the substance takes place at the end of the working day, the exposure to glutaraldehyde following day will be insignificant.

Summary table professional exposure (Food vessel/machinery disinfection- PT4)

| Exposure scenario | PPE | Inhalation uptake Mean event concentration ($mg/m^3$) | Systemic exposure (mg/kg bw/day) |
|---|---|---|---|
| Scenario 9 - Connecting drum to pump - Tier 1 | None | 11 | 1.188 |
| Scenario 9 - Connecting drum to pump - Tier 2 | Gloves, coated coveralls, RPE (10 %) | 1.1 | 0.0155 |
| Scenario 9 - Connecting drum to pump - Tier 3 | Gloves, coated coveralls, RPE (2.5 %) | 0.275 | 0.0125 |
| Scenario 9 - Connecting drum to pump - Tier 4 | Gloves, coated coveralls, RPE (2.5 %) | 0.0348 | 0.0116 |
| Scenario 10 - Maintenance of machines - Tier 1 | None | 0.04 | 0.0806 |
| Scenario 10 - Maintenance of machines - Tier 2 | Gloves, coated coveralls, RPE (10 %) | 0.004 | 0.00804 |

Walls of slaughter houses and other rooms where food is processed/stored need to be disinfected on a regular basis (in the absence of food) with the idea to avoid the contamination of the food that is further processed and to avoid spreading of pathogenic micro-organisms (e.g.: Foot and Mouth Disease, Viruses or Salmonella Bacteria). The solution of disinfectant (0.1 %) is sprayed onto the surfaces, left for soaking (~10 minutes) and then rinsed away with fresh water.

In the above mentioned application the following sequence must be followed:

- Cleaning
- Rinsing
- Disinfection
- Rinsing

Automation ensures that this sequence can be conducted safely without skipping any step. The entire process is expected to take *ca* 30 minutes.

Summary table professional exposure (Food Processing Surface Disinfection- PT4)

| Exposure scenario | PPE | Inhalation uptake | | Systemic exposure |
|---|---|---|---|---|
| | | Mean event concentration ($mg/m^3$) | TWA (8 h) concentration - chronic ($mg/m^3$) | (mg/kg bw/day) |
| Scenario 11- Application of Disinfectant in a Slaughter House – Tier 1 | None | 0.002 | 0.00013 | 7.32E-4 |

#### 2.2.2.4. Product Type 6

Laundry softener, liquid detergents and other aqueous systems used commercially and in the home require an in-can preservative to protect them against bio-spoilage during their shelf life. These systems are prone to microbial growth (both moulds and bacteria). A preservative must be added to these aqueous formulations during their production in the manufacturing plant and the added preservative must prevent the bio-deterioration of these systems until they are used, namely a few months (up to 1 year) after production.

Summary table professional exposure (Preservatives for detergents, car polish and wax emulsion - PT6, these uses are primary exposure to end-use products treated with glutaraldehyde.)

| **Exposure scenario** | **Inhalation uptake** | | **Systemic exposure** (mg/kg bw/day) |
|---|---|---|---|
| | Mean event concentration ($mg/m^3$) | TWA (8-h) concentration - chronic ($mg/m^3$) | |
| Similar to scenario 9 - Connect a drum to a pump - Tier 1 | 11 | - | 1.188 |
| Similar to scenario 9 - Connect a drum to a pump - Tier 2 | 1.1 | - | 0.0155 |
| Similar to scenario 9 - Connect a drum to a pump - Tier 3 | 0.275 | - | 0.0125 |
| Scenario 12 - Laundry Softeners – Loading Tier 1 | 3.96E-05 | 8.25E-07 | 1.67E-05 |
| Scenario 13 - Liquid detergent - Mixing/ Loading | 1.55E-05 | 3.23E-07 | 1.67E-05 |
| Scenario 14 - Liquid detergent – Application | 0.000954 | 1.19E-04 | 0.011 |
| Scenario 15 - Wax Emulsion- Application Tier 1 | 2.7E-05 | 0.0073 | 0.0092 |
| Scenario 16 - Car Polish- Application Tier 1 | 1.93E-05 | 0.0051 | 0.001 |
| Scenario 16 - Car Polish - Application Tier 2 | 0.041 | 0.0051 | 0.0001 |
| Scenario 17 - Manual surface disinfection, - Tier 1 | 0.0052 | 0.00104 | 0.010 |
| Scenario 17 - Manual surface disinfection, - Tier 2 | 0.0052 | 0.00104 | 0.0012 |

Total systemic exposure - mixing and loading and application of liquid detergents (Scenarios 13 and 14)

| Exposure scenario | Mixing and loading (mg/kg bw/day) | Application (mg/kg bw/day) | Total systemic exposure (mg/kg bw/day) |
|---|---|---|---|
| Scenario - Liquid detergent, mixing and loading and application | 1.67E-5 | 0.011 | 0.011 |

Summary table non-professional exposure (Preservatives for detergents, car polish and wax emulsion - PT6, these uses are primary exposure to end-use products treated with glutaraldehyde.)

| **Exposure scenario** | **Inhalation uptake** Mean event concentration ($mg/m^3$) | **Systemic exposure** (mg/kg bw/day) |
|---|---|---|
| Scenario 12 - Laundry Softeners - Loading | 3.69E-05 | 1.67E-5 |
| Scenario 13 - Liquid detergent - Mixing/ Loading | 1.55E-05 | 1.67E-5 |
| Scenario 14 - Liquid detergent – Application | 4.34E-07 | 0.011 |
| Scenario 15 - Wax Emulsion- Application | 2.70E-05 | 0.0092 |
| Scenario 18 - Car Polish- Application | - | 0.0022 |

Total systemic exposure - mixing and loading and application of liquid detergents (Scenarios 13 and 14)

| **Exposure scenario** | **Mixing and loading** (mg/kg bw/day) | **Application** (mg/kg bw/day) | **Total systemic exposure** (mg/kg bw/day) |
|---|---|---|---|
| Scenario - Liquid detergent, mixing and loading and application | 1.67E-5 | 0.011 | 0.011 |

Summary table secondary exposure (Fabric conditioners and liquid detergent - PT6)

| **Exposure scenario** | **Inhalation uptake** | **Systemic exposure** |
|---|---|---|
| | Mean event concentration ($mg/m^3$) | (mg/kg bw/day) |
| Scenario 19 - Fabric Conditioner – Post Application | - | 0.0045 |
| Scenario 20 - Liquid detergent – Post Application | - | 2.8E-06 |

The paper industry uses many additives to produce the various grades of paper and cardboard that are required. Some additives are added to the stock (wet-end), together with the pulp and others are added to the paper once it is formed (dry end). All these additives contain water (slurries or solutions) and are prone to microbial growth (both moulds and bacteria). A preservative must be added to these aqueous formulations during their production in the manufacturing plant; the added preservative must prevent the bio-deterioration of these systems until they are used, namely few days (up to 3 weeks) after production. Glutaraldehyde 50% aqueous solution is pumped into the mixing vessels by

means of dedicated lines and automatic remote control (no direct human involvement) systems. In some cases an additional dose is requested in the storage tank located in the paper mill since the remaining material (heel) might get contaminated after a long period of storage.

Summary table professional exposure (Paper Wet-end Additives Preservation and Paper Coatings Preservation - PT6)

| **Exposure scenario** | **PPE** | **Inhalation uptake** | | **Systemic exposure** |
|---|---|---|---|---|
| | | Mean event concentration ($mg/m^3$) | TWA (8-h) concentration - chronic ($mg/m^3$) | (mg/kg bw/day) |
| Scenario 21 - Loading and unloading slurry tanks – Tier 1 | None | 0.087 | 0.022 | 0.344 |
| Scenario 21 - Loading and unloading slurry tanks – Tier 2 | Gloves, coated coveralls | 0.087 | 0.022 | 0.0368 |
| Scenario 21 - Loading and unloading slurry tanks – Tier 3 | New pair of gloves, coated coveralls, RPE 10% | 0.0087 | 0.022 | 0.0193 |

2.2.2.5. Product Type 11

Preservatives for liquid-cooling and processing systems are used in the paper mills where glutarladehyde is dosed to the systems requiring connecting and disconnecting drums. Bystanders may be exposed to the spray drift of the glutaraldehyde.

For secondary exposure only inhalation was considered relevant. No concern was identified derived for dermal exposure.

**Preservatives used in closed recirculating systems**

Summary table professional exposure (Preservatives used in closed recirculating systems - PT11)

| **Exposure scenario** | **PPE** | **Inhalation uptake** Mean event concentration ($mg/m^3$) | **Systemic exposure** (mg/kg bw/day) |
|---|---|---|---|
| Similar to Scenario 9 –Mixing and Loading Solution for Filling a Closed Recirculating System - Tier 1 | None | 11 | 1.188 |
| Similar to Scenario 9 –Mixing and Loading Solution for Filling a Closed Recirculating System -Tier 2 | Gloves, double coveralls, RPE (10 %) | 1.1 | 0.0155 |
| Similar to Scenario 9 –Mixing and Loading Solution for Filling a Closed Recirculating System - Tier 3 | Gloves, double coveralls, RPE (2.5%) | 0.275 | 0.0125 |
| Scenario 22 –Draining a Closed Recirculating System - Tier 1 | None | 0.0022 | 0.0114 |
| Scenario 22 –Draining a Closed Recirculating System - Tier 2 | Gloves, double coveralls | 0.0022 | 4.8E-04 |

**Preservatives used in Open Recirculating Systems: Small, Shock Dosing**

Summary table professional exposure (Preservatives used in Open Recirculating Systems: Small, Shock Dosing - PT11)

| **Exposure scenario** | **PPE** | **Inhalation uptake** Mean event concentration ($mg/m^3$) | **Systemic exposure** (mg/kg bw/day) |
|---|---|---|---|
| Similar to Scenario 9 –loading (connecting/disconnecting drums) Tier 1 | None | 11 | 1.188 |
| Similar to Scenario 9 –loading (connecting/disconnecting drums) Tier 2 | Gloves and double coveralls, RPE (10 %) | 1.1 | 0.0155 |
| Similar to Scenario 9 –loading (connecting/disconnecting drums) Tier 3 | Gloves and double coveralls, RPE (2.5 %) | 0.275 | 0.0125 |
| Similar to Scenario 9 –loading (connecting/disconnecting drums) Tier 4 | Gloves and double coveralls, RPE (2.5 %) | 0.0348 | 0.0116 |

Summary table secondary exposure (Preservatives Used in Open Recirculating Systems - PT11)

| **Exposure scenario** | **Inhalation uptake** Mean event concentration ($mg/m^3$) | **Systemic exposure** (mg/kg bw/day) |
|---|---|---|
| Scenario 23 -Indirect exposure: Adult – inhalation of spray drift | 0.01 | 1.05E-04 |
| Scenario 23- Indirect exposure: Child – inhalation of spray drift | 0.01 | 5.67E-05 |

#### 2.2.2.6. Product Type 12

Glutaraldehyde is automatically dosed to the wet-end of the paper circuit. The exposure to the worker is limited to disconnecting an empty drum and reconnecting a full drum of glutaraldehyde. Exposure may occur also during cleaning and other daily maintenance tasks related to the pulp tank. Secondary exposure of worker may occur by inhalation of aerosol or vapour phase of the glutaraldehyde.

**Slimicides for paper pulp: wet-end slimicides**

Summary table professional exposure (Slimicides for paper pulp: wet-end slimicides; PT12)

| **Exposure scenario** | **PPE** | **Inhalation uptake** | | **Systemic exposure** (mg/kg bw/day) |
|---|---|---|---|---|
| | | Mean event concentration ($mg/m^3$) | TWA (8-h) concentration - chronic ($mg/m^3$) | |
| Similar to Scenario 9 – Mixing and Loading - Tier 1 | None | 11 | - | 1.188 |
| Similar to Scenario 9 - Mixing and Loading - Tier 2 | Gloves, double coveralls, RPE (10 %) | 1.1 | - | 0.0155 |
| Similar to Scenario 9 - Mixing and Loading - Tier 3 | Gloves, double coveralls, RPE (2.5 %) | 0.275 | - | 0.0125 |
| Scenario 24 – Tank cleaning and paper mill white water - Tier 1 | None | 0.0057 | 0.001 | 0.0153 |
| Scenario 24 – Tank cleaning and paper mill white water - Tier 2 | Gloves, coated coveralls | 0.0057 | 0.001 | 0.00138 |

Summary table secondary exposure (worker exposure to vapor and aerosols of glutaraldehyde used as a slimicide in the paper mill industry; PT12)

| **Exposure scenario** | **Inhalation uptake** Mean event concentration ($mg/m^3$) | **Systemic exposure** (mg/kg bw/day) |
|---|---|---|
| Scenario 25: inhalation of vapour phase | <3.2E-4 | <5.25E-5 |
| Scenario 25 inhalation of aerosol phase | 0.0057 | 0.00095 |

**Slimicides for paper pulp: paper de-inking slimicides**

During the recovery of pulp from old paper, the removal of ink is an important step. This is performed in special pulpers with surfactants and water. Most of the ink is collected with foam on the surface of the pulper but the recycled pulp remains a greyish colour and requires bleaching. Hydrogen peroxide ($H_2O_2$) is used for pulp bleaching. Many micro-organisms can grow in the pulper and they can secrete a fast acting enzyme (catalase) that degrades $H_2O_2$. A biocide is required in order to kill the micro-organisms before they can secrete catalase so that the bleaching step can be successfully performed.

Summary table professional exposure (Slimicides for paper pulp: paper de-inking slimicides; PT12)

| Exposure scenario | PPE | Inhalation uptake | | Systemic exposure (mg/kg bw/day) |
|---|---|---|---|---|
| | | Mean event concentration ($mg/m^3$) | TWA (8-h) concentration - chronic ($mg/m^3$) | |
| Similar to scenario 9 - Mixing and Loading Solution Tier 1 | None | 11 | - | 1.188 |
| Similar to scenario 9 - Mixing and Loading Solution Tier 2 | Gloves, double coveralls, RPE (10%) | 1.1 | - | 0.0155 |
| Similar to scenario 9 - Mixing and Loading Solution Tier 3 | Gloves, double coveralls, RPE (2.5%) | 0.275 | - | 0.0125 |
| Scenario 26 – cleaning/ maintenance of pulp tanks Tier 1 | None | 0.0152 | 0.0076 | 0.0409 |
| Scenario 26 – cleaning/maintenance of pulp tanks Tier 2 | Gloves, coated coveralls | 0.0152 | 0.0076 | 0.00368 |

2.2.2.7. Oilfield applications

Glutaraldehyde is used in several oilfield applications such as:

Industrial product preservative (drilling muds; packing fluids; cementing fluids), PT6

Preservative in hydrostatic pressure testing fluid, PT11

Slimicide in oilfield extraction fluids (flood and injection water), PT11

Summary table professional exposure (oil field applications - preservative in drilling muds (PT6), hydrotesting fluid (PT11), flooding and oil injection water (PT11)).

| **Scenario**<br><br>Mixing and loading (connection/disconnection of feeder system/of lines or hoses) | **Acute inhalation exposure - mean event concentration ($mg/m^3$)** | **Total systemic dose (mg/kg bw/day)** |
|---|---|---|
| Tier 1 (no PPE) | 11 | 1.188 |
| Tier 2 (gloves, coated coveralls, RPE (APF 10)) | 1.1 | 0.0155 |
| Tier 3 (gloves, coated coveralls, REP (APF 40)) | 0.275 | 0.0125 |
| Tier 4 (gloves, coated coveralls, RPE (APF 40)) | 0.0348 | 0.0116 |

2.2.3. ***Risk characterisation***

#### 2.2.3.1. Product Type 2

Qualitative local RC is presented for local dermal effects. Quantitative risk assessment was performed for systemic effects and for local effect following inhalation exposure.

Quantitative local RC was not performed for local dermal or oral effects. Due to skin sensitizing of glutaraldehyde the use of gloves is required. Worker dermal exposure during mixing and loading, application (mopping and wiping) and post application is mostly excluded by the use of protective gloves.

Summary of the quantitative risk assessment for systemic effects following dermal and inhalation exposure and risk for local effects following inhalation exposure in different scenarios is presented in the table below.

| Summary of scenarios assessed in PT 2 | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Scenario** | **Systemic or local RC** | **PPE** | **Relevant reference value** | **% Ref. value ( < 100)** | **MOE** (ref. value / exposure) ( > 1) | **Acceptable** | **Remarks** |
| Scenario 1 - Hard Surface Disinfection - Mixing and Loading | Systemic | Gloves | $AEL_{long-term}$ | 15 | - | Yes | - |
| | Local | - | $AEC_{acute\ inhalation}$ | 4 | 23 | Yes | - |
| | Local | - | $AEC_{inhalation}$ | 5 | 21 | Yes | - |
| Scenario 2 - Hard Surface Disinfection – Application | Systemic | Gloves | $AEL_{long-term}$ | 79 | - | Yes | - |
| | Local | - | $AEC_{acute\ inhalation}$ | 5 | 19 | Yes | - |
| | Local, 330 min | - | $AEC_{inhalation}$ | 175 | <1 | No | - |
| | Local, 180 min | - | $AEC_{inhalation}$ | 95 | 1 | Yes | - |
| Scenario 3 - Hard Surface Disinfection – Post Application | Systemic | - | $AEL_{long-term}$ | <1 | - | Yes | - |
| | Local | | $AEC_{acute\ inhalation}$ | <1 | 290 | Yes | - |
| | Local | | $AEC_{inhalation}$ | <1 | 180 | Yes | - |
| Combined exposure in scenarios 1,2 and 3 | Systemic | Gloves | $AEL_{long-term}$ | 94 | - | Yes | - |
| Scenario 4 - Accidental Exposure to a Child - Hard Surface Disinfection | Systemic | - | ARfD | 40 | - | Yes | Complementary approach only[1] |
| | Local | - | $AEC_{acute\ inhalation}$ | 5 | 19 | Yes | - |

[1] This systemic assessment was performed as a complementary approach to the local RC. Comparison to ARfD is not appropriate, but is provided in the absence of an $AEL_{acute}$.

Professional human exposure during hard surface disinfection is acceptable based on the comparison of the systemic dose to the $AEL_{long\text{-}term}$ and of the calculated glutaraldehyde concentration in the air to the $AEC_{acute\ inhalation}$ and to $AEC_{inhalation,}$ except for mopping and wiping for 330 min (scenario 2), where chronic inhalation exposure is not acceptable. However, this scenario is acceptable if application is done in maximum for 180 min, thus only mopping is acceptable because exposure time is then 110 min (assumption 22 rooms mopped per day, 5 min/room). No adverse health effects are expected in all other scenarios since systemic exposure is below the reference values and all MOE values are more than 1.

For the active substance approval inhalation exposure while mopping and wiping was evaluated using ConsExpo 4.1 model (evaporation, increase release area) with the mass transfer rate (0.052 m/min) estimated by the Sparks et al. (1996) method and using the mopping and wiping time (330 min) agreed by Ad Hoc Human Exposure Group at the WG meeting March 2014. Based on the risk assessment glutaraldehyde PT2 use is acceptable for a maximum duration of 180 min (agreed default time for mopping is 110 min and for wiping 220 min).

The applicant provided in the late stage of the evaluation process, a revised value for the mass transfer rate. However, the mass transfer rate, which was already modified in the CAR was not discussed in the Technical Meeting. Using the mass transfer rate (0.029 m/min) derived by Sparks method (it was revised because the harmonized scenario increased the release area to 46 m2 from 22 $m^2$ and this reduced the value for mass transfer rate) the exposure evaluation for glutaraldehyde is acceptable in scenario 2 for mopping and wiping with the duration of 330 min. According to the study of McCready and Fontaine[1] submitted by applicant the Sparks method should be used for estimating the mass transfer coefficient in ConsExpo calculations because it correlates indoor evaporation to the air flow in the room, temperature and molecular diffusivity. The Langmuir method, one of the defaults given in ConsExpo, should not be used because it provides an unrealistically high estimate of vapour concentration and inhalation exposure. The value for the mass transfer rate could be clarified for the product authorisation when further refinements should also be considered.

Accidental exposure to a child from contact with wet surfaces (scenario 4) following hard surface disinfection is acceptable based on the comparisons of the systemic dose to the ARfD (please see chapter 12.2.3 for the rationale on using ARfD as the reference value) and of the calculated glutaraldehyde concentration in the air to the $AEC_{acute\ inhalation}$. No adverse health effects are expected since systemic exposure is below the reference value and the MOE value is more than 1. Calculated re-entry time 20 minutes (task duration 15 minutes per room, and 5 minutes for last mopped are to dry) for a child was calculated to prevent possible skin sensitisation due to dermal contact with wet residues.

[1]David McCready and Donald Fontaine: Refining ConsExpo Evaporation and Human Exposure Calculations for REACH. Human and Ecological Risk Assessment, Vol. 16, No. 4, 2010, p. 783-800; http://dx.doi.org/10.1080/10807039.2010.501242

**Conclusion on PT 2:** All evaluated use scenarios except scenario 2 (mopping and wiping) for chronic inhalation exposure can be considered as safe uses. Application (scenario 2) is considered safe if only mopping is accepted. PT2 uses are acceptable to support the approval of glutaraldehyde in PT 2 with specific condition to restrict the use only for mopping. The value for the mass transfer rate could be clarified for the product authorisation.

#### 2.2.3.2. Product Type 3

Qualitative local RC is presented for local dermal effects. Quantitative risk assessment was performed for systemic effects and for local effect following inhalation exposure.

Quantitative local RC was not performed for local dermal or oral effects. Direct exposure will mostly be excluded by the use of protective gloves and double coveralls. During mixing and loading, splashes may occur and result in exposure to up to 50 % glutaraldehyde. The use of gloves and double coveralls will be obligatory.

Summary of the quantitative risk assessment for systemic effects following dermal and inhalation exposure and risk for local effects following inhalation exposure in different scenarios is presented in the table below.

| Summary of scenarios assessed in PT 3 | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Scenario** | **Systemic or local RC** | **PPE** | **Relevant reference value** | **% Ref. value (< 100)** | **MOE** (ref. value / exposure) (> 1) | **Acceptable** | **Remarks** |
| Scenario 5 - Mixing and loading solution for disinfection by spraying or fogging | Systemic | - | ARfD | <1 | - | Yes | Complementary approach only[1] |
| | Systemic | - | $AEL_{long-term}$ | 17 | - | Yes | |
| | Local | - | $AEC_{acute\ inhalation}$ | 24 | 4 | Yes | |
| Scenario 6 - Disinfection of a poultry farm by spraying | Systemic | - | ARfD | 34 | - | Yes | Complementary approach only[1] |
| | Systemic | RPE Gloves Double coveralls | $AEL_{long-term}$ | 33 | - | Yes | |
| | Local | RPE | $AEC_{acute\ inhalation}$ | 15 | 7 | Yes | |
| | Local | RPE | $AEC_{inhalation}$ | 18 | 6 | Yes | |
| Scenario 7 - Disinfection of a poultry farm by fogging | Systemic | - | ARfD | - | - | Yes | Negligible exposure |
| | Systemic | - | $AEL_{long-term}$ | - | - | Yes | |
| | Local | - | $AEC_{acute\ inhalation}$ | - | - | Yes | |
| | Local | - | $AEC_{inhalation}$ | - | - | Yes | |
| Combined scenarios 5 and 6 | Systemic | - | ARfD | 35 | - | Yes | |
| | Systemic | - | $AEL_{long-term}$ | 35 | - | Yes | |
| Combined scenarios 5 and 7 | Systemic | - | ARfD | <1 | - | Yes | |
| | Systemic | - | $AEL_{long-term}$ | 17 | - | Yes | |
| Disinfection of a Pig Farm by spraying | - | - | - | - | - | Yes | Covered by scenario 6 |
| Disinfection of a Pig Farm by fogging | - | - | - | - | - | Yes | Covered by scenario 7 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Scenario 8 – Re-entry time | - | - | - | - | - | Yes | A safe re-entry time of 2 h was calculated with sufficient ventilation |
| Scenario 8 - Child acute dermal and oral exposure | Systemic | - | ARfD | 128 | - | No | |

[1] This systemic assessment was performed as a complementary approach to the local RC. Comparison to ARfD is not appropriate, but is provided in the absence of an $AEL_{acute}$.

Professional human exposure during disinfection of a poultry farm or a pig farm by fogging or spraying is acceptable based on the comparison of the systemic dose to the $AEL_{long\text{-}term}$ and of the calculated glutaraldehyde concentration in the air to the $AEC_{acute\ inhalation}$ and to $AEC_{inhalation}$. No adverse health effects are expected since systemic exposure is below the reference values and all MOE values are more than 1. Potential exposure during spraying is very high and all efforts should be made to reduce inhalation exposure e.g. by using full face masks/helmets/hoods and filters.

Acute dermal and oral exposure of a child touching freshly treated surfaces of the animal room is not acceptable. This contact is, however, unlikely to occur, as access should be prohibited until the disinfectant has dried. After disinfection of a barn, a safe re-entry time depends on the adequacy of ventilation. Assuming 3.5 air changes per hour, a safe re-entry time of 2 h was calculated. Entry to the barn shall be prevented during that time.

**Conclusion on PT 3:** Disinfection of a poultry farm or a pig farm by fogging or spraying is acceptable. These uses can be considered as safe uses that are acceptable to support the approval of glutaraldehyde in PT 3. Entering the barn during the re-entry period must be prevented.

#### 2.2.3.3. Product Type 4

Qualitative local RC is presented for local dermal effects. Quantitative risk assessment was performed for systemic effects and for local effect following inhalation exposure.

Quantitative local RC was not performed for local dermal or oral effects. Splashes may occur and result in exposure to up to 50 % glutaraldehyde. The use of gloves and double coveralls will be obligatory.

Summary of the quantitative risk assessment for systemic effects following dermal and inhalation exposure and risk for local effects following inhalation exposure in different scenarios is presented in the table below.

| • Summary of scenarios assessed in PT 4 | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Scenario** | **Systemic or local RC** | **PPE** | **Relevant reference value** | **% Ref. value (< 100)** | **MOE** (ref. value / exposure) (> 1) | **Acceptable** | **Remarks** |
| Scenario 9 - Connecting Drum to Pump | Systemic | Gloves Double coverall RPE (10 %) | ARfD | 3 | - | Yes | Complementary approach only[1] |
| | | Gloves Double coverall RPE (2.5 %) | $AEL_{long-term}$ | 89 | - | Yes | |
| | Local | Gloves Double coverall RPE (2.5 %) | $AEC_{acute\ inhalation}$ | 55 | 1.8 | Yes | |
| Scenario 10 - Exposure during Cleaning/ Maintenance of Machinery | Systemic | Gloves Coated coverall | $AEL_{long-term}$ | 58 | - | Yes | |
| | Local | - | $AEC_{acute\ inhalation}$ | 8 | 13 | Yes | |
| | Local | RPE | $AEC_{inhalation}$ | 19 | 5 | Yes | |
| Scenario 11 - Application of Disinfectant in a Slaughter House | Systemic | - | $AEL_{long-term}$ | 5 | - | Yes | |
| | Local | - | $AEC_{acute\ inhalation}$ | <1 | 250 | Yes | |
| | Local | - | $AEC_{inhalation}$ | 1.2 | 82 | Yes | |

[1] This systemic assessment was performed as a complementary approach to the local RC. Comparison to ARfD is not appropriate, but is provided in the absence of an $AEL_{acute}$.

Professional human exposure during application of disinfectant in a slaughterhouse and during cleaning and maintenance of machinery is acceptable based on the comparison of the systemic dose to the $AEL_{long-term}$ and ARfD, as well as of the calculated glutaraldehyde concentration in the air to the $AEC_{acute\ inhalation}$ and to $AEC_{inhalation}$. No adverse health effects are expected since systemic exposure is below the reference value and the MOE values are more than 1.

In the acute scenario 9, gloves and double coverall are necessary to reduce systemic exposure to an acceptable level, and RPE (APF 40) are required to reach a respiratory concentration below $AEC_{acute\ inhalation}$.

In the chronic scenario 10, gloves and coated coverall are necessary to reduce systemic exposure to an acceptable level, and RPE are necessary to reach a respiratory concentration below $AEC_{inhalation}$.

**Conclusion on PT 4:** None of the scenarios causes concern when the appropriate PPE are used and they are thus acceptable. These scenarios can be considered as safe uses that are acceptable to support the approval of glutaraldehyde in PT 4.

#### 2.2.3.4. Product Type 6

Qualitative local RC is presented for local dermal effects. Quantitative risk assessment was performed for systemic effects and for local effect following inhalation exposure.

Quantitative local RC was not performed for local dermal or oral effects. Direct exposure will mostly be excluded by the use of protective gloves and coveralls. For non-professional uses the glutaraldehyde concentration should be less than 0.1% to prevent the possible risk for skin sensitization.

Summary of the quantitative risk assessment for systemic effects following dermal and inhalation exposure and risk for local effects following inhalation exposure in different scenarios is presented in the table below.

| Summary of scenarios assessed in PT 6 | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Scenario** | **Systemic or local RC** | **PPE** | **Relevant reference value** | **% Ref. value ( < 100)** | **MOE** (ref. value / exposure) ( > 1) | **Acceptable** | **Remarks** |
| Connecting a drum to a pump (similar to #9) | Systemic | Gloves Double coverall RPE (10 %) | ARfD | 3 | - | Yes | Complementary approach only[1] |
| | | Gloves Double coverall RPE (2.5 %) | $AEL_{long-term}$ | 89 | - | Yes | |
| | Local | Gloves Double coverall RPE (2.5 %) | $AEC_{acute\ inhalation}$ | 55 | 1.8 | Yes | |
| Scenario 12 – Loading Laundry Softener | Systemic | - | $AEL_{long-term}$ | <1 | - | Yes | |
| | Local | - | $AEC_{acute\ inhalation}$ | <1 | 14000 | Yes | |
| | Local | - | $AEC_{inhalation}$ | <1 | 2900 | Yes | |
| Scenario 13 - Mixing and Loading Liquid Detergent | Systemic | - | $AEL_{long-term}$ | <1 | - | Yes | |
| | Local | - | $AEC_{acute\ inhalation}$ | <1 | 31000 | Yes | |
| | Local | - | $AEC_{inhalation}$ | <1 | 32800 | Yes | |

| Summary of scenarios assessed in PT 6 | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Scenario** | **Systemic or local RC** | **PPE** | **Relevant reference value** | **% Ref. value (< 100)** | **MOE** (ref. value / exposure) (> 1) | **Acceptable** | **Remarks** |
| Scenario 14 - Applying Liquid Detergent | Systemic | - | $AEL_{long-term}$ | 77 | - | Yes | |
| | Local | - | $AEC_{acute\ inhalation}$ | <1 | 520 | Yes | |
| | Local | - | $AEC_{inhalation}$ | <1 | 89 | Yes | |
| Combined scenario 13 and 14 | Systemic | - | $AEL_{long-term}$ | 77 | - | Yes | |
| Scenario 15 - Applying Wax Emulsion | Systemic | - | $AEL_{long-term}$ | 66 | - | Yes | |
| | Local | - | $AEC_{acute\ inhalation}$ | <1 | 19000 | Yes | |
| | Local | - | $AEC_{inhalation}$ | 69 | 1.5 | Yes | |
| Scenario 16 - Applying Car Polish (professionals) | Systemic | - | $AEL_{long-term}$ | 7 | - | Yes | |
| | Local | - | $AEC_{acute\ inhalation}$ | <1 | 26000 | Yes | |
| | Local | - | $AEC_{inhalation}$ | 48 | 2 | Yes | |

| Summary of scenarios assessed in PT 6 | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Scenario** | **Systemic or local RC** | **PPE** | **Relevant reference value** | **% Ref. value (< 100)** | **MOE** (ref. value / exposure) ( > 1) | **Acceptable** | **Remarks** |
| Scenario 17 - Manual surface disinfection (professionals) | Systemic | - | $AEL_{long-term}$ | 79 | - | Yes | |
| | Local | - | $AEC_{acute\ inhalation}$ | 6 | 17 | Yes | |
| | Local | - | $AEC_{inhalation}$ | 10 | 10 | Yes | |
| Scenario 21 - Loading and unloading slurry tanks | Systemic | - | $AEL_{long-term}$ | 19 | - | Yes | |
| | Local | - | $AEC_{acute\ inhalation}$ | 17 | 6 | Yes | |
| | Local | RPE | $AEC_{inhalation}$ | 82 | 1.2 | Yes | |
| Scenario 18 - Applying Car Polish (non-professionals) | Systemic | - | ARfD | <1 | - | Yes | Complementary approach only[1] |
| | Local | - | $AEC_{inhalation}$ | - | - | Yes | Negligible inhalation exposure |
| Scenario 19 - Indirect Exposure to Laundry Softener | Systemic | - | $AEL_{long-term}$ | 32 | - | Yes | |
| | Local | - | - | - | - | Yes | Negligible inhalation exposure |
| Scenario 20 - Indirect Exposure to Liquid Detergent | Systemic | - | $AEL_{long-term}$ | <1 | - | Yes | |
| | Local | - | - | - | - | Yes | Negligible inhalation exposure |

[1] This systemic assessment was performed as a complementary approach to the local RC. Comparison to ARfD is not appropriate, but is provided in the absence of an $AEL_{acute}$.

Professional human exposure during application of various products containing glutaraldehyde as an in-can preservative has been assessed. All uses are acceptable based on the comparison of the systemic dose to the $AEL_{long-term}$ and ARfD, as well as of the calculated glutaraldehyde concentration in the air to the $AEC_{acute\ inhalation}$ and to $AEC_{inhalation}$. No adverse health effects are expected since systemic exposure is below the reference value and the MOE values are more than 1. RPE is required in loading and unloading slurry tanks (scenario 21) and gloves, double coverall and RPE (APF 40) are required in connecting drum to pump (scenario similar to #9).

Non-professional human exposure to laundry softener, liquid detergent, wax emulsion and car polish has been assessed. All uses are acceptable based on the comparison of the

systemic dose to the $AEL_{long\text{-}term}$ or ARfD, as relevant, and of the calculated glutaraldehyde concentration in the air to the $AEC_{acute\ inhalation}$ and to $AEC_{inhalation}$. No adverse health effects are expected since systemic exposure is below the reference value and the MOE values are more than 1.

**Conclusion on PT 6:** All scenarios are acceptable when the appropriate PPE are used. These scenarios can be considered as safe uses that are acceptable to support the approval of glutaraldehyde in PT 6.

#### 2.2.3.5. Product Type 11

Qualitative local RC is presented for local dermal effects. Quantitative risk assessment was performed for systemic effects and for local effect following inhalation exposure.

Quantitative local RC was not performed for local dermal or oral effects. During loading, splashes may occur and result in exposure to up to 50 % glutaraldehyde. The use of gloves and double coveralls is required to reduce exposure.

Summary of the quantitative risk assessment for systemic effects following dermal and inhalation exposure and risk for local effects following inhalation exposure in different scenarios is presented in the table below.

| Summary of scenarios assessed in PT 11 | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Scenario** | **Systemic or local RC** | **PPE** | **Relevant reference value** | **% Ref. value (< 100)** | **MOE** (ref. value / exposure) (> 1) | **Acceptable** | **Remarks** |
| Mixing and Loading Solution for Filling a Closed Recirculating System (similar to #9) | Systemic | Gloves Double coverall RPE (10 %) | ARfD | 3 | - | Yes | Complementary approach only[1] |
| | Local | Gloves Double coverall RPE (2.5 %) | $AEC_{acute\ inhalation}$ | 55 | 1.8 | Yes | |
| Scenario 22 – Draining a Closed Recirculating System | Systemic | - | ARfD | 1.9 | - | Yes | Complementary approach only[1] |
| | Systemic | - | $AEL_{long\text{-}term}$ | 81 | - | Yes | |
| | Local | - | $AEC_{acute\ inhalation}$ | <1 | 230 | Yes | |
| | Local | - | $AEC_{inhalation}$ | <1 | 5 | Yes | |
| Loading (connecting / disconnecting drums) (similar to #9) | Systemic | Gloves Double coverall RPE (10 %) | ARfD | 3 | - | Yes | Complementary approach only[1] |
| | Local | Gloves Double coverall RPE (2.5 %) | $AEC_{acute\ inhalation}$ | 55 | 1.8 | Yes | |
| Scenario 23 – Bystander Exposure; Child | Systemic | - | ARfD | <1 | - | Yes | Complementary approach only[1] |
| | Local | - | $AEC_{acute\ inhalation}$ | <1 | 500 | Yes | |
| Scenario 23 – Bystander Exposure; Adult | Systemic | - | ARfD | <1 | - | Yes | Complementary approach only[1] |
| | Local | - | $AEC_{acute\ inhalation}$ | <1 | 500 | Yes | |

[1] This systemic assessment was performed as a complementary approach to the local RC. Comparison to ARfD is not appropriate, but is provided in the absence of an $AEL_{acute}$.

Professional human exposure during draining a closed recirculating system (scenario 22), mixing and loading solution for filling a closed recirculating system and connecting and disconnecting drums (both are similar to scenario 9) is acceptable based on the comparison of the systemic dose to the $AEL_{long\text{-}term}$ and ARfD, as well as of the calculated glutaraldehyde concentration in the air to the $AEC_{acute\ inhalation}$ and to

$AEC_{inhalation}$. No adverse health effects are expected since systemic exposure is below the reference value and the MOE value is more than 1.

Above mentioned scenarios mixing and loading and connecting and disconnecting drums cause a high potential exposure and are acceptable only when gloves, double coverall and RPE (APF 40) are used. The use of these PPE is required.

Bystander exposure (scenario 23) reveals very low exposure levels. This scenario is acceptable for both an adult and a child.

**Conclusion on PT 11:** None of the professional scenarios causes concern when the appropriate PPE are used and they are all thus acceptable. These scenarios can be considered as safe uses that are acceptable to support the approval of glutaraldehyde in PT 11. This conclusion is also supported by the acceptable indirect exposure scenario 23.

#### 2.2.3.6. Product Type 12

Qualitative local RC is presented for local dermal effects. Quantitative risk assessment was performed for systemic effects and for local effect following inhalation exposure.

Quantitative local RC was not performed for local dermal or oral effects. Direct exposure will mostly be excluded by the use of protective gloves and double coveralls. During connecting or disconnecting (scenario loading wet-end slimicide), splashes may occur and result in exposure to higher glutaraldehyde concentrations. The use of gloves and double coveralls will be obligatory.

Summary of the quantitative risk assessment for systemic effects following dermal and inhalation exposure and risk for local effects following inhalation exposure in different scenarios is presented in the table below.

| Summary of scenarios assessed in PT 12 | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Scenario** | **Systemic or local RC** | **PPE** | **Relevant reference value** | **% Ref. value (< 100)** | **MOE** (ref. value / exposure) (> 1) | **Acceptable** | **Remarks** |
| Wet-end slimicide – loading (connecting/disconnecting drums) (similar to #9) | Systemic | Gloves Double coverall RPE (10 %) | ARfD | 3 | - | Yes | Complementary approach only[1] |
| | | Gloves Double coverall RPE (2.5 %) | $AEL_{long-term}$ | 89 | - | Yes | |
| | Local | Gloves Double coverall RPE (2.5 %) | $AEC_{acute\ inhalation}$ | 55 | 1.8 | Yes | |
| Scenario 24 – Wet-end slimicide – cleaning and maintenance of pulp tanks | Systemic | - | ARfD | <1 | - | Yes | Complementary approach only[1] |
| | Systemic | - | $AEL_{long-term}$ | 43 | - | Yes | |
| | Local | - | $AEC_{acute\ inhalation}$ | <1 | 250 | Yes | |
| | Local | - | $AEC_{inhalation}$ | 9 | 11 | Yes | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Mixing and Loading Solution (similar to #9) | Systemic | Gloves Double coverall RPE (10 %) | ARfD | 3 | - | Yes | Complementary approach only[1] |
| | Local | Gloves Double coverall RPE (2.5 %) | $AEC_{acute\ inhalation}$ | 55 | 1.8 | Yes | |
| Scenario 26 - Exposure during Cleaning/Maintenance of Pulp Tanks - Deinking | Systemic | Gloves Coated coveralls | $AEL_{long-term}$ | 26 | - | Yes | |
| | Local | - | $AEC_{acute\ inhalation}$ | 3 | 33 | Yes | |
| | | - | $AEC_{inhalation}$ | 72 | 1.4 | Yes | |
| Scenario 25 - Indirect worker exposure, vapour phase | Systemic | - | $AEL_{long-term}$ | <290 | - | No | |
| | Local | | $AEC_{acute\ inhalation}$ | <52 | <2 | Yes | |
| | Local | - | $AEC_{inhalation}$ | <2500 | <1 | No | |
| Scenario 25 - Indirect worker exposure, aerosol phase | Systemic | - | $AEL_{long-term}$ | 7 | - | Yes | |
| | Local | - | $AEC_{acute\ inhalation}$ | 1 | 88 | Yes | |
| | Local | - | $AEC_{inhalation}$ | 54 | 2 | Yes | |
| Scenario 25 - Total indirect inhalation exposure | Systemic | - | $AEL_{long-term}$ | <280 | - | No | |
| | Local | - | $AEC_{acute\ inhalation}$ | <53 | <2 | Yes | |
| | Local | - | $AEC_{inhalation}$ | <2500 | <1 | No | |

[1] This systemic assessment was performed as a complementary approach to the local RC. Comparison to ARfD is not appropriate, but is provided in the absence of an $AEL_{acute}$.

Professional human exposure during cleaning and maintenance of pulp tanks (scenarios 24 and 26), connecting and disconnecting drums (scenario loading wet-end slimicide) and mixing and loading solution (scenario mixing and loading) is acceptable based on the comparison of the systemic dose to the $AEL_{long-term}$ and ARfD, as well as of the calculated glutaraldehyde concentration in the air to the $AEC_{acute\ inhalation}$ and to $AEC_{inhalation}$. No adverse health effects are expected since systemic exposure is below the reference value and the MOE value is more than 1.

Indirect worker exposure (scenario 25) exceeded the AEL and $AEC_{inhalation}$ values. However, exposure approximated using Henry's law is not accurate enough to

demonstrate that there is a risk although the result exceeded the previously mentioned reference values. This estimation is a very conservative worst case approximation and cannot be used to decide that exposure is unacceptable. Local ventilation must be used to get the systemic and long term inhalation exposure below the $AEC_{inhalation}$ if needed. The use of respiratory protective equipment (RPE) is obligatory unless other risk mitigation measures can reduce exposure to acceptable level. This should be verified with the measurements or modelling in the product authorization stage.

No PPE are required in scenario 24 due to systemic effects. However, gloves and coated coveralls are required in this scenario due to skin sensitizing effect of glutaraldehyde. Gloves and coated coveralls are required in scenario 26. Scenarios loading wet-end slimicide and mixing and loading cause a high potential exposure and are acceptable only when gloves, double coverall and RPE (APF 40) are used. The use of these PPE is required.

**Conclusion on PT 12:** None of the professional scenarios causes concern when the appropriate PPE are used and they are all thus acceptable. These scenarios can be considered as safe uses that are acceptable to support the approval of glutaraldehyde in PT 12.

#### 2.2.3.7. Oilfield applications

Qualitative local RC is presented for local dermal effects. Quantitative risk assessment was performed for systemic effects and for local effect following inhalation exposure.

Quantitative local RC was not performed for local dermal or oral effects. Direct exposure will mostly be excluded by the use of coated coveralls and protective gloves. Splashes may occur and result in exposure to up to 50 % glutaraldehyde. The use of PPE will be obligatory.

Summary of the quantitative risk assessment for systemic effects following dermal and inhalation exposure and risk for local effects following inhalation exposure in different scenarios is presented in the table below.

| Summary of scenarios assessed | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Scenario** | **Systemic or local RC** | **PPE** | **Relevant reference value** | **% Ref. value (< 100)** | **MOE** (ref. value / exposure) (> 1) | **Acceptable** | **Remarks** |
| Drilling mud preservative – adding concentrate: connecting/disconnecting feeder system | Systemic | Gloves Double coveralls RPE (2.5 %) | $AEL_{long-term}$ | 89 | - | Yes | |
| | Local | Gloves Double coveralls RPE (2.5 %) | $AEC_{acute\ inhalation}$ | 55 | 1.8 | Yes | |
| | | Gloves Double coveralls RPE (2.5 %) | $AEC_{inhalation}$ | 81 | 1.2 | Yes | |
| Drilling mud preservative – adding concentrate to hydrotesting fluid | Systemic | Gloves Double coveralls RPE (2.5 %) | $AEL_{long-term}$ | 89 | - | Yes | |
| | Local | Gloves Double coveralls RPE (2.5 %) | $AEC_{acute\ inhalation}$ | 55 | 1.8 | Yes | |
| | | Gloves Double coveralls RPE (2.5 %) | $AEC_{inhalation}$ | 81 | 1.2 | Yes | |
| Mixing and loading: (diluted biocide) – semi- automatically | Systemic | Gloves Double coveralls RPE (2.5 %) | $AEL_{long-term}$ | 89 | - | Yes | |

| Summary of scenarios assessed | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Scenario** | **Systemic or local RC** | **PPE** | **Relevant reference value** | **% Ref. value (< 100)** | **MOE** (ref. value / exposure) (> 1) | **Acceptable** | **Remarks** |
| | Local | Gloves Double coveralls RPE (2.5 %) | $AEC_{acute\ inhalation}$ | 55 | 1.8 | Yes | |
| | | Gloves Double coveralls RPE (2.5 %) | $AEC_{inhalation}$ | 81 | 1.2 | Yes | |

Professional human exposure during the oilfield applications presented in scenarios drilling mud preservative - adding concentrate to feeder system or hydrotesting fluid and mixing and loading slimicide for mineral oil extrcation is acceptable based on the comparison of the systemic dose to the $AEL_{long\text{-}term}$, as well as of the calculated glutaraldehyde concentration in the air to the $AEC_{inhalation}$. No adverse health effects are expected since systemic exposure is below the reference value and the MOE values are more than 1.

The presented oilfield applications result in high potential exposure rates, but the professional users can be protected using gloves, double coveralls and RPE with assigned protection factors (APF) of 40. The use of these PPE will be required.

**Conclusion on PT 6 and 11 in oilfield applications:** None of the scenarios cause concern when the appropriate PPE are used and they are thus acceptable. These scenarios can be considered as safe uses that are acceptable to support the approval of glutaraldehyde in PTs 6 and 11 in oilfield applications.

## 2.3. Summary of Environmental Risk Assessment

### *2.3.1. Fate and distribution in the environment*

Glutaraldehyde is highly hydrophilic and lipophobic substance. It is non-ionisable and fully soluble in water. Glutaraldehyde is volatile, but does not easily evaporate from water. Glutaraldehyde is subject to rapid photochemical degradation in air with a half-life of 8.2 h. Glutaraldehyde is readily biodegradable and has a potential to biodegrade in the marine environment, but it is hydrolytically and photolytically stable under environmental relevant conditions.

Under aerobic water/sediment system Glutaraldehyde dissipated from the water phase with a half-life of 1.25 d (12 °C). The major metabolite in the aqueous phase was glutaric acid that was detected at maximum 20.2% of the applied radioactivity during the first day. Glutaric acid was not detected thereafter. The amount of non-extractable radioactivity in the sediment was 12.6% of applied radioactivity in the end of the experiment (30 days). Total proportion of CO2 formed in the test was 67.9% of the applied radioactivity indicating significant mineralization.

Under anaerobic conditions Glutaraldehyde is not degraded, but rather transformed to three major metabolites; 5-hydroxy-pentanal (37.0%), 1,5-pentanediol (76.1%) and a dimer of Glutaraldehyde, 2-hydroxy-3,4,4a,7,8,8a-hexahydro-2H-chromene-6-carbaldehyde (17.7%). The first metabolite was not detected after first day and is considered non-persistent, but the two latter metabolites were present over 10% of the applied radioactivity in the end of the experiment (123 day) and are hence regarded as persistent metabolites under the test conditions. The 1,5-pentanediol would be expected to degrade in aerobic environments and the dimer of Glutaraldehyde would not be kinetically favoured to form in an anaerobic sediment were only very low concentrations of Glutaraldehyde are possibly present. The amount of non-extractable radioactivity in the sediment was 8.4% in the end of the test. A dissipation half-life of 0.91 d (12 °C) was calculated based on Glutaraldehyde in the aqueous phase using pseudo-first order kinetics.

Glutaraldehyde is considered to be mobile in sandy sediment (Koc 120) and moderately mobile in soil (Koc 210-500) on the basis of adsorption/desorption study. The arithmetic mean Koc of 326 l/kg will be used for the risk assessment. The adsorption/desorption study indicated rapid degradation or irreversible adsorption (chemisorption) of Glutaraldehyde in soil as it could not be measured in the desorption supernatants.

In a study on degradation and adsorption of Glutaraldehyde in the activated sludge biodegradation and chemisorption where shown to be main removal processes. As a result of chemisorption Glutaraldehyde is likely bound by covalent bonds to proteinaceous material and loses its identity as Glutaraldehyde. The overall disappearance rate was 2.9 $h^{-1}$ (15 °C) corresponding to a half-life of 0.2 h. The rate constant is used to model degradation rate in the activated sludge in the exposure calculations.

Glutaraldehyde is not expected to bioaccumulate in aquatic or terrestrial organisms based on the low log octanol/water partition coefficient (-0.33, -0.36). Taken into account the low bioaccumulation potential and ready biodegradation there is no need to further testing or risk assessment of secondary poisoning.

### *2.3.2. Effects assessment*

Acute toxicity has been studied in both freshwater and marine organisms. No systematic difference in sensitivity between marine and freshwater species could be observed. The difference in sensitivity between freshwater and marine taxa was less than 10 in all three trophic levels in those cases where studies with equal quality could be compared. Considering the chronic toxicity algae were the most sensitive species and the PNEC was based on the lowest valid NOEC of 0.025 mg/L from algae test. The PNECwater and PNECseawater are 2.5 and 0.25 µg/L, respectively.

Toxicity of metabolites formed in the aerobic and anaerobic water sediment studies have not been studied because they are either covered by the aquatic ecotoxicity tests (glutaric acid) or the metabolites formed in the anaerobic water/sediment test are not likely to be formed in the natural anaerobic sediment as Glutaraldehyde is unlikely to partition there due to high water solubility, low log Kow and ready biodegradability.

Toxicity of Glutaraldehyde to sediment dwelling organisms has not been studied and it is neither required as the sediment risk assessment is not needed for Glutaraldehyde according to the TGD: it's log Koc and log Kow are ≤ 3 and it's readily biodegradable. Glutaraldehyde starts to inhibit activated sludge micro-organism above 16 mg/L (NOEC), the EC50 is > 51 mg/L. The $PNEC_{STP}$ is 0.51 mg/L.

Glutaraldehyde is not particularly toxic to plants or earthworms. Soil micro-organisms are the most sensitive group among soil organisms and the PNECsoil was determined from the carbon transformation test with the assessment factor of 50. The PNECsoil is 0.184 mg/kg ww.

### *2.3.3. PBT and POP assessment*

Glutaraldehyde does not fulfil PBT or vPvB criteria according to Commission Regulation 253/2011 amending the Annex XIII of Regulation 1907/2006. Glutaraldehyde is readily biodegradable, has a low bioaccumulation potential (Log Kow -0.33) and does not have any NOEC less than 0.01 mg/l. Glutaraldehyde does not meet the criteria for classification as carcinogenic (category 1A or 1B), germ cell mutagenic (category 1A or 1B), toxic for reproduction (category 1A, 1B or 2) or specific target organ toxicity after repeated exposure (STOT RE category 1 or 2) according to Regulation 1272/2008. It is concluded that Glutaraldehyde is not a PBT or vPvB substance.

Glutaraldehyde does not fulfil criteria for being persistent organic pollutant (POP). Glutaraldehyde does not have potential for long-range transboundary atmospheric transport, its vapour pressure is below 1000 PA (44 Pa, 20 °C), but the estimated atmospheric half-life is less than two days (8.2 hours). As stated above in the context of PBT assessment Glutaraldehyde does not meet criteria for persistence and bioaccumulation.

### *2.3.4. Exposure assessment*

The emissions for PT 2, 3, 4, 6, 11 and 12 have been calculated according the respective Emission Scenario Documents, ESDs. The emissions have mostly been calculated according to average consumption based scenarios. In confidential Annex to Documents IIB and IIC the tonnage based scenarios are given when such are described in the ESDs. The Predicted Environmental Concentrations, PECs, have been calculated according to the TGD and calculations have been done with EUSES Version 2.1.2. The default values of TGD/EUSES have been used in calculations unless stated otherwise. The emission and exposure calculations are reported in detail in Doc IIB.

The PECs are usually calculated for STP, surface water, soil, groundwater and air. The PECs are given as 100 % Glutaraldehyde. The PECs have been calculated for Tier 0, Tier 1 and 2. In Tier 0 the default rate constant of 1 $h^{-1}$ is used for the STP. In the Tier 1 calculations the experimentally derived rate constant of 2.9 $h^{-1}$ is used for the STP (Doc IIA, 5.1.1.4). The refinement is based on an adsorption and degradation study in the activated sludge owned by both applicants. Very limited desorption from the activated sludge could be observed in this study demonstrating irreversible nature of adsorption. The adsorption/desorption experiment in soil (Doc IIIA7.2.3.1, Dow, BASF) provided evidence of reactions with soil organic matter during the adsorption phase. As Glutaraldehyde reacted with the soil matrix, it was not available in the desorption experiment. Therefore, in Tier 2 the concentration in dry sewage sludge is set to 0.

A specific refinement is used for paper industry (PT 6 and PT 12). The refinement is based on the monitoring study in a paper mill [redacted]. In that study Glutaraldehyde is added twice a day to pulper resulting in concentration of 13 ppm. After addition Glutaraldehyde was measured in the headbox, the pulper and in wastewater treatment plant several times for ten successive hours. Glutaraldehyde was not detected above the detection limit of 0.05 ppm. The applicants suggested adding a fraction of elimination (Felim) of 0.996 in the calculation of Elocalwater which was agreed by the RMS. In addition, there is another monitoring study of BASF (A6.14_03) from a different paper mill than the study of Dow. The report show similar dissipation. This refinement based on two monitoring studies and specific reactive nature of Glutaraldehyde was accepted in TM III 2013 and is called Tier 3 and it also includes refinements of Tier 2.

#### 2.3.4.1. Product Type 2

Glutaraldehyde is used for disinfection of hard surfaces in industry and hospitals. For calculations the concentration of 3 g/l is used. Glutaraldehyde is applied on the surfaces such as floor, walls, and tables, rinsing is sometimes performed but most of the time the treated surfaces are let to dry out. This application is used by professionals only. The PECs are presented below.

PECs for PT 2 scenarios. Tiers 0-2 are explained in Section 2.2.2.5.

| Scenario | $Elocal_{water}$ kg/d | $PEC_{stp}$ mg/l | $PEC_{water}$ µg/l | $PEC_{soil}$ mg/kg ww | $PEC_{gw}$ µg/l | $PEC_{air}$ mg/m$^3$ |
|---|---|---|---|---|---|---|
| Industrial areas | | | | | | |
| Tier 0 | 0.06 | 0.0037 | 0.37 | 0.0024 | 0.131 | 3.8E-10 |
| Tier 1 | 0.06 | 0.0014 | 0.139 | 0.0023 | 0.127 | 2.56E-10 |
| Tier 2 | 0.06 | 0.0014 | 0.139 | 4.62E-11 | 7.87E-12 | 2.56E-10 |
| Sanitary purposes in hospitals | | | | | | |
| Tier 0 | 0.113 | 0.0069 | 0.693 | 0.0044 | 0.246 | 5.08E-10 |
| Tier 1 | 0.113 | 0.0026 | 0.261 | 0.0043 | 0.239 | 3.42E-10 |
| Tier 2 | 0.113 | 0.0026 | 0.261 | 6.17E-11 | 1.05E-11 | 3.42E-10 |

#### 2.3.4.2. Product Type 3

Glutaraldehyde is applied for disinfection of poultry and pig fattening farms. Disinfection is performed by spraying with a 1 g/l Glutaraldehyde solution. The intended use volume is 0.4 l/m$^2$. The product remains on the treated surfaces and is not rinsed off. The scenarios 'Sows in group' and 'Laying hens in free range with litter floor' were chosen by the applicants. The sow scenario was identified as the worst case scenario (highest PECs) among the pig and sow scenarios and the hen scenario had direct emissions to slurry/manure and STP.

PIEC for soil and PEC for groundwater for PT 3 scenarios with release to slurry/manure.

| Scenario | PIECgrs-N mg/kg | PIECars-N mg/kg | $PEC_{gw}$-grass µg/l | $PEC_{gw}$-arab µg/l |
|---|---|---|---|---|
| Without degradation (one application to arable land and four applications to grassland) | | | | |
| No refinement | | | | |
| Sows in groups | 0.1328 | 0.0322 | 22.6 | 5.7 |
| Laying hens in free range with litter floor | 0.0305 | 0.0076 | 5.2 | 1.3 |
| Refinement: Fresidue 0.01% | | | | |
| Sows in groups | 1.33E-05 | 3.32E-06 | 2.26E-03 | 5.65E-04 |
| Laying hens in free range with litter floor | 3.05E-06 | 7.63-E07 | 5.20E-04 | 1.30E-04 |

| | | | | |
|---|---|---|---|---|
| 10 successive years of manure application | | | | |
| No refinement | | | | |
| Sows in groups | 0.0337 | 0.0239 | 5.7 | 4.1 |
| Laying hens in free range with litter floor | 0.0077 | 0.0055 | 1.32 | 0.94 |
| Refinement: Fresidue 0.01% | | | | |
| Sows in groups | 3.37E-06 | 2.39E-06 | 5.73E-04 | 4.08E-04 |
| Laying hens in free range with litter floor | 7.74E-07 | 5.50E-07 | 1.32E-04 | 9.38E-05 |

PECs for PT 3 scenario 'Laying hens in free range with litter floor' with release to STP. Tiers 0-2 are explained in Section 2.2.2.5.

| **Scenario** | **$Elocal_{water}$ kg/d** | **$PEC_{stp}$ mg/l** | **$PEC_{water}$ µg/l** | **$PEC_{soil}$ mg/kg ww** | **$PEC_{gw}$ µg/l** | **$PEC_{air}$ mg/m$^3$** |
|---|---|---|---|---|---|---|
| Laying hens in free range with litter floor | | | | | | |
| Tier 0 | 0.369 | 0.0277 | 2.27 | 0.015 | 0.807 | 2.35E-09 |
| Tier 1 | 0.369 | 0.0086 | 0.856 | 0.014 | 0.783 | 1.58E-09 |
| Tier 2 | 0.369 | 0.0086 | 0.856 | 1.85E-10 | 4.85E-08 | 1-58E-09 |

#### 2.3.4.3. Product Type 4

Glutaraldehyde is used for disinfection of vessels and machinery and food processing surfaces within PT 4. The emissions are led either to an on-site STP and thereafter to surface water or to off-site (municipal) STP. Food processing vessels are disinfected on a daily basis or after each batch of food. A solution of Glutaraldehyde at a concentration of 1 g/l is used for this application and is replaced on a weekly basis. The walls and other surfaces of a slaughter house or similar food processing/storage area are disinfected on a daily basis by applying a solution of 1 g/l Glutaraldehyde. In both uses Glutaraldehyde is left to soak for approximately 10 minutes and is then rinsed with water which is discharged to the drain.

PECs for PT 4 scenarios. Tiers 0-2 are explained in Section 2.2.2.5.

| Scenario | $Elocal_{water}$ kg/d | $PEC_{STP}$ mg/l | $PEC_{water}$ µg/l | $PEC_{soil}$ mg/kg ww | $PEC_{gw}$ µg/l | $PEC_{air}$ mg/m$^3$ |
|---|---|---|---|---|---|---|
| Entire plant: on-site STP | | | | | | |
| Tier 0 | 0.032[1] | - | 16 | - | - | - |
| Tier 1 | 0.0024[1] | - | 1.224 | - | - | - |
| Entire plant: off-site STP | | | | | | |
| Tier 0 | 0.294[3] | 0.018 | 1.81 | 0.012 | 0.643 | 1.87E-03 |
| Tier 1 | 0.294[3] | 0.007 | 0.682 | 0.011 | 0.624 | 1.26E-09 |
| Tier 2 | 0.294[3] | 0.007 | 0.682 | 2.27E-10 | 3.87E-08 | 1.26E-09 |
| Surfaces in food processing areas: slaughterhouses | | | | | | |
| Tier 0 | 1 | 0.062 | 6.16 | 0.040 | 2.19 | 4.51E-9 |
| Tier 1 | 1 | 0.023 | 2.32 | 0.038 | 2.12 | 3.04E-9 |
| Tier 2 | 1 | 0.023 | 2.32 | 5.48E-10 | 9.34E-11 | 3.04E-9 |
| Surfaces in large scale kitchens | | | | | | |
| Tier 0 | 0.2 | 0.012 | 1.23 | 0.008 | 0.437 | 9.02E-10 |
| Tier 1 | 0.2 | 0.005 | 0.464 | 0.008 | 0.424 | 6.07E-10 |
| Tier 2 | 0.2 | 0.005 | 0.464 | 1.1E-10 | 1.87E-08 | 6.07E-10 |

[1]This corresponds to $C_{effluent}$ of 0.016 mg/l calculated in the ESD for PT 4.

[2]This corresponds to $C_{effluent}$ of 0.0012 mg/l calculated in the ESD for PT 4.

[3]This corresponds to $C_{influent}$ of 0.147 mg/l calculated in the ESD for PT 4.

#### 2.3.4.4. Product Type 6

Glutaraldehyde is used as a preservative in household and professional detergents. In paper industry Glutaraldehyde is used to preserve paper wet-end additives and paper coatings. Some of the PT 6 scenarios are based on tonnages and are given in Confidential Annex to Doc IIB and IIC. Laundry softener, liquid detergents and other aqueous formulations used in the home require an in-can preservative to protect them against bio-spoilage during their shelf life. The concentration of Glutaraldehyde in detergents is 1 g/l. It is assumed that 100% of the product is discharged to a STP. Paper wet-end additives and paper coatings are used by professionals in the paper making industry. Glutaraldehyde concentration is 0.5 g/l and it is used 100 g per tonne of produced paper.

The PECs for Glutaraldehyde as in-can preservative in detergents and paper additives are presented below. The waste water volume was increased to 5000 m$^3$/day for newsprint in all Tiers. This refinement is based on the default waste water volume of 15 m$^3$/tonne of produced paper and is explained in detail in Doc IIB, Section 8.3.6.4.

PECs for PT 6 scenarios. Tiers 0-3 are explained in Section 2.2.2.5.

| Scenario | $Elocal_{water}$ (kg/d) | $PEC_{STP}$ (mg/l) | $PEC_{water}$ (µg/l) | $PEC_{soil}$ (mg/kg ww) | $PEC_{gw}$ (µg/l) | $PEC_{air}$ (mg/m$^3$) |
|---|---|---|---|---|---|---|
| Detergents for sanitary purpose (PT 2) | | | | | | |
| Tier 0 | 0.025 | 0.0015 | 0.154 | 0.001 | 0.055 | 1.13E-10 |
| Tier 1 | 0.025 | 0.0005 | 0.058 | 0.001 | 0.053 | 7.59E-11 |
| Tier 2 | 0.025 | 0.0005 | 0.058 | 1.37E-11 | 2.33E-12 | 7.59E-11 |
| Detergents for professional use | | | | | | |
| Tier 0, $F_{penetr}$=1 | 0.144 | 0.0089 | 0.887 | 0.006 | 0.351 | 2.51E-12 |
| Tier 0, $F_{penetr}$=0.5 | 0.072 | 0.0044 | 0.443 | 0.003 | 0.157 | 1.25E-12 |
| Tier 1, $F_{penetr}$=1 | 0.144 | 0.0033 | 0.334 | 0.006 | 0.305 | 1.69E-12 |
| Tier 1, $F_{penetr}$=0.5 | 0.072 | 0.0017 | 0.167 | 0.003 | 0.153 | 8.44E-13 |
| Tier 2, $F_{penetr}$=1 | 0.144 | 0.0033 | 0.334 | 3.05E-13 | 5.19E-12 | 1.69E-12 |
| Tier 2, $F_{penetr}$=0.5 | 0.072 | 0.0017 | 0.167 | 1.52E-13 | 2.59E-12 | 8.44E-13 |
| Paper production: preservative for additives (newspaper) | | | | | | |
| Tier 0 | 0.494 | 0.012 | 1.22 | 0.008 | 0.432 | 2.57E-09 |
| Tier 1 | 0.494 | 0.005 | 0.46 | 0.008 | 0.419 | 1.73E-09 |
| Tier 2 | 0.494 | 0.005 | 0.46 | 3.1E-10 | 5.32E-08 | 1.73E-09 |
| Tier 3 | 0.002 | 0.00002 | 0.002 | 1.26E-12 | 2.15E-10 | 7.0E-12 |
| Paper production: preservative for additives (printing and writing paper) | | | | | | |
| Tier 0 | 0.429 | 0.026 | 2.64 | 0.017 | 0.94 | 2.06E-09 |
| Tier 1 | 0.429 | 0.010 | 1.0 | 0.016 | 0.91 | 1.39E-09 |
| Tier 2 | 0.429 | 0.010 | 1.0 | 3.14E-10 | 5.34E-08 | 1.39E-09 |
| Tier 3 | 0.002 | 0.00005 | 0.005 | 1.45E-12 | 2.49E-10 | 6.47E-12 |

#### 2.3.4.5. Product Type 11

Glutaraldehyde as a preservative has been evaluated for open and closed recirculating cooling systems. In an open recirculating cooling system, the cooling water circulates in an open loop. In addition water is recycled in cooling towers. In small recirculating cooling systems, the dose of 100 ppm is used for the defouling treatment which is assumed to be needed once a year. For maintenance treatment a dosing of 50 ppm once per day daily is used. Small open systems were assessed with and without a STP connection.

In closed systems, the cooling water recirculates in a closed loop. The cooling water is not discharged after cooling. These systems have minimal loss of water, since there is no direct contact with the atmosphere. The system is filled before use and then drained and refilled very infrequently. Glutaraldehyde is added directly to the system at maximum concentration of 100 ppm. The applicants propose to restrict the use of Glutaraldehyde to closed systems where releases are emitted to STP.

PECs for PT 11 scenarios - small-recirculation cooling systems without STP (direct release to surface water).

| **Scenario** | **$PEC_{water}$ µg/l** | **$PEC_{seawater}$ µg/l** | **$PEC_{soil\ drift}$ mg/kg ww** | **$PEC_{air}$ mg/m$^3$** |
|---|---|---|---|---|
| Small open recirculation cooling systems | | | | |
| Defouling treatment | | 887 | 0.002 | 1.62E-06 |
| Dilution factor 350 | 253 | | | |
| Dilution factor 1000 | 88.7 | | | |
| Maintenance treatment | | 2010 | 0.200 | 0.0011 |
| Dilution factor 350 | 574 | | | |
| Dilution factor 1000 | 201 | | | |

The dilution factors from small recirculating cooling systems were used as agreed at TM III/2011. The dilution to coastal water was 100 according to TGD.

PECs for PT 11 scenarios - small and closed recirculation cooling systems with STP.

| **Scenario** | **$PEC_{STP}$ mg/l** | **$PEC_{water}$ µg/l** | **$PEC_{soil}$ mg/kg ww** | **$PEC_{gw}$ µg/l** | **$PEC_{soildrift}$ mg/kg ww** | **$PEC_{air}$ mg/m$^3$** |
|---|---|---|---|---|---|---|
| Small open recirculation cooling systems | | | | | | |
| Defouling treatment | | | | | | |
| Tier 0 | 0.262 | 26.2 | 0.168 | 9.31 | 0.002 | 7.41E-11 |
| Tier 1 | 0.0987 | 9.87 | 0.163 | 9.03 | 0.002 | 4.99E-11 |
| Tier 2 | 0.0897 | 9.87 | 9.03E-12 | 1.53E-12 | 0.002 | 1.53E-12 |
| Maintenance treatment | | | | | | |
| Tier 0 | 0.594 | 59.4 | 0.381 | 21.1 | 0.200 | 5.04E-08 |
| Tier 1 | 0.224 | 22.4 | 0.369 | 20.5 | 0.200 | 3.39E-08 |
| Tier 2 | 0.224 | 22.4 | 6.12E-09 | 1.04-09 | 0.200 | 3.39E-08 |
| Closed recirculation cooling systems | | | | | | |
| Defouling treatment | | | | | | |
| Tier 0 | 5.92E-05 | 0.0059 | 3.79E-05 | 0.0021 | | 1.67E-14 |
| Tier 1 | 2.23E-05 | 0.0022 | 3.68E-05 | 0.002 | | 1.12E-14 |
| Tier 2 | 2.23E-05 | 0.0022 | 2.03E-15 | 3.46E-13 | | 1.12E-14 |
| Mantenance treatment | | | | | | |
| Tier 0 | 1.48E-05 | 0.0015 | 9.47E-06 | 5.25E-04 | | 4.18E-15 |
| Tier 1 | 5.57E-06 | 5.56E-04 | 9.19E-06 | 5.09E-04 | | 2.81E-15 |
| Tier 2 | 5.57E-06 | 5.56E-04 | 5.08E-16 | 8.65E-17 | | 2.81E-15 |

### 2.3.4.6. Product Type 12

Glutaraldehyde is used to control slime producing micro-organisms in paper industry where the main function of the slimicide is to suppress the growth of the micro-organisms.

Emissions from paper production are calculated with the reasonable worst case and typical case scenarios. In the reasonable worst case scenario both the short and long circulation water are treated with slimicide and there is no connection to a pulp mill or WWTP. The primary receiving compartment is surface water. A range of dilution factors (10, 100 and 1000) are used in the calculations. Dilution factor of 100 is used for seawater. In the typical case scenario, only the short circulation is treated, and there is a connection to a pulp mill. The wastewater from the paper mill is diluted with the wastewater from the pulp mill as they are connected to the same WWTP. The effluent discharge of the local WWTP is set to 5000 $m^3/d^1$. Slimicides are applied by a continuous low dose (37.5 ppm) or by a single defouling treatment with elevated doses (75 ppm).

PECs for PT 12 paper production processes - the reasonable worst case scenario (no connection to WWTP, direct release to surface water). Tiers 0 and 3 are explained in Section 2.2.2.5.

| **Treatment** | **Dilution factor** | **$PEC_{water}$ µg/l** |
|---|---|---|
| Defouling treatment | | |
| Tier 0 | | |
| | 10 | 4000 |
| | 100 | 4000 |
| | 1000 | 40 |
| Tier 3 | | |
| | 10 | 18 |
| | 100 | 1.8 |
| | 1000 | 0.18 |
| | | |
| Maintenance treatment | | |
| Tier 0 | | |
| | 10 | 2000 |
| | 100 | 200 |
| | 1000 | 20 |
| Tier 3 | | |
| | 10 | 9 |
| | 100 | 0.9 |
| | 1000 | 0.09 |

Table 6.1.8.2.2 PECs for PT 12 paper production processes - the typical case scenario (connection to WWTP). Tiers 0-3 are explained in Section 2.2.2.5.

| Treatment | $PEC_{wwtp}$ mg/l | $PEC_{water}$ µg/l | $PEC_{soil}$ mg/kg ww | $PEC_{gw}$ µg//l | $PEC_{air}$ mg/m$^3$ |
|---|---|---|---|---|---|
| Defouling | | | | | |
| Tier 0 | 1.93 | 193 | 1.24 | 68.5 | 4.09E-07 |
| Tier 1 | 0.727 | 72.7 | 1.20 | 66.4 | 2.75E-07 |
| Tier 2 | 0.727 | 72.7 | 4.96E-08 | 8.46E-06 | 2.75E-07 |
| Tier 3 | 0.0033 | 0.33 | 2.22E-10 | 3.78E-11 | 1.23E-09 |
| Maintenance | | | | | |
| Tier 0 | 0.97 | 96.6 | 0.619 | 34.3 | 2.05E-07 |
| Tier 1 | 0.364 | 36.4 | 0.600 | 33.3 | 1.38E-07 |
| Tier 2 | 0.364 | 36.4 | 2.49E-08 | 4.23E-06 | 1.38E-07 |
| Tier 3 | 0.0016 | 0.161 | 1.10E-10 | 1.88E-08 | 6.11E-10 |

### 2.3.4.7. Oilfield applications

Glutaraldehyde is also used in the mineral oil extraction and these uses are described here as PTs for oilfield applications are currently under discussion among the MS and the Commission, no specific PTs are assigned for the different oilfield uses[2].

Emissions and exposure from the oil production have been estimated according to CHARM (2005). Within CHARM, chemicals are categorised into four application groups: production chemicals, drilling chemicals, cementing chemicals and hydrotest chemicals. Glutaraldehyde is used in all applications groups.

Production chemicals are added either to the injection water or to the produced fluids in order to protect the installation, protect the reservoir, maintain production efficiency, or to separate the oil/gas and water. They partition between the produced fluids according to their hydrophilic properties. The fraction of the chemicals which dissolves in the produced water is released into the ambient seawater. Glutaraldehyde is used to control slime forming organisms in the injection water stream. The CHARM calculations estimate daily emissions to wastewater, taking into account of daily dose, and do not consider the interval between applications. A calculation was conducted adopting this approach, assuming a dose of 300 ppm for 1 hour (Tier 1). For further calculations, the application interval was taken into account to calculate an average daily dose and release. In order to investigate this, a maximum daily average dosage of 4.30 mg/l was considered (Tier 2).

[2] The PTs for oilfield uses were decided at 57th CA meeting in September 2014. Production chemicals (injection water) and hydrotesting water belong to PT 11 and drilling muds and cementing chemicals belong to PT 6. In the assessment report the oilfield uses are included in specific chapters, but in the opinions the oilfield uses are included in the opinions of PT 6 and PT 11 together with other uses allocated to these PTs.

Drilling muds are liquids used in drilling operations to cool and lubricate the bit, carry away drill cutting and to balance underground hydrostatic balance. Glutaraldehyde is used for preservation of water-based muds, typically within a use range of 125 - 300 ppm. In CHARM two scenarios for drilling muds are presented: continuous and batchwise. Due to their expense and perceived environmental impact, drilling muds are recovered and reused as much as possible. However, in order to take account of a worst-case situation, the batchwise scenario, which covers bulk discharge of muds following the completion of drilling section, was also considered. A dose rate of 300 ppm has been considered for both scenarios.

Glutaraldehyde is also used in the cementing chemicals. After the first sections of a well have been drilled, casings are inserted in the well and cemented into place. This is done by injecting cement down into the casing. The last casings to be cemented in a well are called the liners. A liner is a standard casing which does not extend all the way to the surface, but is hung from the inside of the previous casing string. When cementing a liner, a spacer is pumped into the annular prior to the cement slurry to separate the drilling fluid and the cement. Glutaraldehyde may be used in the spacer at a rate up to 500 ppm. The volume of cement slurry to be used is normally overestimated in order to ensure that there will be adequate cementing throughout the annulus. This excess cement is brought back to the surface along with the spacer, both of which will be heavily contaminated with the drilling mud. The CHARM manual presents a simple calculation for estimating potential release of chemical associated with spacer fluid.

For hydrotesting in oilfields Glutaraldehyde is used to control microbially induced corrosion to the inner surfaces of transit pipes during hydrostatic pressure testing. Glutaraldehyde should be dosed to give a final concentration in the total fluid of between 2 - 30 ppm. However, for the purposes of the calculation presented here, a realistic dose rate of 5 ppm has been assumed. Since hydrotesting chemicals are discharged with batches, no equilibrium situation will exist, and therefore it is irrelevant to estimate the sediment concentration.

According to applicant the Tier 1 calculations present unrealistic worst case as they do not take into account the potential dissipation during storage and use of drilling muds, cementing chemicals or hydrotest chemicals. The applicant has not provided measurements to support this statement. The dissipation is taken into account in Tier 2 calculations, but triggers a requirement in the label to measure Glutaraldehyde in oil production chemicals before release to the seawater. In order to achieve a PEC/PNEC ratio < 1 Glutaraldehyde must not exceed 0.4 ppm in drilling muds, 4 ppm in spacer fluid (cementing chemicals) and 0.05 ppm in hydrotest water.

The PECs for use of Glutaraldehyde as a slimicide or preservative in production, drilling, cementing and hydrotesting chemicals in mineral oil extraction are given below.

PECs for use of Glutaraldehyde in oil production.

| **Scenario** | **$PEC_{seawater}$ µg/l** |
|---|---|
| Produced water | |
| Tier 1 | 0.142 |
| Tier 2 | 0.0499 |
| Drilling chemical | |
| Continuous discharge | 0.0438 |
| Batchwise discharge, Tier 1 | 36.9 |
| Batchwise discharge, Tier 2 | 0.0492 |
| Cementing fluids | |
| Tier 1 | 6 |
| Tier 2 | 0.048 |
| Hydrotesting fluids | |
| Tier 1 | 5 |
| Tier 2 | 0.049 |

### *2.3.5. Risk characterisation*

The risk characterisation is done only for Glutaraldehyde since it does not contain additives or impurities which are considered as substances of concern. Glutaraldehyde does not form metabolites exceeding 10% in normal environmental conditions (Doc IIA, Section 5.1.1). Risk quotients (PEC/PNEC) based on the average consumption are reported here, but the PEC/PNEC ratios based on the tonnage scenarios are presented only in the Confidential Annex IIB and IIC.

Glutaraldehyde is applied for six product types and most of uses in these product types have a direct release to municipal sewage treatment plant (STP) or industrial waste water treatment plant (WWTP). Subsequently the risk characterisation is conducted for STP (WWTP), surface water (freshwater and for some uses also seawater) and soil. The PEC/PNEC ratios for these compartments are presented in separate sections for each product types. Risk characterisation for sediment has not been done, since Glutaraldehyde does not fulfil criteria for sediment risk assessment: it's readily biodegradable and it is not expected to adsorb to sediment, both log Kow and log Koc are less than three. Predicted No Effect Concentrations (PNECs) for STP, freshwater, seawater, marine sediment and soil are reported below. The PNECs are given as 100 % Glutaraldehyde.

PNECs for STP, freshwater, seawater and soil.

| PNEC | Unit | Value |
|---|---|---|
| $PNEC_{STP}$ | mg a.s./l | 0.51 |
| $PNEC_{water}$ | µg a.s./l | 2.5 |
| $PNEC_{seawater}$ | µg a.s./l | 0.25 |
| $PNEC_{soil}$ | mg a.s./kg ww | 0.184 |

#### 2.3.5.1. Product Type 2

Glutaraldehyde is used for disinfection of hard surfaces in industry and hospitals. Acceptable risk is identified in surface water in all Tiers in the average consumption based scenario, and in the tonnage based scenario in Tiers 1 and 2. In STP and soil no unacceptable risk is identified. The groundwater concentrations are < 0.1 µg/l in Tier 2 in both the average consumption and tonnage based scenarios. According to ESD for PT 2 the risk assessment should be based on the tonnage based scenario in this case as the tonnage exceeds the break-even point and in such situations the average consumption based scenario would underestimate the emissions to the STP. Different guidance is given in the PT 1-6 Workshop Report (CA-Nov-08-Doc.6.3) which recommends using tonnage scenarios only for comparative purposes to check the validity of default values in the average consumption based scenarios. In this case the RMS considers that the tonnage based scenario confirms and validates the average consumption based scenarios.

The RMS' conclusion is that the applied uses of Glutaraldehyde in PT 2 (disinfection of industrial areas and sanitary purposes in medial sector) are acceptable concerning the environment.

PEC/PNEC ratios for STP, surface water and soil and PEC for groundwater for PT 2 scenarios. Tiers 0-2 are explained in Section 2.2.2.5.

| Scenario | PEC/PNEC STP | PEC/PNEC Water | PEC/PNEC Soil | PEC (µg/l) Groundwater |
|---|---|---|---|---|
| Industrial areas | | | | |
| Tier 0 | 0.002 | 0.148 | 0.013 | 0.131 |
| Tier 1 | 0.001 | 0.056 | 0.013 | 0.127 |
| Tier 2 | 0.001 | 0.056 | 0.000 | 7.87E-12 |
| Sanitary purposes in hospitals | | | | |
| Tier 0 | 0.004 | 0.277 | 0.024 | 0.246 |
| Tier 1 | 0.001 | 0.104 | 0.023 | 0.239 |
| Tier 2 | 0.001 | 0.104 | 0.000 | 1.05E-11 |

#### 2.3.5.2. Product Type 3

Glutaraldehyde is used for disinfection of poultry and pig fattening farms.

No unacceptable risk is identified in the STP and in the surface water in the scenario 'Laying hens in free range with litter floor' where a fraction of Glutaraldehyde released to STP is 0.2. No unacceptable risk is identified in the scenarios 'Sows in groups' and 'Laying hens in free range with litter floor' where direct release is assumed to slurry/manure which is later spread to soil. Neither unacceptable risk is identified for soil in the scenario 'Laying hens in free range with litter floor' where direct release is assumed to the STP and the sewage sludge is later spread to soil. Glutaraldehyde exceeds the groundwater quality standard of 0.1 µg/l (Directive 2006/118/EC) in the scenarios 'Sows in groups' where direct release is assumed to slurry/manure after one application to arable land and four application to grassland and after 10 successive years of manure application. However, when the refinement based on the reactivity of Glutaraldehyde in slurry/manure (Fresidue 0.01%) is applied, the concentration of Glutaraldehyde is below the quality standard. The quality standard is also exceeded in Tier 0 and 1, but not in Tier 2, in the scenario 'Laying hens in free range with litter floor' with an emission fraction of 0.2 directed to the STP.

Glutaraldehyde can be approved for PT 3 with respect to the environmental risk.

PIEC/PNEC ratios for soil (grassland and arable land) and PEC for groundwater for animal housing scenarios with exposure to slurry or manure.

| Scenario | PIEC/PNEC Grassland-N | PIEC/PNEC Arable-N | PEC (µg/l) Groundwater Grassland | PEC (µg/l) Groundwater Arable land |
|---|---|---|---|---|
| Without degradation (one application to arable land and four applications to grassland) | | | | |
| No refinement | | | | |
| Sows in groups | 0.722 | 0.180 | 22.6 | 5.7 |
| Laying hens in free range with litter floor | 0.165 | 0.041 | 5.2 | 1.3 |
| Refinement: Fresidue 0.01% | | | | |
| Sows in groups | 7.22E-05 | 1.84E-05 | 2.26E-03 | 5.65E-04 |
| Laying hens in free range with litter floor | 1.66E-05 | 4.14E-04 | 5.20E-04 | 1.30E-04 |
| 10 successive years of manure application | | | | |
| No refinement | | | | |
| Sows in groups | 0.183 | 0.130 | 5.7 | 4.1 |
| Laying hens in free range with litter floor | 0.042 | 0.030 | 1.32 | 0.94 |
| Refinement: Fresidue 0.01% | | | | |
| Sows in groups | 1.83E-05 | 1.30E-05 | 5.73E-04 | 4.08E-04 |
| Laying hens in free range with litter floor | 4.20E-06 | 3.0E-06 | 1.32E-04 | 9.38E-05 |

PEC/PNEC ratios for STP, surface water and soil and PEC for groundwater for the scenario 'Laying hens in free range with litter floor' with exposure to the wastewater. Tiers 0-2 are explained in Section 2.2.2.5.

| Scenario | PEC/PNEC STP | PEC/PNEC Water | PEC/PNEC Soil | PEC (µg/l) Groundwater |
|---|---|---|---|---|
| Laying hens in free range with litter floor | | | | |
| – Tier 0 | 0.045 | 0.908 | 0.082 | 0.807 |
| – Tier 1 | 0.017 | 0.342 | 0.076 | 0.783 |
| – Tier 2 | 0.017 | 0.342 | 1.5E-09 | 4.85E-08 |

### 2.3.5.3. Product Type 4

None of the scenarios leads to unacceptable risk in STP or soil. Unacceptable risk is identified in Tier 0 in scenarios "Entire plant: on-site STP" and "Surfaces in food processing areas: slaughterhouses". In other Tiers and all other scenarios no unacceptable risk is identified. The estimated groundwater concentrations exceed the quality standard of 0.1 µg/l (2006/118/EC) in Tier 0 and 1, but not in Tier 2 in following scenarios "Entire plant: off-site STP" and "Surfaces in food processing areas: slaughterhouses" and "Surfaces in large scale kitchens". The estimated groundwater concentration is below the quality standard in all relevant scenarios in Tier 2.

The conclusion of the RMS is that the environmental criteria for approval of glutaraldehyde for PT4 are fulfilled.

PEC/PNEC ratios for STP, surface water and soil and PEC for groundwater for PT 4 scenarios. Tiers 0-2 are explained in Section 2.2.2.5.

| Scenario | PEC/PNEC STP | PEC/PNEC Water | PEC/PNEC Soil | PEC (µg/l) Groundwater |
|---|---|---|---|---|
| Entire plant: on-site (WWTP) | | | | |
| Tier 0 | - | 6.4 | - | - |
| Tier 1 | - | 0.499 | - | - |
| Entire plant: off-site (STP) | | | | |
| Tier 0 | 0.035 | 0.724 | 0.065 | 0.643 |
| Tier 1 | 0.014 | 0.273 | 0.06 | 0.624 |
| Tier 2 | 0.014 | 0.273 | 1.23E-09 | 3.78E-08 |
| Surfaces in food processing areas: slaughterhouses | | | | |
| Tier 0 | 0.122 | 2.46 | 0.217 | 2.19 |
| Tier 1 | 0.045 | 0.928 | 0.207 | 2.12 |
| Tier 2 | 0.045 | 0.928 | 2.98E-09 | 9.34E-11 |
| Surfaces in large scale kitchens | | | | |
| Tier 0 | 0.023 | 0.492 | 0.043 | 0.437 |
| Tier 1 | 0.010 | 0.186 | 0.043 | 0.424 |
| Tier 2 | 0.010 | 0.186 | 5.98E-10 | 1.87E-08 |

### 2.3.5.4. Product Type 6

Glutaraldehyde is used a preservative in household detergents and in paper additives in paper industry. Preservation of household detergents is recognized as a safe use, i.e. no unacceptable risk is identified in STP, surface water and soil and the predicted groundwater concentration is less than 0.1 µg/l. Glutaraldehyde can also be used safely as a preservative in detergents for professional use and in paper industry as demonstrated in the Tier 2 or 3 calculations. Based on the safe use in detergents Glutaraldehyde can be approved for PT 6 with respect to the environmental risk.

PEC/PNEC ratios for STP, surface water and soil and PEC for groundwater for PT 6 scenarios. Tiers 0-2 are explained in Section 2.2.2.5.

| Scenario | PEC/PNEC STP | PEC/PNEC Water | PEC/PNEC Soil | PEC (µg/l) Groundwater |
|---|---|---|---|---|
| Sanitary purpose (PT 2) | | | | |
| Tier 0 | 0.003 | 0.062 | 0.005 | 0.055 |
| Tier 1 | 0.001 | 0.023 | 0.005 | 0.053 |
| Tier 2 | 0.001 | 0.023 | 7.45E-11 | 2.33E-12 |
| Detergents for professional use | | | | |
| Tier 0, Fpenetr = 1 | 0.018 | 0.359 | 0.033 | 0.351 |
| Tier 1, Fpenetr = 1 | 0.006 | 0.134 | 0.033 | 0.305 |
| Tier 2, Fpenetr = 1 | 0.006 | 0.134 | 1.66E-12 | 5.19E-12 |
| Paper production: preservative for additives(newsprint) | | | | |
| Tier 0 | 0.024 | 0.488 | 0.043 | 0.432 |
| Tier 1 | 0.010 | 0.184 | 0.043 | 0.419 |
| Tier 2 | 0.010 | 0.184 | 1.68E-09 | 5.32E-08 |
| Tier 3 | 0.00004 | 0.00008 | 6.85E-12 | 2.15E-10 |
| Paper production: preservative for additives (printing and writing paper) | | | | |
| Tier 0 | 0.051 | 1.06 | 0.092 | 0.94 |
| Tier 1 | 0.020 | 0.40 | 0.087 | 0.91 |
| Tier 2 | 0.020 | 0.40 | 1.70E-09 | 5.34E-08 |
| Tier 3 | 0.00010 | 0.002 | 7.88E-12 | 2.49E-10 |

### 2.3.5.5. Product Type 11

Glutaraldehyde is used as a preservative in open and closed recirculating cooling systems. Preservation of water in closed recirculating cooling systems with connection to the STP is recognized as a safe use, i.e. no unacceptable risk is identified in STP, surface water and soil. The groundwater concentration closest to the 80$^{th}$ percentile were < 0.001 µg/l in all scenarios in both PEARL 4.4.4 and PELMO 5.5.3 simulations. Thus, Glutaraldehyde can be included approved for PT 11 with respect to the environmental risk. Concerning the use in small open recirculating cooling systems the refinement of the risk assessment and/or risk reduction measures are needed. At the TM III 2013 it was agreed that the applicants will provide more data for the inclusion of degradation rate in cooling systems for the product authorization stage.

PEC/PNECs for PT 11 scenarios without connection to STP (direct release to surface water).

| Scenario | PEC/PNEC Freshwater | PEC/PNEC Seawater | PEC/PNEC Soil drift |
|---|---|---|---|
| Small open recirculation cooling systems | | | |
| Defouling treatment | | 354.8 | 0.011 |
| Dilution factor 350 | 101.2 | | |
| Dilution factor 1000 | 35.48 | | |
| Maintenance treatment | | 804 | 1.09 |
| Dilution factor 350 | 229.6 | | |
| Dilution factor 1000 | 80.4 | | |

PEC/PNEC ratios for STP, surface water and soil and PEC for groundwater for PT 11 scenarios with connection to the STP. Tiers 0-2 are explained in Section 2.2.2.5.

| Scenario | PEC/PNEC STP | PEC/PNEC Water | PEC/PNEC Soil | PEC/PNEC Soil drift | PEC (µg/l) Groundwater |
|---|---|---|---|---|---|
| Small open recirculation cooling systems | | | | | |
| Defouling treatment | | | | | |
| Tier 0 | 0.514 | 10.5 | 0.913 | 0.011 | 9.31 |
| Tier 1 | 0.194 | 3.9 | 0.886 | 0.011 | 9.03 |
| Tier 2 | 0.194 | 3.9 | 3.6E-12 | 0.011 | 1.53E-12 |
| Maintenance treatment | | | | | |
| Tier 0 | 1.163 | 23.8 | 2.071 | 1.09 | 21.1 |
| Tier 1 | 0.439 | 9 | 2.071 | 1.09 | 20.5 |
| Tier 2 | 0.439 | 9 | 3.3E-08 | 1.09 | 1.04E-09 |
| Closed recirculation cooling systems | | | | | |
| Defouling treatment | | | | | |
| Tier 0 | 0.0001 | 0.002 | 0.0002 | | 0.0021 |
| Tier 1 | 4.37E-05 | 0.0009 | 0.0002 | | 0.002 |
| Tier 2 | 4.37E-05 | 0.0009 | 1.10E-14 | | 3.46E-13 |
| Maintenance treatment | | | | | |
| Tier 0 | 2.90E-05 | 0.0006 | 5.15E-05 | | 5.25E-04 |
| Tier 1 | 1.09E-05 | 0.0002 | 4.99E-05 | | 5.09E-04 |
| Tier 2 | 1.09E-05 | 0.0002 | 2.76E-16 | | 8.65E-17 |

### 2.3.5.6. Product Type 12

Glutaraldehyde is used as a slimicide in pulp and paper industry. Safe use is recognized in Tier 3 both in the reasonable worst case and typical case scenario. Unacceptable risk was identified in Tiers 0-2 in the reasonable worst case scenario. In the typical case scenario unacceptable risk was identified in Tier 0 in the WWTP, in Tier 0-2 in the surface water and in Tier 0-1 in soil. The groundwater quality standard was exceeded in Tier 0-1 in the typical case scenario, but not in Tier 2-3. To conclude, Glutaraldehyde can be approved for PT 12 with respect to the environmental risk.

PEC/PNECs for PT 12 paper production processes - the worst case scenario (no connection to WWTP, direct release to surface water).

| **Treatment** | **Dilution factor**[1] | **PEC/PNEC Freshwater** | **PEC/PNEC Seawater** |
|---|---|---|---|
| Defouling treatment | | | |
| Tier 0 | | | |
| | 10 | 1600 | |
| | 100 | | 1600 |
| | 1000 | 16 | |
| Tier 3 | | | |
| | 10 | 7.2 | |
| | 100 | | 7.2 |
| | 1000 | 0.072 | |
| Maintenance treatment | | | |
| Tier 0 | | | |
| | 10 | 800 | |
| | 100 | | 800 |
| | 1000 | 8 | |
| Tier 3 | | | |
| | 10 | 3.6 | |
| | 100 | | 3.6 |
| | 1000 | 0.036 | |

[1]The dilution factors 10,100 and 1000 were selected since TMIII/2011 agreed that dilution factors cannot be lower than 10 and the maximum dilution factor is 1000. Dilution factor of 100 is used for coastal dilution.

PEC/PNECs for PT 12 paper production processes - the typical case scenario (connection to WWTP).

| Scenario | PEC/PNEC WWTP | PEC/PNEC Water | PEC/PNEC Soil | PEC (µg/l) Groundwater |
|---|---|---|---|---|
| Defouling | | | | |
| Tier 0 | 3.784 | 77.2 | 6.739 | 68 |
| Tier 1 | 1.425 | 29.08 | 6.522 | 66.4 |
| Tier 2 | 1.425 | 29.08 | 4.598E-05 | 8.48E-06 |
| Tier 3 | 0.006 | 0.132 | 2.0154E-10 | 4.78E-11 |
| Maintenance | | | | |
| Tier 0 | 1.902 | 38.84 | 3.364 | 34.3 |
| Tier 1 | 0.714 | 14.56 | 3.261 | 33.3 |
| Tier 2 | 0.714 | 14.56 | 2.49E-08 | 4.23E-06 |
| Tier 3 | 0.003 | 0.064 | 1.10E-10 | 1.88E-08 |

#### 2.3.5.7. Oilfield applications

Glutaraldehyde is used in various applications in mineral oil extraction and these uses are reported here because the PTs for oilfield uses are currently under discussion[3]. An unacceptable risk for seawater is identified for all oil production uses when dissipation is not taken into account (Tier 1) apart from the produced water and the drilling chemical use with continuous release. In all cases the risk is acceptable when the degradation is taken into account (Tier 2). It is concluded that Glutaraldehyde can be approved with the following specific provision: The label must include an obligation to measure Glutaraldehyde in oil production chemicals before they are released to seawater. Glutaraldehyde must not exceed 0.4 ppm in drilling mud, 4 ppm in spacer fluid (cementing chemical) and 0.05 ppm in hydrotest water.

[3] The PTs for oilfield uses were decided at 57th CA meeting in September 2014. Production chemicals (injection water) and hydrotesting water belong to PT 11 and drilling muds and cementing chemicals belong to PT 6. In the assessment report the oilfield uses are included in specific chapters, but in the opinions the oilfield uses are included in the opinions of PT 6 and PT 11 together with other uses allocated to these PTs.

PEC/PNEC ratios for oil production.

| Scenario | PEC/PNEC Seawater |
|---|---|
| Produced water | |
| Tier 1 | 0.568 |
| Tier 2 | 0.200 |
| Drilling chemical | |
| Continuous discharge | 0.180 |
| Batchwise discharge, Tier 1 | 146 |
| Batchwise discharge, Tier 2 | 0.197 |
| Cementing fluids | |
| Tier 1 | 24 |
| Tier 2 | 0.192 |
| Hydrotesting fluids | |
| Tier 1 | 20 |
| Tier 2 | 0.196 |

### *2.3.6. Aggregated exposure*

According to the Article 10(1) of the Biocidal Products Directive 98/8/EC cumulation effects from the use of biocidal products containing the same active substance should be taken into account, where relevant. A cumulative risk assessment for Glutaraldehyde is relevant, since there might be overlapping emissions from one or several PTs into the same environmental compartment. The cumulative assessment is explained in detail in Doc IIC, Section 13.9 and the exact values from the calculations can be found in Confidential Annex to IIB and IIC.

The emission estimates (Elocals) were added up, if possible overlapping emissions into same environmental compartment was identified within one PT or between PTs. Tonnage based scenarios were used for formulation and service-life of detergents and formulation of paper additives in PT 6 and paper deinking in PT 12, for other uses the average consumption based scenarios were used. The cumulative Elocal then served as an input value for EUSES calculations of PECs.

Within PTs all emissions into same environmental compartment were considered relevant with three exceptions:

- The emissions of Glutaraldehyde in slurry/manure were not added up in PT 3. The overlapping application of slurry/manure to arable land from both piggery and henhouse was considered unrealistic due to the requirements of the nitrogen immission standard, i.e. a maximum load on an agricultural soil or grassland is assumed in the PIEC-calculations and therefore it is not allowed to spread further amounts of slurry or manure to the soil.

- It was assumed that emissions from the service life of paper production (PT 6) are discharged to an industrial wastewater treatment plant (WWTP), whereas emissions from the formulation phase were released to a municipal sewage treatment plant.

Relevant scenarios for cumulative risk assessment within PT are marked with an "x" in Table below.

For cumulative assessment between PTs the emissions from detergent uses in PT 2 and PT 6 are added up, since they represent wide dispersive use pattern. These scenarios are marked with "a" in Table below. Generally the emissions of non-dispersive uses (e.g. industrial use) are not relevant for cumulative assessment, since it is unlikely that the emissions end up into the same local STP or environmental compartment. However, the non-dispersive uses may become relevant if they overlap with wide dispersive uses. In the case of Glutaraldehyde there are numerous possible overlapping combinations of emissions from wide dispersive uses and industrial, non-dispersive disinfection/preservation uses. These scenarios are marked with "(a)". For the cumulative assessment RMS selected a combination of wide dispersive use and one industrial use at a time, since it is unlikely that all industries are situated in the same catchment area.

Concerning the paper production, the RMS assumed that there is a common WWTP (wastewater volume 5000 $m^3$/d) for wet-end and dry-end operations of newspaper in PT 12 and PT 6, respectively. These possible overlapping emissions from paper production are marked with "b". RMS further recognized that newsprint paper is produced mainly from recycled paper and thus the emissions from paper deinking may also overlap with wet-end and dry-end operations. However, since the default wastewater volume of 2000 $m^3$/d is adequate for the emissions of printing and writing paper and for paper deinking, it is assumed that their wastewater are released to a separate WWTP (wastewater volume 2000 $m^3$/d).

The cumulative assessment for oil production not performed and thus they are not included in the Summary Table.

Summary of local emissions and their relevance for cumulative risk assessment within PT and between PTs. Tier 3 has been used for service-life of paper additives in PT 6 and for slimicides in PT 12.

| Product Type | Scenario type | Emission point | Elocal | Relevance within PT | Relevance between PTs |
|---|---|---|---|---|---|
| **PT 2** | | | | | |
| Disinfection of industrial areas | Cons. | STP | 0.06 kg/d | x | a |
| Sanitary purposes in hospitals | Cons. | STP | 0.113 kg/d | x | a |
| | Tonn. | STP | See Conf. Annex | | |
| **PT 3** | | | | | |
| Disinfection of animal housing | | | | | |
| Sows in group | Cons. | Slurry/manure | 0.444 kg/application | | |
| Laying hens in free range with litter floor | Cons. | STP<br>Slurry/manure | 0.369 kg/d<br>0.553 kg/application | | (a) |
| **PT 4** | | | | | |
| Food vessels/machinery disinf. | Cons. | STP | 0.2 and 1 kg/d | x | (a) |
| Food processing surface disinf. | Cons. | STP | 0.294 kg/d | x | (a) |
| **PT 6** | | | | | |
| In-can preservative in detergents | | | | | |
| Formulation | Tonn. | STP | See Conf. Annex | x | (a) |
| Service life, private use | Cons. | STP | 0.025 kg/d | | |
| professional use | Cons. | STP | 0.144 and 0.072 kg/d | | |
| | Tonn. | STP | See Conf. Annex | x | a |
| In-can preservatives in paper additives | | | | | |
| Formulation | Tonn. | STP | See Conf. Annex | x | (a) |
| Service life (newspaper), Tier 3 | Cons. | WWTP (5000 $m^3$/d) | 0.004kg/d | | b |
| Service life (printing and writing paper), Tier 3 | Cons. | WWTP | 0.001 kg/d | | |
| **PT 11** | | | | | |
| Preservatives for open recirculating cooling systems | | | | | |
| Small | Cons. | Surface water or STP | 4.26 kg/d defouling | x | (a) |
| | | | | | |
| Preservatives for closed recirculating cooling systems | Cons. | STP | 9.6E-04 kg/d defouling | x | (a) |
| **PT 12** | | | | | |
| Slimicides for paper production | | | | | |
| Worst case, Tier 3 | Cons. | Surface water | 0.9 kg/d defouling | | |
| Typical case, Tier 3 | Cons. | WWTP (5000 $m^3$/d) | 0.35 kg/d defouling | | b |
| Paper de-inking, Tier 3 | Tonn. | WWTP | See Conf. Annex | | |

No unacceptable risk is identified in STP or soil and the groundwater concentrations are < 0.1 µg/l either within PT or between PTs. No unacceptable risk is identified within PT 2 and PT 6 in surface water. The unacceptable risk, however, is identified in surface water within PT 4and PT 11, in combination of wide dispersive use (PT 2, PT 6) and one industrial use of PT4 or PT 11 at a time (PT 3, PT 4, PT 6, PT 11). Since confidential tonnage data is used in almost all PEC calculations, the PECs and exact PEC/PNEC ratios are presented in the Confidential Annex to Doc IIB and IIC. Here only an overview of whether PEC/PNEC ratios exceed or undercut one is given (Table below).

At the moment there is no regulatory interpretation how an identified unacceptable cumulative risk should be taken into account when approving active substances, since for approval one safe use is sufficient. Thus, approval of Glutaraldehyde is not based on the outcome of this cumulative risk assessment. However, it is important to bring out that a potential cumulative risk is identified.

For the time being the methodology for the cumulative risk assessment is not harmonized. This assessment was performed also to gain experience of how to perform a cumulative risk assessment and to bring out issues that should be taken into account when the guidance is developed. The main issues noticed were the reliability of tonnage data, from which PTs the emissions are summed up and what kind of and how many industrial factories are present in catchment area of a STP.

Cumulative PEC/PNEC ratios for STP, surface water and soil and within PTs. The exact PEC/PNEC ratios are given in Confidential Annex to Doc IIB and IIC.

| Product Type | PEC/PNEC STP | PEC/PNEC Water | PEC/PNEC Soil |
|---|---|---|---|
| PT 2 | < 1 | < 1 | < 1 |
| PT4 | < 1 | > 1 | < 1 |
| PT 6 | < 1 | <1 | < 1 |
| PT 11 (defouling) | < 1 | > 1 | < 1 |

Cumulative PEC/PNEC ratios for STP, surface water and soil and between PTs. The exact PEC/PNEC ratios are given in Confidential Annex to Doc IIB and IIC.

| Uses and Relevant Product Types | PEC/PNEC STP | PEC/PNEC Water | PEC/PNEC Soil |
|---|---|---|---|
| Wide dispersive use (PT 2, 6) | < 1 | <1 | < 1 |
| Wide dispersive use (PT 2, 6) and laying hens (PT 3) | < 1 | <1 | < 1 |
| Wide dispersive use (PT 2, 6) and food vessels/machinery disinfection (PT 4) | < 1 | > 1 | < 1 |
| Wide dispersive use (PT 2, 6) and formulation of in-can preservative in detergents (PT 6) | < 1 | <1 | < 1 |
| Wide dispersive use (PT 2, 6) and formulation in paper production (PT6) | < 1 | <1 | < 1 |
| Wide dispersive use (PT 2, 6) and preservatives for small open recirculating cooling system (PT 11), defouling | < 1 | > 1 | < 1 |
| Wide dispersive use (PT 2, 6) and preservatives for closed recirculating cooling systems (PT 11) | < 1 | > 1 | < 1 |
| Paper production (PT6, PT12) | < 1 | <1 | < 1 |

## 2.4. Assessment of endocrine disruptor properties

Glutaraldehyde is not included in the priority list of substances for further evaluation of their role in endocrine disruption established within the Community Strategy for Endocrine Disrupters (COM (1999) 706, COM (2001) 262). Available evidence at this time indicates that glutaraldehyde does not have endocrine-disrupting properties (classification criteria specified in Art. 5(3) are not met, no effects on endocrine organs and/or reproduction were observed in standard toxicity studies to raise a concern for potential endocrine disruption).

## 2.5. Overall conclusions

### a) Presentation of the active substance and representative biocidal product including classification of the active substance

Please refer to 2.1.1 and 2.1.3.

### b) Intended use, target species and effectiveness: containing a description of the use(s) evaluated in the assessment report

Please refer to 2.1.2.

### c) Risk characterization for human health

Please refer to 2.2.1.

### d) Risk characterisation for environment

Please refer to 2.2.2.

### e) Substitution and exclusion criteria

Glutaraldehyde does not meet any of the exclusion criteria of Article 5(1). Glutaraldehyde is a respiratory sensitizer and meets therefore the substitution criteria of Article 10(1b). Glutaraldehyde does not meet other substitution criteria.

### f) Overall conclusion evaluation including need for risk management measures

Glutaraldehyde has been assessed for approval of Directive 98/8/EC in Product Types 2, 3, 4, 6, 11 and 12.

Glutaraldehyde poses no risks to humans through the physical-chemical properties of the active substance. There are sufficient analytical methods for glutaraldehyde for approval, but the methods need to be updated for product authorization in order to meet the requirements as updated in the guidance agreed at the 33rd meeting of representatives of Members States Competent Authorities for the implementation of Directive 98/8/EC concerning the placing of biocidal products on the market (May 2009).

Sufficient efficacy has been demonstrated against bacteria in a number of real and simulated uses. The fungicidal, sporicidal, mycobactericidal, virucidal and algicidal efficacy and efficacy against biofilms were not demonstrated for the intended use concentration. Resistance to glutaraldehyde in certain mycobacteria strains has been reported in hospitals. The recommended resistance management strategy is to vary the products used, to use more than one product simultaneously, or to alternate treatment regimes and monitor occurrence of resistance.

Glutaraldehyde is a respiratory sensitizer category 1 according to the CLP Regulation. Respiratory sensitization has been linked with high peak exposure concentrations, and therefore $AEC_{acute\ inahalation}$ (122 ppb) should be regarded as a ceiling value that should never be exceeded. The $AEC_{inhalation}$ (2.6 ppb) is considered as a reference value that is likely to be protective for sensitization effects as well.

Due to skin sensitisation of glutaraldehyde, gloves and coverall must always be used when exposure is possible to the glutaraldehyde containing products classified as skin sensitising.

The risk characterisation for human health indicates that there are uses for which no unacceptable risk is anticipated based on conventional Tier 1 or Tier 2 assessment methods for professional or non-professional users with the intended use of the biocidal product in Product Types 3, 4, 6, 11 and 12. There were some critical scenarios (no. 9 and other 8 similar scenarios in connecting drum to pump or mixing and loading) at Tier 2 level where risk was identified for the professional user. However, refinement of the

assessment by using more efficient RPE (APF 40) it is concluded that the risk for professional users is at acceptable level also in those scenarios. Child entering the barn disinfected by the PT3 product during the re-entry period must be prevented. An unacceptable risk was identified in the application scenario 2 (mopping and wiping) in PT 2. Chronic inhalation exposure in this scenario is acceptable if only mopping is performed. No risk was identified due to secondary indirect exposure.

A repeated dose toxicokinetics study is usually required for risk assessment of biocidal active substances. Since single dose studies provided no indication of accumulation in any tissue, and because of the rapid metabolism, the eCA does not consider the lack of this study to be a data gap.

At least one use of glutaraldehyde in Product Types 2, 3, 4, 6, 11 and 12 has been recognized as a safe use concerning the environment, i.e. the PEC/PNEC ratio is less than 1. In addition, glutaraldehyde concentration in groundwater is predicted to be below 0.1 µg/L. Glutaraldehyde does not fulfil the exclusion criteria of Art. 5 in regulation (EU) No 528/2012, i.e. it does not meet criteria of being a PBT, vPvB or POP substance. Glutaraldehyde has not been suspected for endocrine disrupting effects.

## 2.6. List of endpoints

The most important endpoints, as identified during the evaluation process, are listed in Appendix I.

## 2.7. Elements to be taken into account by Member States when authorising products

- While the active as manufactured is the product this does not negate the need to determine relevant physical and chemical properties related to the product. The data generated for the active does not cover all aspects. A two year storage stability and shelf-life test at ambient temperature is required. Furthermore other product information should be submitted on technical properties including information on persistent foaming and dilution stability for relevant for types of application (spraying), as well as application relevant information on compatibilities with other products.

## 2.8. Requirement for further information

Sufficient data have been provided to verify the conclusions on the active substance, permitting the proposal for the approval of glutaraldehyde.

- A new analytical method for the determination of glutaraldehyde in air should be submitted. Data must be provided as soon as possible but no later than 6 months before the date of approval to the evaluating Competent Authority (eCA).

- A confirmatory analytical method for the determination of glutaraldehyde in the technical material should be submitted for one of the applicants (BASF). The applicant should also submit an analytical method for determination of impurities in the technical material, or submit adequate validation data on the existing ones including recovery, repeatability, and LOQ. Data must be provided as soon as possible but no later than 6 months before the date of approval to the evaluating Competent Authority (eCA).

- Confirmatory methods should be submitted for one of the applicants (Dow) for determination of glutaraldehyde and the impurity in aqueous formulations of glutaraldehyde. Data must be provided as soon as possible but no later than 6 months before the date of approval to the evaluating Competent Authority (eCA).

## 2.9. Updating this Assessment Report

This assessment report may need to be updated periodically in order to take account of scientific developments and results from the examination of any of the information referred to in Regulation (EU) 528/2012. Such adaptations will be examined and finalised in connection with any amendment of the conditions for the Approval of glutaraldehyde.

## 2.10. Candidacy for substitution

The active substance glutaraldehyde is considered as a candidate for substitution, and consequently the competent authority shall perform a comparative assessment as part of the evaluation of an application for either national or Union authorisation.

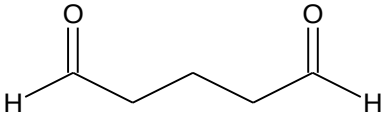
A public consultation on glutaraldehyde in PT 2, 3, 4, 6, 11 and 12 took place from 17/12/2013 to 15/02/2014. Comments included information on the availability of alternative active substances and information claiming the essentiality of glutaraldehyde in product types 2, 3 and 4. Summary of public consultation can be found in Confidential Annex.

# Appendix I: List of endpoints

## Chapter 1: Identity, Physical and Chemical Properties, Classification and Labelling

| | |
|---|---|
| Active substance (ISO Common Name) | Glutaraldehyde |
| Product-type | 2, 3, 4, 6, 11, 12 |

**Identity**

| | |
|---|---|
| Chemical name (IUPAC) | 1,5-pentanedial |
| Chemical name (CA) | Glutaraldehyde |
| CAS No | 111-30-8 |
| EC No | 203-856-5 |
| Other substance No. | |
| Minimum purity of the active substance as manufactured (g/kg or g/l) | Glutaraldehyde content in the aqueous solution is in a range of 48.5-52.5 % (wt), 485-525 g/kg. The theoretical dry weight specification: minimum purity is 95.0 % (wt), 950 g/kg. The applicant specific information and specifications are in the confidential documents [Doc III A4.1/02 confidential (Dow) and Doc V Confidential (BASF) in detail]. |
| Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg) | [redacted]. The specifications are in the confidential documents [Doc III A4.1/02 confidential (Dow) and Doc V Confidential (BASF)]. |
| Molecular formula | $C_5H_8O_2$ |
| Molecular mass | 100.11 g/mol |
| Structural formula |  |

**Physical and chemical properties**

| | |
|---|---|
| Melting point (state purity) | Peak maximum ca. -18 ºC (BASF)<br>-18 to -21.2 ºC ( ) (Dow) |
| Boiling point (state purity) | 101.5 °C at 987.1 hPa ( ) (BASF)<br>100.7 ºC at 1013 hPa ( ) (Dow) |
| Temperature of decomposition | 1.Peak:<br>Onset temperature: 85 °C<br>Peak temperature: 246 °C<br>2.Peak:<br>Onset temperature: 330 °C<br>Peak temperature: 385 °C<br>(BASF)<br>For Dow, there is no information, but this is not an absolute requirement in case the temperatures of melting and boiling have been determined, according to Guidance on information requirements. |
| Appearance (state purity) | Free flowing clear liquid ( ) (BASF)<br>Clear colourless liquid, sharp odour ( ) (Dow) |
| Relative density (state purity) | 1.129 ( ) (BASF, Dow) |
| Surface tension | ca. 68 mN/m at 20 °C, ( ) (BASF)<br>72.4 mN/m at 20 ºC, ( ) (Dow) |
| Vapour pressure (in Pa, state temperature) | 44 Pa at 20 °C (BASF, Dow), |
| Henry's law constant (Pa $m^3$ $mol^{-1}$) | 0.0086 Pa×$m^3$/mol (calculated by RMS) |
| Solubility in water (g/l or mg/l, state temperature) | pH 5, 7, 9 (20.2+/- 0.1 °C): miscible (BASF)<br>pH not measured: ≥ 51.3 g/100ml at 21 °C (Dow)<br>Glutaraldehyde is not expected to ionize in water based on its chemical structure, therefore testing at different pH values was not considered necessary (Dow). |
| Solubility in organic solvents (in g/l or mg/l, state temperature) | Methanol: fully soluble<br>1,4-dioxane: fully soluble<br>at 20 °C and at 30 °C<br>(BASF)<br><br>Isopropanol: fully soluble (≥ 51.3 g/100 ml)<br>Acetone: fully soluble (≥ 51.3 g/100 ml)<br>Ethyl acetate: 59 g/100 ml<br>Dichloromethane: 70 g/100 ml<br>n-hexane: 0.19 g/100 ml<br>Toluene: 8.5 g/100 ml<br>at 21 °C<br>(Dow) |
| | |
| Stability in organic solvents used in biocidal | Not applicable (organic solvents not used in biocidal |

| | |
|---|---|
| products including relevant breakdown products | products) |
| | |
| Partition coefficient (log $P_{OW}$) (state temperature) | pH 5 : -0.41 at 23 +/- 1 °C<br>pH 9 : -0.80 at 23 +/- 1 °C<br>pH 7 :-0.36 at 23 +/- 1 °C<br>(BASF)<br>pH not reported: -0.33 at 25 ºC<br>(Dow) |
| Hydrolytic stability ($DT_{50}$) (state pH and temperature) | See Ch. 4: Fate and Behaviour in the Environment |
| Dissociation constant | Glutaraldehyde has no ionisable groups, and no ionisation/dissociation in water is expected. |
| UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength) | Medium $\lambda_{max}$ [nm] ε [$l*mol^{-1}*cm^{-1}$]<br>neutral 234 14.9<br>neutral 282 5.9<br>acidic 234 14.5<br>acidic 282 6.1<br>basic 235 478.2<br>basic 283 22.3<br>max. at 234 nm. There are no peaks above 290 nm. The ε is below 10 at wavelengths of 290 nm or greater. (BASF, Dow) |
| Photostability ($DT_{50}$) (aqueous, sunlight, state pH) | See Ch. 4: Fate and Behaviour in the Environment |
| Quantum yield of direct phototransformation in water at Σ > 290 nm | See Ch. 4: Fate and Behaviour in the Environment |
| Flammability | Not flammable , [redacted] (BASF, Dow)<br>Auto Ignition Temperature = 395 °C at 1002 – 1006 hPa (BASF) |
| Explosive properties | Not explosive (BASF, Dow) |

**Classification and proposed labelling**

| | |
|---|---|
| with regard to physical/chemical data | No classification |
| with regard to toxicological data | **RAC 29 (2-6 June 2014) opinion on classification and labelling of glutaraldehyde (100%) according to Regulation 1272/2008:**<br>Acute Tox. 3; H301<br>Acute Tox. 2; H330<br>Skin Corr. 1B; H314<br>Resp. Sens. 1; H334<br>Skin Sens. 1A; H317<br>STOT SE 3; H335, SCL C ≥ 0.5 %<br>EUH071 |
| with regard to ecotoxicological data | **RAC 29 (2-6 June 2014) opinion on classification of glutaraldehyde (100%) according to Regulation 1272/2008:**<br>Aquatic Acute 1; H400<br>Aquatic Chronic 2; H411<br>M Factor:<br>M = 1; Aquatic Acute 1 |

## Chapter 2: Methods of Analysis

**Analytical methods for the active substance**

| | |
|---|---|
| Technical active substance (principle of method) | Potentiometric titration (BASF)<br>HPLC-UV (Dow)<br>Titration (Dow)<br>For additional information required at product authorisation see Doc IIA and the Doc IIIAs. |
| Impurities in technical active substance (principle of method) | GC-MS-FID (BASF)<br>Karl-Fisher titration (BASF)<br>GC-TCD (Dow)<br>IEC-CD (Dow)<br>For additional information required at product authorisation see Doc IIA and the Doc IIIAs. |

**Analytical methods for residues**

| | |
|---|---|
| Soil (principle of method and LOQ) | Waived, Persistence or accumulation of glutaraldehyde or its metabolites in soil is not expected (BASF)<br>LC-MS/MS, 0.05 mg/kg (Dow)<br>The method is not required since the $DT_{50}$ < 3 days |
| Air (principle of method and LOQ) | [HPLC/UV, 18 µg/m$^3$ (BASF)<br>HPLC/UV, 55.0 ng/sample (STS: 0.44 ppb or 1.8 µg/m$^3$; LTS: 0.027 ppb or 0.11 µg/m$^3$ ) (Dow) ]<br>It has been agreed that a new method will be submitted before product authorisation |
| Water (principle of method and LOQ) | GC-MS, LOQ = 0.05 µg/l (for drinking water and surface water) (BASF)<br>LC-MS-MS, 0.1 µg/l (for drinking water and surface water) (Dow) |

| | |
|---|---|
| Body fluids and tissues (principle of method and LOQ) | Rat blood: GC-MS, 20 ng/g (Dow)<br>Body tissues: waived (BASF, Dow) It is technically impossible at this time to analyse glutaraldehyde in animal tissues as the glutaraldehyde will react with the biological material, followed by rapid metabolisation and elimination. |
| Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) | Waived (BASF, Dow) The product is not intended to be added to food and feedstuffs or be used in facilities during food processing. Only by accident may trace amounts of glutaraldehyde be on the surface of food and feedstuffs. Due to evaporation, photodegradation and rapid reactions with proteins, only trace amounts would be expected even in the case of accident. |
| Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) | Waived (BASF, Dow). It is technically impossible at this time to analyse glutaraldehyde in animal tissues as the glutaraldehyde will react with the biological material, followed by rapid metabolisation and elimination. |

## Chapter 3: Impact on Human Health

**Absorption, distribution, metabolism and excretion in mammals**

| | |
|---|---|
| Rate and extent of oral absorption: | Approx. 37 to 51 % for both sexes depending on dose level and method of calculation (measured as radioactivity of $^{14}C$ labelled GA). (Dow, BASF)<br>Oral absorption of 40 % is proposed for estimating the systemic dose. |
| Rate and extent of dermal absorption for the active substance: | 10 % is proposed based on weight of evidence. |
| Rate and extent of dermal absorption for the representative product(s)[4]: | |
| Distribution: | All organs and tissues (radioactive label) |
| Potential for accumulation: | No potential for accumulation |
| Rate and extent of excretion: | Rapid and almost complete, independent of the sex |
| Toxicologically significant metabolite(s) | Metabolites are poorly known, but none expected to be toxicologically significant |

**Acute toxicity**

| | |
|---|---|
| Rat $LD_{50}$ oral | 77 mg/kg bw (for pure GA); R25 (Dow) |
| Rat $LD_{50}$ dermal | > 1000 mg/kg bw (for pure GA; highly dependent on concentration) (BASF) |
| Rat $LC_{50}$ inhalation | 0.35 mg/L in male rats and 0.s8 mg/L in female rats; R23 (BASF, Dow) |
| Skin irritation | Corrosive, R34 (Dow, BASF) |
| Eye irritation | Corrosive, R41 (Dow, BASF) |
| Skin sensitization (test method used and result) | Sensitising; Guinea pig maximisation test R43 (Dow, BASF) |

**Repeated dose toxicity**

| | |
|---|---|
| Species/ target / critical effect | Rat / kidney / increased kidney weight coupled with a slight increase in urea nitrogen in females (Dow, BASF)<br>Mouse / kidney / increased kidney weight (Dow)<br>Dog / GI tract / increased incidence of vomiting (Dow) |
| Lowest relevant oral NOAEL / LOAEL | NOAEL 2.9 mg/kg bw/day (2.9 and 3.6 mg/kg bw/day for males and females, respectively), rat (Dow, BASF) |
| Lowest relevant dermal NOAEL / LOAEL | NOAEL/LOAEL not established: skin irritation but no systemic effects |
| Lowest relevant inhalation NOAEL / LOAEL | LOAEC 0.26 µg GA/L, mice (local irritant effects; no indications of systemic toxicity other than secondary to irritation) (Dow) |

| | |
|---|---|
| **Genotoxicity** | *In vitro*: Positive results in Ames test (Dow, BASF), |

[4] Please consider Q5 on *Derivation of dermal absorption values* of section 4.1.1 of the Manual of Technical Agreements (MOTA) version 5.

| | |
|---|---|
| | sister chromatid exchange assay (BASF), *in vitro* chromosomal aberration assay (BASF), Forward mutation assay (Dow, BASF).<br>*In vivo*: Slightly positive in an intraperitoneal *in vivo* micronucleus test and equivocal in all oral studies presumed due to test substance not reaching the target organ. (BASF) |

**Carcinogenicity**

| | |
|---|---|
| Species/type of tumour | Large Granular Lymphocytic Leukaemia in female rats (Dow)<br>Testis Leydig cell adenomas in male rats (BASF) |
| lowest dose with tumours | LGLL: 5.5 mg/kg bw/day (2-year oral study; not treatment related) (Dow)<br>Leydig cells: 3.5 mg/kg bw/day (2-year oral study) (BASF) |

**Reproductive toxicity**

| | |
|---|---|
| Species/ Reproduction target / critical effect | 1. Increased resorption rate, increased post-implantation losses, reduction in mean placental weights (Teratogenicity study in rabbits; Dow, BASF)<br>2. Testes Leydig cell hyperplasia, cystic degeneration (2-year oral study in [redacted] rats; BASF)<br>3. Testes consistency changes (2-year oral study in [redacted] rats; Dow)<br>4. Diffuse degeneration of the testes (1-year oral study in [redacted] rats; BASF)<br>Due to the nature and incidence of the findings there is no ground for classification for teratogenicity. Glutaraldehyde had little effect on any reproduction parameters even at maternally toxic doses and there is no ground for classification for fertility effects. |
| Lowest relevant reproductive NOAEL / LOAEL | 1. NOAEL 15 mg/kg bw/day<br>2. LOAEL 3.5 mg/kg bw/day<br>3. NOAEL 3.6 mg/kg bw/day<br>4. NOAEL 3.2 mg/kg bw/day<br>(The numbers refer to the studies as indicated above) |
| Species/Developmental target / critical effect | None in rabbits or rats (Dow, BASF) |
| Developmental toxicity | |
| Lowest relevant developmental NOAEL / LOAEL | Not relevant |

**Neurotoxicity / Delayed neurotoxicity**

| | |
|---|---|
| Species/ target/critical effect | None |
| Lowest relevant developmental NOAEL / LOAEL. | Not relevant |

**Other toxicological studies**

| | |
|---|---|
| Respiratory irritation | Moderately potent peripheral sensory irritant; Peripheral sensory irritation test, in mice (BASF) |
| Respiratory sensitisation | Potential respiratory sensitizer; Mouse IgE test (Dow) |

**Medical data**

| |
|---|
| Cohort studies and case studies have identified respiratory and skin sensitization as the main effects on human health. Glutaraldehyde is among the most common causes of occupational asthma among health care workers.<br>Other health risks are due to the corrosive properties of glutaraldehyde. |

| **Summary** | Value | Study | Safety factor |
|---|---|---|---|
| **Non-professional user** | | | |
| ADI (acceptable daily intake, external long-term reference dose) | Not relevant | - | - |
| $AEL_{medium-term}$ | 0.014 mg/kg bw/day | Rat 90-day oral study | 100 |
| $AEL_{long-term}$ | 0.014 mg/kg bw/day | Rat 90-day oral study | 100 |
| $AEC_{inhalation}$ | 10.6 µg/m$^3$ (2.6 ppb) | 2-year inhalation study in the mouse | 24 |
| $AEC_{acute\ inhalation}$ | 0.5 mg/m$^3$ (120 ppb) | Human study on odour detection and chemesthetic detection | 3.2 |
| $AEC_{dermal}$ | not established | | |
| Drinking water limit | 0.1 µg/L | As set by EU Drinking Water Directive (98/83/EC) | Not relevant |
| ARfD (acute reference dose) | 0.60 mg/kg bw/day | Rabbit teratogenicity study | 25 |
| **Professional user** | | | |
| Reference value for inhalation (proposed OEL) | - | - | - |
| Reference value for dermal absorption concerning the active substance: | 10% estimated value | - | - |
| Reference value for dermal absorption concerning the representative product(s)[4]: | 10% estimated value | - | - |

**Acceptable exposure scenarios (including method of calculation)**

| | |
|---|---|
| Professional users | **PT2**: Hard Surface Disinfection<br>Mixing and Loading (*Dermal: Mixing and loading model 2 (TNsG 2002), Inhalation: ConsExpo4.1, evaporation, constant release area*)<br>Application by mopping (*Dermal: surface disinfection model 1 (TNsG 2002), Inhalation: ConsExpo4.1, evaporation, increase release area*)<br>Post application (*Dermal: Mixing and loading model 2 (TNsG 2002), Inhalation: ConsExpo4.1, evaporation, constant release area*) |
| | **PT3**: Veterinary hygiene biocidal product<br>Mixing and loading (*EUROPOEM II data)*<br>Disinfection by spraying (*Spraying model 2, TNsG 2002)*<br>Disinfection by fogging (*covered by spraying scenario*) |
| | **PT4**: Food vessel/Machinery Disinfection<br>Food Processing Surface Disinfection<br>Connecting drum to pump (*Mixing and loading Model 7 –, TNG 2002, and measurement data)*<br>Cleaning and maintenance of machinery (*TGD Appendix II, Table 2, Stoffenmanager)*<br>Application of disinfectant in a slaughter house *(Disinfection Model 9, TNsG 2002*) |
| | **PT6:** Preservatives for Detergents, Paper Wet-End Additives Preservation and Paper Coatings Preservation<br>Connecting drum to pump (*Mixing and loading Model 7 –, TNG 2002, and measurement data)*<br>Loading laundry softener (*ConsExpo 4.1)*<br>Mixing and loading liquid detergent (*ConsExpo 4.1)*<br>Applying liquid detergent (*ConsExpo 4.1)*<br>Applying wax emulsion (*ConsExpo 4.1)*<br>Applying car polish (*ConsExpo 4.1)*<br>Manual surface disinfection (*Dermal: Manual surface disinfection model 1, TNsG 2002, Inhalation: ConsExpo 4.1)*<br>Loading and unloading slurry tanks *(Dermal: RISKOFDERM, inhalation: EASE)* |
| | **PT11:** Preservatives for liquid-cooling and processing systems<br>Closed Recirculating Systems:<br>Mixing and loading *(Mixing and loading Model 7 –, TNG 2002, and measurement data)*<br>Draining *(Mixing and loading Model 7 – TNG 2002)*<br>Open Recirculating Cooling Systems:<br>Loading *(Mixing and loading Model 7 –, TNG 2002, and measurement data* ) |

| | |
|---|---|
| | **PT12:**<br>Slimicide for paper pulp: wet-end slimicides :<br>Mixing and loading *(Mixing and loading Model 7 –, TNG 2002, and measurement data*)<br>Cleaning and maintenance of pulp tanks (*Spraying model 2, TNsG 2002)*<br>Slimicide for paper pulp: paper de-inking:<br>Mixing and loading (*(Mixing and loading Model 7 –, TNG 2002, and measurement data*)<br>Cleaning and maintenance of pulp tanks *(Spraying model 2, TNsG 2002)* |
| | **Oilfield uses:**<br>Slimicide for oilfield injection water PT11,<br>Preservative for drilling muds/fluids PT6,<br>Preservative for hydrotesting water PT11: mixing and loading (connecting/disconnecting)): *(Mixing and loading Model 7 –, TNG 2002, and measurement data)* |
| Production of active substance: | Not applicable |
| Formulation of biocidal product | Not applicable |
| Secondary (indirect) exposure as a result of use exposure | **PT2**: Child secondary exposure *(scenarios outlined in the TNG Human Exposure Part 3)* |
| | **PT6:** Secondary exposure to laundry softerner (*ConsExpo 4.1)*<br>Secondary exposure to liquid detergent (*ConsExpo 4.1)* |
| | **PT11**: Secondary inhalation exposure, adult and child *(calculations based on measured concentration)* |
| | **PT12**: Worker inhalation exposure to vapour and aerosol phase to be demonstrated at product authorisation by measurement or modelling *(Henry's law, Spraying model 2, TNsG 2002)* |
| Non-professional users | **PT6:** Loading laundry softener (*ConsExpo 4.1)*<br>Mixing and loading liquid detergent (*ConsExpo 4.1)*<br>Applying liquid detergent (*ConsExpo 4.1)*<br>Applying wax emulsion (*ConsExpo 4.1)*<br>Applying car polish (*US EPA scenarios)* |

## Chapter 4: Fate and Behaviour in the Environment

**Route and rate of degradation in water**

| | |
|---|---|
| Hydrolysis of active substance and relevant metabolites ($DT_{50}$) (state pH and temperature) | pH 5: 508-628 days at 25°C (1 437-1 777 d at 12 °C) (BASF, Dow) |
| | pH 7:102-394 days at 25°C (289-1 115 d at 12 °C) (BASF, Dow) |
| | pH 9: 46-63 days at 25°C (130-178 d at 12 °C) (BASF, Dow) |
| Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites | 196 days of natural sunlight at pH 5 and 25°C<br>No metabolites detected > 10%. (Dow) |

| | |
|---|---|
| | Waived (BASF): Waiving was accepted at TM III 2011 because Glutaraldehyde has its adsorption max below 290 nm which is the cutoff value for direct photolysis. Due to ready biodegradability photolysis is not considered a relevant degradation pathway for Glutaraldehyde. |
| Readily biodegradable (yes/no) | Yes (Dow, BASF) |
| STP Simulation Study | k 4.95 h-1 at 20-25 °C, DT50 0.14 h at 20-25 °C. (DT50= 0.2 h at 15 °C) (Dow, BASF ) |
| Biodegradation in seawater | Yes, 73.4% degradation after 28 days (Dow) and 90-100% degradation after 70 days (BASF) |
| Non-extractable residues | **Bound residues in water/sediment systems (% of initial applied radioactivity)**<br>Aerobic system: max. 15.8% after 14 days.<br>Anaerobic system: max. 2.3% after 3 days.<br>(Dow, BASF) |
| Distribution in water / sediment systems (active substance) | **Distribution in river water/sediment systems at 25°C (% of applied radioactivity)**<br><u>Aerobic system</u><br>Water: max 94.0% at 4 hour; DT50 10.6 hours (1.25 d at 12 °C)<br>Sediment: max 25.3% at 48 hour<br>Cumulative % mineralisation to $CO_2$ was 67.9% after 30 days.<br><u>Anaerobic system</u><br>Water: max 95.1% at Day 1; DT50 7.7 hours (0.91 d at 12 °C)<br>Sediment: max 8.4% at Day 123<br>(Dow, BASF) |
| Distribution in water / sediment systems (metabolites) | <u>Aerobic system</u><br>18.9 to 21.5% glutaric acid in water phase at 12 hours, which was then completely metabolised by 48 h.<br>49.8 to 52.9% carbon dioxide in water phase at 48 h.<br><u>Anaerobic system</u><br>12.62 to 22.86% Compound A (2-hydroxy-3,4,4a,7,8,8a-hexahydro-2H-chromene-6-carbaldehyde) in the water phase at Day 90.<br>35.11 to 38.97% 5-hydroxy-pentanal in the water phase at Day 1.<br>74.34 to 77.86% 1,5-pentanediol in the water phase at Day 14.<br>(Dow, BASF) |

**Route and rate of degradation in soil**

| | |
|---|---|
| Mineralization (aerobic) | Not available |
| Laboratory studies (range or median, with number of measurements, with regression coefficient) | $DT_{50lab}$ (20°C, aerobic): Not available |
| | $DT_{90lab}$ (20°C, aerobic): Not available |
| | $DT_{50lab}$ (10°C, aerobic): Not available |

| | |
|---|---|
| | $DT_{50lab}$ (20°C, anaerobic): Not available |
| | degradation in the saturated zone: Not available |
| Field studies (state location, range or median with number of measurements) | $DT_{50f}$: Not required |
| | $DT_{90f}$: Not required |
| Anaerobic degradation | See distribution in water / sediment systems |
| Soil photolysis | Not applicable |
| Non-extractable residues | Not applicable |
| Relevant metabolites - name and/or code, % of applied active ingredient (range and maximum) | Not applicable |
| Soil accumulation and plateau concentration | Not applicable |

**Adsorption/desorption**

| | |
|---|---|
| Ka , Kd<br>$Ka_{oc}$ , $Kd_{oc}$<br>pH dependence (yes / no) (if yes type of dependence) | **Ka**: 2.06 (sandy loam), 4.94 (silty clay loam), 4.83 (silt loam), 1.10 (loamy sand), 0.59 (sediment<br>**$Ka_{oc}$**: 210 (sandy loam), 500 (silty clay loam), 340 (silt loam), 460 (loamy sand), 120 (sediment)<br>Arithmetic mean 326 L/kg<br>pH dependence: No<br>(Dow, BASF) |

**Fate and behaviour in air**

| | |
|---|---|
| Direct photolysis in air | Not available |
| Quantum yield of direct photolysis | Not required |
| Photo-oxidative degradation in air | Model calculation (Aopwin v1.91)<br>$DT_{50}$ 8.2 hours (24 hours, 5.0 x $10^5$ OH radicals per $cm^3$<br>Latitude: ..... Season: ..... $DT_{50}$ ..... |
| Volatilization | Glutaraldehyde has a low potential for volatilization based on the vapour pressure and the Henry's Law Constant.<br>Henry's Law Constant for 100% glutaraldehyde:<br>0.0086 $Pa.m3.mol^{-1}$ at 20°C<br>(calculated from data of Dow) |

**Monitoring data, if available**

| | |
|---|---|
| Soil (indicate location and type of study) | No monitoring data are available. |
| Surface water (indicate location and type of study) | No monitoring data are available. |
| Ground water (indicate location and type of study) | No monitoring data are available. |
| Air (indicate location and type of study) | Glutaraldehyde was not detected (ND) when air samples were taken outside 4 paper mills using glutaraldehyde. (Dow)<br>The concentrations in the air in the paper mill were below the lowest measured value of 2.5 ppb (BASF) |

## Chapter 5: Effects on Non-target Species

**Toxicity data for aquatic species (most sensitive species of each group)**

| Species | Time-scale | Endpoint | Toxicity |
|---|---|---|---|
| **Fish** | | | |
| *Oncorhynchus mykiss* | 62 day | NOEC | 1.0 mg a.i./L (measured) (Dow) |
| **Invertebrates** | | | |
| *Daphnia magna* | 21 day | NOEC | 0.12 mg a.i./L (measured) (Dow) |
| **Algae** | | | |
| *Scenedesmus subspicatus* | 72 hour | $E_rC_{50}$<br>$NOE_rC$ | 0.6 mg a.i./L (measured) (BASF)<br>0.025 (measured) |
| **Microorganisms** | | | |
| Activated sludge | 30 min | $EC_{50}$ | >51 mg a.i./L (nominal) (Dow) |

**Effects on earthworms or other soil non-target organisms**

| | |
|---|---|
| Acute toxicity to *Eisenia foetida* | LC50 > 150 mg a.i./kg ww (nominal) (BASF, Dow) |
| Reproductive toxicity to *Eisenia foetida* | Not required |
| Acute toxicity to terrestrial plants (*Vicia sativa*) | LC50 1079 mg a.i./kg ww (nominal) (BASF, Dow) |

**Effects on soil micro-organisms**

| | |
|---|---|
| Nitrogen mineralization | EC10 15.4 mg a.i./kg ww (nominal) (BASF, Dow)<br>EC50 483 mg a.i./kg ww (nominal) |
| Carbon mineralization | EC10 9.2 mg a.i./kg ww (nominal) (BASF, Dow)<br>EC50 > 925 mg a.i./kg ww (nominal) |

**Effects on terrestrial vertebrates**

| | |
|---|---|
| Acute toxicity to mammals | Not required |
| Acute toxicity to birds | Not required |
| Dietary toxicity to birds | Not required |
| Reproductive toxicity to birds | Not required |

**Effects on honeybees**

| | |
|---|---|
| Acute oral toxicity | Not required |
| Acute contact toxicity | Not required |

**Effects on other beneficial arthropods**

| | |
|---|---|
| Acute oral toxicity | Not required |
| Acute contact toxicity | Not required |
| Acute toxicity to …….. | Not required |

**Bioconcentration**

| | |
|---|---|
| Bioconcentration factor (BCF) | Calculated according to the TGD using log Kow -0.33 (Dow)<br>$BCF_{fish}$: 1.41 (Eq. 75)<br>$BCF_{earthworm}$: 0.846 (Eq. 82d) |
| Depuration time($DT_{50}$)<br>($DT_{90}$) | Not required |
| Level of metabolites (%) in organisms accounting for > 10 % of residues | Not applicable |

## Chapter 6: Other End Points

None required.

## Appendix II: List of Intended Uses

**Note: Active substance (a.s.) refers to 100% glutaraldehyde**

| Product type | Product name | Organisms controlled | Formulation | | Application | | | Applied amount per treatment | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Type | Conc of a.s. g/kg | method kind | number min max | interval between applications (min) | g a.s./L min max | water L/m$^2$ min max | g as/m$^2$ min max |
| PT 02 | [redacted] | **Bacteria** [redacted]<br>**Fungi** [redacted]<br>**Yeast** [redacted]<br>**Viruses**: [redacted]<br>**Green algae**: [redacted]<br>**Cyanobacteria**: | SL-Water soluble concen-trate<br>Liquid formulation containing [redacted] | [redacted] | Hard surface disinfection in hospitals and industrial areas | Min: 1/week max: 4/day | 24h for hard surface disinfection. | 0.5-3.0 | 0.02 | 0.01-0.06 |

| Product type | Product name | Organisms controlled | Formulation | | Application | | | Applied amount per treatment | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Type | Conc of a.s. g/kg | method kind | number min max | interval between applications (min) | g a.s./L min max | water L/m$^2$ min max | g as/m$^2$ min max |
| | | [redacted]<br>**Diatoms:** [redacted]<br>Biofilms | | | | | | | | |
| PT 03 | See PT 02 | See PT 02 for bacteria, fungi and yeast<br>**Viruses** [redacted] | See PT 02 | [redacted] | Disinfection of animal housing (poultry and pig farms) by spraying or fogging. | Min: 2/year max: <24h | 6 months for pig farms and 2 months for poultry farms. | Spraying 1<br>Fogging 20 | Spraying 0.4 L<br>Fogging 0.02 | Spraying 0.4<br>Fogging 0.4 |

| Product type | Product name | Organisms controlled | Formulation | | Application | | | Applied amount per treatment | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Type | Conc of a.s. g/kg | method kind | number min max | interval between applications (min) | g a.s./L min max | water L/$m^2$ min max | g as/$m^2$ min max |
| PT 04 | See PT 02 | See PT 02 for bacteria, fungi and yeast<br>Biofilms | See PT 02 | [redacted] | Disinfection of food vessels/machinery | Min: daily<br>max: daily | 24h | 0.5-1 | 0.1 | 0.05-0.1 |
| PT 04 | See PT 02 | See PT 02 for bacteria, fungi and yeast<br>Biofilms | See PT 02 | [redacted] | Food processing (e.g. slaughter house) surface disinfection | Min: daily<br>max: daily | 24h | 0.5-1 | 0.1 | 0.05-0.1 |
| PT 06 | See PT 02 | See PT 02 for bacteria, fungi, yeast and algae | See PT 02 | [redacted] | In-can preservative for detergents (e.g. laundry softeners, liquid detergent, wax emulsion, car polish) | Incorporated during manufacture. | 24h | 0.1-1 | NA | NA |
| PT 06 | See PT 02 | See PT 02 for bacteria, fungi , yeast and algae | See PT 02 | [redacted] | Preservation of Paper Wet-End Additives and Paper Coatings | | | 0.05-0.5 | NA | NA |
| PT 11 | See PT 02 | **Bacteria** e.g [redacted] | See PT 02 | [redacted] | Open re-circulating cooling systems | Min: 1/ week<br>Max: 7/week | As required | 0.02-0.1 | NA | NA |

| Product type | Product name | Organisms controlled | Formulation | | Application | | | Applied amount per treatment | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Type | Conc of a.s. g/kg | method kind | number min max | interval between applications (min) | g a.s./L min max | water L/m$^2$ min max | g as/m$^2$ min max |
| PT 11 | See PT 02 | [redacted]<br>**Fungi** [redacted]<br>**Yeast** e[redacted]<br>See PT 02 for algae<br>Biofilms | See PT 02 | [redacted] | Closed re-circulating cooling systems | System drained and re-filled twice per year | 6 months | 0.02-0.1 | NA | NA |
| PT 12 | See PT 02 | See PT 02 for bacteria, fungi, yeast and algae<br>Biofilms | See PT 02 | [redacted] | Slimicide for paper pulp: wet-end slimicide | Min: 2 daily additions<br>Max:6 daily additions | 4 hours | 0.0075-0.075 | NA | NA |
| PT 12 | See PT 02 | See PT 02 for bacteria, fungi, yeast and algae<br>Biofilms | See PT 02 | [redacted] | Slimicide for paper pulp: paper de-inking | Min: 2 daily additions<br>Max:6 daily additions | 4 hours | 0.05-0.2 | NA | NA |
| PT 11 | See PT 02 | **Bacteria** [redacted] | See PT 02 | [redacted] | Preservative for oilfield injection water | 1 (continuous application of between 1 to 6 hours) | 1 week | 0.05-3 | NA | NA |

| Product type | Product name | Organisms controlled | Formulation | | Application | | | Applied amount per treatment | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Type | Conc of a.s. g/kg | method kind | number min max | interval between applications (min) | g a.s./L min max | water L/m$^2$ min max | g as/m$^2$ min max |
| PT 06 | See PT 02 | [redacted] | See PT 02 | [redacted] | Preservative for drilling muds/fluids | 1 application on manufact-ure or recon-ditioning | No repeat application necessary during use | 0.1-0.5 | NA | NA |
| PT 06 | See PT 02 | [redacted] **Fungi** e[redacted] | See PT 02 | [redacted] | Preservative for cementing fluids | 1 application | No repeat application necessary | 0.1-0.5 | NA | NA |
| PT 11 | See PT 02 | [redacted] **Yeast** e[redacted] See PT 02 for algae Biofilms | See PT 02 | [redacted] | Preservative for hydrotesting water | 1 application | No repeat application necessary | 0.002-0.03 | NA | NA |

## Appendix III: Summary of public consultation - CONFIDENTIAL

## Appendix IV: List of Studies of BASF

Data protection is claimed by the applicant in accordance with Article 60 of Regulation (EU) No 528/2012.

| Section No./ Reference No. | Author(s) | Year | Title<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant)/(Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| A3.1.1_01 | [redacted] | 2002 | Determination of the Melting Temperature of "Protectol GA [redacted] Study [redacted],<br>BPD ID A3.01.1_01<br>GLP, Unpublished | Yes | BASF |
| A3.1.2_01 | [redacted] | 1999 | Product Chemistry for Glutaraldehyde ([redacted], Series 63 - Physical and Chemical Characteristics.<br>[redacted]<br>BPD ID A3.01.2_01<br>GLP, Unpublished | Yes | BASF |
| A3.1.2_02 | [redacted] | 1995 | Dampfdruck von Glutardialdehyd, wässerig.<br>[redacted]<br>BPD ID A3.01.2_02<br>Non GLP, Unpublished | Yes | BASF |
| A3.1.2_03 | [redacted] | 1992 | Dampfdruck von [redacted].<br>[redacted]<br>BPD ID A3.01.2_03<br>Non GLP, Unpublished | Yes | BASF |
| A3.1.3_01 | [redacted] | 1999 | Product Chemistry for Glutaraldehyde [redacted] Series 63 - Physical and Chemical Characteristics.<br>[redacted]<br>BPD ID A3.01.2_01<br>GLP, Unpublished | Yes | BASF |
| A3.1.3_02 | [redacted] | 1987 | Temperaturabhängigkeit der Dichte von [redacted]<br>BPD ID A3.01.3_02<br>Non GLP, Unpublished | Yes | BASF |
| A3.1.3_03 | [redacted] | 1992 | Dichte von [redacted] bei -26 bis 40 °C.<br>[redacted]<br>BPD ID A3.01.3_03<br>Non GLP, Unpublished | Yes | BASF |

| Section No./ Reference No. | Author(s) | Year | Title<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant)/(Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| A3.2_01 | [redacted] | 1999 | Product Chemistry for Glutaraldehyde ([redacted], Series 63 - Physical and Chemical Characteristics.<br>[redacted]<br>BPD ID A3.01.2_01<br>GLP, Unpublished | Yes | BASF |
| A3.2_02 | [redacted] | 1993 | Dampfdruck [redacted],<br>and Translation of the Report (1994).<br>[redacted]<br>BPD ID A3.02_02<br>GLP, Unpublished | Yes | BASF |
| A3.2_03 | Olson JD | 1998 | The vapour pressure of pure and aqueous glutaraldehyde.<br>Fluid Phase Equilibria 150-151: 713-720,<br>BPD ID A3.02_03<br>Non GLP, Published | No | Public |
| A3.2_04 | [redacted] | 1995 | Dampfdruck von Glutardialdehyd, wässerig.<br>[redacted]<br>BPD ID A3.01.2_02<br>Non GLP, Unpublished | Yes | BASF |
| A3.2_05 | [redacted] | 1992 | Dampfdruck von [redacted].<br>[redacted]<br>BPD ID A3.01.2_03<br>Non GLP, Unpublished | Yes | BASF |
| A3.2_06 | [redacted] | 1983 | Glutardialdehydpartialdruck über wässrigen Lösungen (Teil 4).<br>[redacted]<br>BPD ID A3.02_06<br>Non GLP, Unpublished | Yes | BASF |
| A3.2.1_01 | [redacted] | 2005 | Glutaraldehyde, SRC EPIWIN calculations.<br>[redacted]<br>BPD ID A3.02.1_01<br>Non GLP, Unpublished | No | BASF |
| A3.3.1_01 | [redacted] | 1999 | Product Chemistry for Glutaraldehyde ([redacted]), Series 63 - Physical and Chemical Characteristics.<br>[redacted]<br>BPD ID A3.01.2_01<br>GLP, Unpublished | Yes | BASF |

| Section No./ Reference No. | Author(s) | Year | Title<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant)/(Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| A3.3.2_01 | [redacted] | 1999 | Product Chemistry for Glutaraldehyde ([redacted]), Series 63 - Physical and Chemical Characteristics.<br>[redacted]<br>BPD ID A3.01.2_01<br>GLP, Unpublished | Yes | BASF |
| A3.3.3_01 | Siemann L | 1999 | Product Chemistry for Glutaraldehyde [redacted] Series 63 - Physical and Chemical Characteristics.<br>[redacted]<br>BPD ID A3.01.2_01<br>GLP, Unpublished | Yes | BASF |
| A3.4.1_01 | [redacted] | 2004 | Characterization of "[redacted]" for the notification in the Netherlands.<br>[redacted]<br>BPD ID A3.04.1_01<br>GLP, Unpublished | Yes | BASF |
| A3.4.2_01 | [redacted] | 2006 | Characterization of "[redacted]" before start of toxicological and ecological studies and 1. Amendment to Final Report.<br>[redacted],<br>BPD ID A3.04.2_01<br>GLP, Unpublished | Yes | BASF |
| A3.4.3_01 | [redacted] | 2006 | Characterization of "[redacted]" before start of toxicological and ecological studies and 1. Amendment to Final Report.<br>[redacted]<br>BPD ID A3.04.2_01<br>GLP, Unpublished | Yes | BASF |
| A3.4.4_01 | [redacted] | 2004 | Characterization of "[redacted]" for the notification in the Netherlands.<br>[redacted]<br>BPD ID A3.04.1_01<br>GLP, Unpublished | Yes | BASF |
| A3.5_01 | [redacted] | 2002 | Water Solubility of "[redacted]".<br>[redacted]<br>BPD ID A3.05_01<br>GLP, Unpublished | Yes | BASF |

| Section No./ Reference No. | Author(s) | Year | Title<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant)/(Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| A3.5_02 | [redacted] | 1999 | Product Chemistry for Glutaraldehyde ([redacted], Series 63 - Physical and Chemical Characteristics.<br>[redacted]<br>BPD ID A3.01.2_01<br>GLP, Unpublished | Yes | BASF |
| A3.5_03 | [redacted] | 1987 | Glutardialdehyd [redacted],and Translation of the Report (1994).<br>[redacted]<br>BPD ID A3.05_03<br>Non GLP, Unpublished | Yes | BASF |
| A3.6_01 | [redacted] | 1999 | Product Chemistry for Glutaraldehyde ([redacted]), Series 63 - Physical and Chemical Characteristics.<br>[redacted]<br>BPD ID A3.01.2_01<br>GLP, Unpublished | Yes | BASF |
| A3.7_01 | [redacted] | 2006 | Physico-chemical properties of "[redacted]".<br>[redacted]<br>BPD ID A3.07_01<br>GLP, Unpublished | Yes | BASF |
| A.3.7_02 | [redacted] | 1999 | Product Chemistry for Glutaraldehyde ([redacted]), Series 63 - Physical and Chemical Characteristics.<br>[redacted]<br>BPD ID A3.01.2_01<br>GLP, Unpublished | Yes | BASF |
| A3.9_01 | [redacted] | 2002 | Partition Coefficient n-Octanol/Water (log Pow) of "[redacted]".<br>[redacted]<br>BPD ID A3.09_01<br>GLP, Unpublished | Yes | BASF |
| A3.9_02 | [redacted] | 1987 | Glutardialdehyd [redacted],<br>and Translation of the Report (1994).<br>[redacted]<br>BPD ID A3.05_03<br>Non GLP, Unpublished | Yes | BASF |

| Section No./ Reference No. | Author(s) | Year | Title<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant)/(Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| A3.10_01 | [redacted] | 2004 | Evaluation of physical and chemical properties according to Directive 92/69/EC: Annex A.9-A.17.<br>[redacted]<br>BPD ID A3.10_01<br>GLP, Unpublished | Yes | BASF |
| A3.10_02 | [redacted] | 2006 | [redacted] - Thermal Decomposition. [redacted], Statement,<br>BPD ID A3.10_02<br>Non GLP, Unpublished | Yes | BASF |
| A3.10_03 | [redacted] | 1998 | Dynamische Differenzkalorimetrie (DSC).<br>[redacted]<br>BPD ID A3.10_03<br>Non GLP, Unpublished | Yes | BASF |
| A3.11_01 | [redacted] | 2004 | Evaluation of physical and chemical properties according to Directive 92/69/EC: Annex A.9-A.17.<br>[redacted]<br>BPD ID A3.10_01<br>GLP, Unpublished | Yes | BASF |
| A3.12_01 | [redacted] | 1999 | Product Chemistry for Glutaraldehyde ([redacted]), Series 63 - Physical and Chemical Characteristics.<br>[redacted]<br>BPD ID A3.01.2_01<br>GLP, Unpublished | Yes | BASF |
| A3.12_02 | [redacted] | 1970 | Kennzahlen Explosionsfähiger Stoffe.<br>[redacted]<br>BPD ID A3.12_02<br>GLP, Unpublished | Yes | BASF |
| A3.13_01 | [redacted] | 2004 | Physico-chemical Properties of "[redacted]" for the Notification in the Netherlands.<br>[redacted]<br>BPD ID A3.13_01<br>GLP, Unpublished | Yes | BASF |
| A3.14_01 | [redacted] | 1999 | Product Chemistry for Glutaraldehyde ([redacted]), Series 63 - Physical and Chemical Characteristics.<br>[redacted]<br>BPD ID A3.01.2_01<br>GLP, Unpublished | Yes | BASF |

| Section No./ Reference No. | Author(s) | Year | Title<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant)/(Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| A3.14_02 | [redacted] | [redacted] | Physico-chemical Properties of "[redacted]" for the Notification in the Netherlands.<br>[redacted]<br>BPD ID A3.13_01<br>GLP, Unpublished | Yes | BASF |
| A3.15_01 | [redacted] | 2004 | Evaluation of physical and chemical properties according to Directive 92/69/EC: Annex A.9-A.17.<br>[redacted]<br>BPD ID A3.10_01<br>GLP, Unpublished | Yes | BASF |
| A3.15_02 | [redacted] | 2000 | Expert judgement - Absence of explosive and oxidizing properties of glutaral.<br>[redacted]<br>BPD ID A3.15_02<br>Non GLP, Unpublished | Yes | BASF |
| A3.16_01 | [redacted] | 1999 | Product Chemistry for Glutaraldehyde ([redacted]), Series 63 - Physical and Chemical Characteristics.<br>[redacted]<br>BPD ID A3.01.2_01<br>GLP, Unpublished | Yes | BASF |
| A3.16_02 | [redacted] | 2000 | Expert judgement - Absence of explosive and oxidizing properties of glutaral.<br>[redacted]<br>BPD ID A3.15_02<br>Non GLP, Unpublished | Yes | BASF |
| A3.17_01 | [redacted] | 1999 | Product Chemistry for Glutaraldehyde ([redacted], Series 63 - Physical and Chemical Characteristics.<br>[redacted]<br>BPD ID A3.01.2_01<br>GLP, Unpublished | Yes | BASF |
| A3.17_02 | [redacted] | 2004 | Product Information: Glutaraldehyde - Materials Compatibility.<br>[redacted]<br>BPD ID A3.17_02<br>Non GLP, Unpublished | Yes | BASF |

| Section No./ Reference No. | Author(s) | Year | Title<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant)/(Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| A4.1_01 | [redacted] | 2000 | Product Chemistry for Glutaraldehyde ([redacted]), Series 62 - Preliminary Analysis. [redacted]<br>BPD ID A4.01_01<br>GLP, Unpublished | Yes | BASF |
| A4.1_02 | [redacted] | 2005 | Validation of the method of analysis used for the determination of Glutaraldehyde within [redacted] and [redacted] in compliance with Good Laboratory Practice and 1st Addendum to Report. [redacted]<br>BPD ID A4.01_02<br>GLP, Unpublished | Yes | BASF |
| A4.1_03 | [redacted] | 2004 | Determination of Methanol in "[redacted]" for the notification in the Netherlands. [redacted]<br>BPD ID A4.01_03<br>GLP, Unpublished | Yes | BASF |
| A4.1_04 | [redacted] | 2006 | Analysenbericht, and GC Lab Method 'Determination of the oligomers in [redacted]. [redacted]<br>BPD ID A4.01_04<br>Non GLP, Unpublished | Yes | BASF |
| A4.1_05 | [redacted] | 2001 | Product Chemistry for Glutaraldehyde; Series 62 - Preliminary Analysis. [redacted]<br>BPD ID A4.01_05<br>GLP, Unpublished | Yes | BASF |
| A4.2b_01 | Hendricks W | 1987 | Glutaraldehyde.<br>Organic Methods Evaluation Branch, OSHA Analytical Laboratory, Salt Lake City, Utah, SHA Method No. 64,<br>BPD ID A4.02b_01<br>Non GLP, Published | No | Public |
| A4.2b_02 | Neumeister CE, Hill G | 1994 | Glutaraldehyde.<br>NIOSH Manual of Analytical Methods (NMAM), Method: 2532,<br>BPD ID A4.02b_02<br>Non GLP, Published | No | Public |
| A4.2b_03 | Anonymous | 1998 | Methods for the Determination of Hazardous Substances - Glutaraldehyde in air.<br>HSE Books, MDHS 93,<br>BPD ID A4.02b_03<br>Non GLP, Published | No | Public |

| Section No./ Reference No. | Author(s) | Year | Title<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant)/(Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| A4.2b_04 | [redacted] | 1992 | Bestimmung von Glutardialdehyd (Pentandial).<br>[redacted],<br>BPD ID A4.02b_04<br>Non GLP, Unpublished | Yes | BASF |
| A4.2c_01 | [redacted] | 2007 | Method Validation for the Determination of Glutaraldehyde in Water.<br>[redacted]<br>BPD ID A4.02c_01<br>GLP, Unpublished | Yes | BASF |
| A4.2c_02 | [redacted] | 2007 | Product Information - [redacted] Analysis by HPLC.<br>[redacted]<br>BPD ID A4.02c_02<br>Non GLP, Unpublished | Yes | BASF |

| Section No. / Reference No. | Author(s) | Year | Title<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant)/(Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| A5.3.1_01 | [redacted] | 1999 | Determination of the Minimum Inhibitory Concentrations (MIC) of [redacted] Glutaraldehyde)<br>[redacted]<br>Unpublished<br>Non GLP | Yes | BASF |
| A5.3.1_02 | Borick et al | 1968 | Chemical Sterilizers, Adv. Appl. Microbiol., *10*, 291-312<br>BPD ID A5.3.1_02<br>Published | No | Public |
| A5.3.1_03 | Borick et al | 1964 | Alkalinised Glutaraldehyde, a new antimicrobial agent,<br>J. Pharm. Sci., *53*, 1273-1275<br>BPD ID A5.3.1_03<br>Published | No | Public |
| A5.3.1_05 | Dyas and Das | 1985 | The activity of Glutaraldehyde against *Clostridium difficile*.<br>J. Hosp. Infect., *6*, 41-45<br>BPD ID A5.3.1_05<br>Published | No | Public |
| A5.3.1_06 | Orsi et al | 1995 | In vitro activity of commercially manufactured disinfectants against Pseudomonas aeruginosa.<br>Eur. J. Epidemiol., *11*, 453-457<br>BPD ID A5.3.1_06<br>Published | No | Public |
| A5.3.1_11 | [redacted] | 2001 | An Investigation into the Efficacy of [redacted] Glutaraldehyde) as a Disinfectant in Veterinary and Animal Husbandry Applications | Yes | BASF |

| Section No. / Reference No. | Author(s) | Year | Title<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant)/(Un)Published | Data Protection Claimed (Yes/No) | Owner |
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| | | | [redacted]<br>Unpublished<br>Non GLP | | |
| A5.3.1_12 | [redacted] | 2000 | EN1276 testing of an All purpose cleaner containing [redacted] Glutaraldehyde)<br>[redacted]<br>Unpublished<br>Non GLP | Yes | BASF |
| A5.3.1_13 | [redacted] | 2002 | Efficacy of [redacted] against [redacted]<br>Unpublished<br>Non GLP | Yes | BASF |
| A5.3.1_14 | [redacted] | 2007 | Efficacy of [redacted] against [redacted]<br>Unpublished<br>Non GLP | Yes | BASF |
| A5.3.1_17 | [redacted] | 2003 | The efficacy of [redacted] in the preservation of drilling muds and workover fluids and Addendum<br>[redacted]<br>Unpublished<br>Non GLP | Yes | BASF |
| A5.3.1_20 | [redacted] | 2007 | Efficacy Testing of [redacted] against Bacterial spores<br>[redacted]<br>Unpublished<br>Non GLP | Yes | BASF |
| A5.3.1_21 | [redacted] | 2007 | EN1275 & EN1650 Efficacy Testing of [redacted] Glutaraldehyde)<br>[redacted]<br>Unpublished<br>Non GLP | Yes | BASF |
| A5.3.1_22 | [redacted] | 2012 | Test report: EN 14476: 2005 Chemical disinfectants and antiseptics – Virucidal quantitative suspension test for chemical disinfectants and antiseptics used in human medicine - Test method and requirements under clean conditions (phase 2/step 1). [redacted]. Unpublished. Revised report dated [redacted], 2012. | Yes | BASF |

| Section No. / Reference No. | Author(s) | Year | Title<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant)/(Un)Published | Data Protection Claimed (Yes/No) | Owner |
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| A5.3.1_23 | [redacted] | 2012 | Test report: EN 14476: 2005 Chemical disinfectants and antiseptics – Virucidal quantitative suspension test for chemical disinfectants and antiseptics used in human medicine - Test method and requirements under dirty conditions (phase 2/step 1). [redacted] Unpublished. Revised report dated [redacted], 2012. | Yes | BASF |
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| A5.4.1_02 | Hughes and Thurman | 1970 | Cross-linking of bacterial cell walls with glutaraldehyde. Biochem. J., *119*, 925-926<br>BPD ID A5.4.1_02<br>Published | No | Public |
| A5.7.1_01 | Carson et al | 1978 | Growth characteristics of atypical Mycobacteria in water and their comparative resistance to disinfectants.<br>Appl. Environ. Microbiol., *36*, 839-846<br>BPD ID A5.7.1_01<br>Published | No | Public |
| A5.7.1_02 | Deva et al | 1998 | Detection of persistent vegetative bacteria and amplified viral nucleic acid from in-use testing of gastro-intestinal endoscopes.<br>J. Hosp. Infect., *39*, 149-157<br>BPD ID A5.7.1_02<br>Published | No | Public |
| A5.7.1_03 | Ayliffe et al | 1979 | Decontamination of gastroscopes.<br>Health and Social Services Journal, *89*, 238-540.<br>BPD ID A5.7.1_03<br>Published | No | Public |
| A5.7.1_04 | Willinghan et al | 1996 | Investigation of bacterial resistance to hatchery disinfectants<br>Avian Diseases, 40, 510-515<br>BPD ID A5.7.1_04<br>Published | No | Public |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
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| A6.01.1_01 | [redacted] | 1994a | Report on the study of the acute oral toxicity [redacted]; rat/oral.<br>[redacted] (original report in German dated 1981),<br>[redacted]<br>Non GLP, Unpublished | Yes | BASF |
| A6.01.2_01 | [redacted] | 1995 | Acute dermal toxicity study of glutaraldehyde in [redacted] rabbits.<br>[redacted] | Yes | BASF |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| | | | [redacted]<br>GLP, Unpublished | | |
| A6.01.2_02 | [redacted] | 1994b | Report on the study of the acute dermal toxicity of "Glutaraldehyde" in the rat.<br>[redacted] (original report in German dated 1981),<br>[redacted]<br>Non GLP, Unpublished | Yes | BASF |
| A6.01.3_01 | [redacted] | 1994a | Acute inhalation toxicity LC50 4 hours (rat) of "glutaraldehyde [redacted] liquid aerosol study ([redacted]). [redacted] (original report in German dated 1982),<br>[redacted]<br>Non GLP, Unpublished<br>Addendum: [redacted] - Technical Trial [redacted] non GLP, Unpublished | Yes | BASF<br>Dow |
| A6.01.3_02 | [redacted] | 2001 | Acute inhalation toxicity LC50 4 hours (rat) of "glutaraldehyde [redacted]" ([redacted]), liquid aerosol study.<br>[redacted]<br>Non GLP, Unpublished | Yes | BASF |
| A6.01.3_03 | [redacted] | 1994b | Study of the acute inhalation toxicity in rats in the inhalation hazard test.<br>[redacted] (original report in German dated 1981),<br>[redacted]<br>Non GLP, Unpublished | Yes | BASF |
| A6.01.4_01 | [redacted] | 1994a | Study on the irritation to the intact dorsal skin of the [redacted] rabbit (short-term test).<br>[redacted] (original report in German dated [redacted] 1981),<br>[redacted]<br>Non GLP, Unpublished | Yes | BASF |
| A6.01.4_02 | [redacted] | 1994b | Study on the irritation to the intact dorsal skin of the [redacted] rabbit (short-term test).<br>[redacted] (original German report dated [redacted] 1981), | Yes | BASF |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
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| | | | [redacted]<br>Non GLP, Unpublished | | |
| A6.01.4_03 | [redacted] | 1994c | Report on the study of the irritation to the eye of white rabbits based on Draize.<br>[redacted] (original German report [redacted] 1981),<br>Non GLP, Unpublished | Yes | BASF |
| A6.01.4_04 | Werley MS, Burleigh-Flayer HD, Ballantyne B | 1995 | Respiratory peripheral sensory irritation and hypersensitivity studies with glutaraldehyde vapor.<br>Toxicol. Ind. Health 11(5): 489-501, BPD ID A6.01.4_04<br>Non GLP, Published | No | Public |
| A6.01.5_01 | [redacted] | 1975 | Bericht ueber die Pruefung von Methoxidihydropyran im Vergleich zu Methoxidihydropyran, roh und [redacted] auf etwaige hautsensibilisierende Wirkung.<br>[redacted]<br>Non GLP, Unpublished | Yes | BASF |
| A6.01.5_02_a | Ulrich P, Grenet O, Bluemel J, Vohr HW, Wiemann C, Grundler O, Suter W | 2001 | Cytokine expression profiles during murine contact allergy: T helper 2 cytokines are expressed irrespective of the type of contact allergen.<br>Arch. Toxicol. 75: 470-479,<br>BPD ID A6.01.5_02_a<br>Non GLP, Published | No | Public |
| A6.01.5_02_b | Ulrich P, Streich J, Suter W | (2001) | Intralaboratory validation of alternative endpoints in the murine local lymph node assay for the identification of contact allergic potential: primary ear skin irritation and ear-draining lymph node hyperplasia induced by topical chemicals.<br>Arch. Toxicol. 74(12): 733-744,<br>BPD ID A6.1.5_02_b<br>Non GLP, Published | No | Public |
| A6.01.5_02_c | Ulrich P, Homey B, Vohr HW | 1998 | A modified murine local lymph node assay for the differentiation of contact photoallergy from phototoxicity by analysis of cytokine expression in skin-draining lymph node cells.<br>Toxicology 125(2-3): 149-168,<br>BPD ID A6.01.5_02_c<br>Non GLP, Published | No | Public |
| A6.02_01 | [redacted] | 2004 | Report on 14C-GDA - Study of the biokinetics in rats.<br>[redacted]<br>GLP, Unpublished | Yes | BASF<br>Dow |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
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| A6.02_02_a<br>A6.02_02_b<br>A6.02_02_c | [redacted] | 2004 | Glutaraldehyde: pharmacokinetics in [redacted] rats following oral gavage or dermal application.<br>[redacted]<br>GLP, Unpublished | Yes | BASF<br>Dow |
| A6.02_05 | [redacted] | 2007 | Glutaraldehyde: Identification of metabolites in the [redacted] rat. [redacted]<br>Unpublished, | Yes | Dow<br>BASF |
| A6.02_09 | [redacted] | 2007 | Glutaraldehyde: Pharmacokinetics Of Drinking Water Administered Glutaraldehyde [redacted] Rats<br>[redacted]<br>GLP, Unpublished | Yes | BASF<br>Dow |
| A6.03.1_01 | [redacted] | 1985 | Glutaraldehyde: Two-week inclusion in drinking water of rats.<br>[redacted]<br>GLP, Unpublished | Yes | BASF<br>Dow |
| A6.03.2_01 | Ballantyne B | 1986 | Glutaraldehyde review of toxicological studies and human health effects.<br>Union Carbide Corporation, Specialty Chemicals Division, Danbury,<br>BPD ID A6.03.2_01<br>Non GLP, Published | No | Public |
| A6.03.3_01 | Ballantyne B, Greenspan BJ, Fowler EH, Snellings WM | 1985 | Subchronic inhalation toxicity of glutaraldehyde.<br>The Toxicologist 5: 29, Abstract 115,<br>BPD ID A6.03.3_01<br>Non GLP, Published | No | Public |
| A6.04.1_01 | [redacted] | 2001 | [redacted] Glutaraldehyde) - Subchronic oral toxicity and neurotoxicity study in [redacted] rats - Administration in drinking water for 3 months.<br>[redacted]<br>GLP, Unpublished | Yes | BASF |
| A6.04.1_02 | [redacted] | 1985 | Glutaraldehyde: ninety-day inclusion in drinking water of rats.<br>[redacted] | Yes | BASF<br>Dow |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
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| | | | [redacted] &<br>Addendum,<br>[redacted]<br>GLP, Unpublished | | |
| A6.04.2_01 | [redacted] | 2000 | 13-week toxicity study by cutaneous route in rats.<br>[redacted]<br>GLP, Unpublished | Yes | BASF |
| A6.04.3_01_a | Kari FW | 1993 | NTP technical report on toxicity studies of glutaraldehyde administered by inhalation to F344/N rats and B6C3F1 mice.<br>US Department of Health and Human Services, Public Health Service, National Institutes of Health NIH, Toxicity Report Series No: 25, NIH Publication No: 93-3348,<br>BPD ID A6.04.3_01_a<br>GLP, Published | No | Public |
| A6.05_01 | [redacted] | 2002 | [redacted] Glutaraldehyde) - Chronic toxicity study in Wistar rats - Administration in the drinking water for 12 months.<br>[redacted]<br>GLP, Unpublished | Yes | BASF |
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| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
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| A6.06.1_02 | Kari FW | 1993 | NTP technical report on toxicity studies of glutaraldehyde administered by inhalation to F344/N rats and B6C3F1 mice.<br>US Department of Health and Human Services, Public Health Service, National Institutes of Health NIH, Toxicity Report Series No: 25, NIH Publication No: 93-3348,<br>BPD ID A6.04.3_01_a<br>GLP, Published | No | Public |
| A6.06.2_01 | [redacted] | 2002 | In vitro chromosome aberration assay with [redacted] Glutaraldehyde).<br>GLP, Unpublished | Yes | BASF |
| A6.06.2_02 | Kari FW | 1993 | NTP technical report on toxicity studies of glutaraldehyde administered by inhalation to F344/N rats and B6C3F1 mice.<br>US Department of Health and Human Services, Public Health Service, National Institutes of Health NIH, Toxicity Report Series No: 25, NIH Publication No: 93-3348,<br>BPD ID A6.04.3_01_a<br>GLP, Published | No | Public |
| A6.06.3_01 | [redacted] | 1994 | AS52/XPRT Mammalian cell forward gene mutation assay on [redacted]<br>GLP, Unpublished | Yes | BASF |
| A6.06.3_02 | Kari FW | 1993 | NTP technical report on toxicity studies of glutaraldehyde administered by inhalation to F344/N rats and B6C3F1 mice.<br>US Department of Health and Human Services, Public Health Service, National Institutes of Health NIH, Toxicity Report Series No: 25, NIH Publication No: 93- | No | Public |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
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| | | | 3348,<br>BPD ID A6.04.3_01_a<br>GLP, Published | | |
| A6.06.4_01 | [redacted] | 1994 | In vivo micronucleus test with [redacted] in mouse bone marrow erythropoietic cells.<br>[redacted]<br>GLP, Unpublished | Yes | BASF |
| A6.06.5_01 | [redacted] | 2002 | In vivo unscheduled DNA synthesis (UDS) assay with [redacted] Glutaraldehyde) in rat hepatocytes - single oral administration.<br>[redacted]<br>GLP, Unpublished | Yes | BASF |
| A6.06.6_01 | Kari FW | 1993 | NTP technical report on toxicity studies of glutaraldehyde administered by inhalation to F344/N rats and B6C3F1 mice.<br>US Department of Health and Human Services, Public Health Service, National Institutes of Health NIH, Toxicity Report Series No: 25, NIH Publication No: 93-3348,<br>BPD ID A6.04.3_01_a<br>GLP, Published | No | Public |
| A6.07_01 | [redacted] | 2003 | [redacted] glutaradeldehyde) - Carcinogenicity study in [redacted] rats - Administration in the drinking water for 24 months.<br>[redacted]<br>GLP, Unpublished | Yes | BASF |
| A6.08.1_01 | [redacted] | 1991 | Study of the prenatal toxicity of glutaraldehyde in rabbits after oral administration (gavage).<br>[redacted]<br>GLP, Unpublished | Yes | BASF<br>Dow |
| A6.08.1_02 | [redacted] | 1987 | Report on the study of the prenatal toxicity of glutaraldehyde in rats after oral administration (drinking water). [redacted]<br>[redacted]<br>GLP, Unpublished | Yes | BASF<br>Dow |
| A6.08.1_03 | [redacted] | 1991a | Range-finding study of the prenatal | Yes | BASF |

| Section No / Reference No | Author(s) | Year | Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
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| | [redacted] | | toxicity of glutaraldehyde in rabbits after oral administration (drinking water). [redacted] GLP, Unpublished | | |
| A6.08.1_04 | [redacted] | 1991b | Range-finding study of the prenatal toxicity of glutaraldehyde in rabbits after oral administration (gavage). [redacted] GLP, Unpublished | Yes | BASF |
| A6.08.1_05 | [redacted] | 1991c | Range-finding study of the prenatal toxicity of glutaraldehyde in rats after oral administration (drinking water). [redacted] GLP, Unpublished | Yes | BASF |
| A6.08.1_06 | [redacted] | 1991d | Range-finding study of the prenatal toxicity of glutaraldehyde in rats after oral administration (gavage). [redacted] GLP, Unpublished | Yes | BASF |
| A6.08.2_01 | [redacted] | 2001 | [redacted] Glutaraldehyde) - Two-generation reproduction toxicity study in [redacted] rats - Continuous administration in the drinking water. [redacted] GLP, Unpublished | Yes | BASF |
| A6.09 _ 01 | [redacted] | 2001 | [redacted] Glutaraldehyde) - Subchronic oral toxicity and neurotoxicity study in [redacted] rats - Administration in drinking water for 3 months. [redacted] GLP, Unpublished | Yes | BASF |
| A6.11_01 | [redacted] | 1970 | [redacted] Ergebnis der Gewerbetoxikologischen Vorprüfung. [redacted] Non GLP, Unpublished | Yes | BASF |
| A6.11_02 | [redacted] | 1970 | [redacted] Ergebnis | Yes | BASF |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
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| | [redacted] | | der Gewerbetoxikologischen Vorpruefung.<br>[redacted]<br>Non GLP, Unpublished | | |
| A6.12.1_01 | [redacted] | 2007 | Monitoring of manufacturing plant personnel. [redacted]<br>Non GLP, Unpublished | Yes | BASF |
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| A6.12.2_08 | [redacted] | 2007 | Odor and chemesthesis from exposures to glutaraldehyde vapor. [redacted]<br>Non GLP, In press | No | Public |
| A6_12_4/01 | [redacted] | 2006 | Odor and Chemesthesis from Exposures to Glutaraldehyde Vapor.<br>[redacted] | Yes | Dow<br>BASF |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
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| A6.12.4_06 | Corrado OJ, | 1986 | Asthma and rhinitis after exposure to | No | Public |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
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| A6.12.4_09 | Norbaeck D | 1988 | Skin and respiratory symptoms from exposure to alkaline glutaraldehyde in medical services.<br>Scand. J. Work Environ. Health 14: 366-371,<br>BPD ID A6.12.4_09<br>Non GLP, Published | No | Public |
| A6.12.4_10 | Jachuck SJ, Bound CL, Steel J, Blain PG | 1989 | Occupational hazard in hospital staff exposed to 2 per cent glutaraldeyhde in an endoscopy unit.<br>J. Soc. Occup. Med. 39 69-71,<br>BPD ID A6.12.4_10<br>Non GLP, Published | No | Public |
| A6.12.4_11 | McDonald JC, Keynes HL, Meredith SK | 2000 | Reported incidence of occupational asthma in the United Kingdom, 1989-97. Occup. Environ. Med. 57: 823-829,<br>BPD ID A6.12.4_11<br>Non GLP, Published | No | Public |
| A6.12.5_01 | Anadol D, Özcelik U, Kiper N, Göcmen A | 2001 | Chemical pneumonia caused by glutaraldehyde. Pediatric International 43:701–702,<br>BPD ID A6.12.5_01<br>Non GLP, Published | No | Public |
| A6.12.5_02 | Murray WJ, Ruddy MP | 1985 | Toxic eye injury during induction of anesthesia. South. Med. J. 78: 1012-1013,<br>BPD ID A6.12.5_02<br>Non GLP, Published | No | Public |
| A6.12.5_03 | Ünal M, Yucel I,Akar Y, Oner A, Altin M | 2006 | Outbreak of toxic anterior segment syndrome associated with glutaraldehyde after cataract surgery. J Cataract Refract Surg. 32(10):1696-701,<br>BPD ID A6.12.5_03<br>Non GLP, Published | No | Public |
| A6.12.5_04 | Karpelowsky JS, Maske CP, Sinclair-Smith C, Rode H | 2006 | Glutaraldehyde-induced bowel injury after laparoscopy. J Pediatr Surg. 2006 Jun;41(6):e23-52,<br>BPD ID A6.12.5_04<br>Non GLP, Published | No | Public |
| A6.12.5_05 | Caprilli R, Viscido A, Frieri G, Latella G | 1998 | Acute colitis following colonscopy. Endoscopy 30: 428-431,<br>BPD ID A6.12.5_05<br>Non GLP, Published | No | Public |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| A6.12.5_06 | West AB, Kuan S-F, Bennick M, Lagarde S | 1995 | Gastroenterology 108: 1250-1255,<br>BPD ID A6.12.5_06<br>Non GLP, Published | No | Public |
| A6.12.6_01 | Reifenrath WG, Prystowsky SD, Nonomura JH, Robinson PB | 1985 | Topical glutaraldehyde-percutaneous penetration and skin irritation.<br>Arch. Dermatol. Res. 277: 242-244,<br>BPD ID A6.12.6_01<br>Non GLP, Published | No | Public |
| A6.12.6_02 | Ballantyne B, Berman B | 1984 | Dermal sensitizing potential of glutaraldehyde: a review and recent observations.<br>J. Toxicol. - Cut. & Ocular Toxicol. 3: 251-262,<br>BPD ID A6.12.6_02<br>Non GLP, Published | No | Public |
| A6.12.6_03 | Fowler JF | 1989 | Allergic contact dermatitis from glutaraldehyde exposure.<br>J. Occup. Med. 31: 852-853,<br>BPD ID A6.12.6_03<br>Non GLP, Published | No | Public |
| A6.12.6_04 | Shaffer MP, Belsito DV | 2000 | Allergic contact dermatitis from glutaraldehyde in health-care workers.<br>Contact Dermatitis 43: 150-156,<br>BPD ID A6.12.6_04<br>Non GLP, Published | No | Public |
| A6.12.6_05 | Kiec-Swierczynska M, Krecisz B | 2001 | Occupational allergic contact dermatitis in hairdressers due to glutaraldehyde. Contact Dermatitis 44: 185-186,<br>BPD ID A6.12.6_05<br>Non GLP, Published | No | Public |
| A6.12.6_06 | Juhlin L, Hansson H | 1968 | Topical glutaraldehyde for plantar hyperhydrosis.<br>Arch. Derm. 97: 327-330,<br>BPD ID A6.12.6_06<br>Non GLP, Published | No | Public |
| A6.12.7_01 | None | 2007 | PAN Pesticides Database – Chemicals<br>Non GLP, Published (online data) | No | Public |
| A6.12.8_01 | Anadol D, Özcelik U, Kiper N, Göcmen A | 2001 | Chemical pneumonia caused by glutaraldehyde. Pediatric International 43:701–702,<br>BPD ID A6.12.5_01<br>Non GLP, Published | No | Public |
| A6.12.8_02 | Ünal M, Yucel I,Akar Y, Oner A, Altin M | 2006 | Outbreak of toxic anterior segment syndrome associated with glutaraldehyde after cataract surgery. J Cataract Refract Surg. 32(10):1696-701,<br>BPD ID A6.12.5_03<br>Non GLP, Published | No | Public |
| A6.12.8_03 | Karpelowsky JS, Maske CP, Sinclair-Smith C, Rode H | 2006 | Glutaraldehyde-induced bowel injury after laparoscopy. J Pediatr Surg. 2006 Jun;41(6):e23-52,<br>BPD ID A6.12.5_04<br>Non GLP, Published | No | Public |
| A6.12.8_04 | Caprilli R, Viscido A, Frieri G, Latella G | 1998 | Acute colitis following colonscopy.<br>Endoscopy 30: 428-431,<br>BPD ID A6.12.5_05<br>Non GLP, Published | No | Public |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| A6.14_01 | [redacted] | 2006 | Glutaraldehyde release into the air during simulated manual processing of endoscopes.<br>[redacted]<br>Non GLP, Unpublished | Yes | BASF |
| A6.14_02 | [redacted] | 1994 | Measurement of glutaraldehyde concentrations in [redacted]<br>Non GLP, Unpublished | Yes | BASF |
| A6.14_03 | [redacted] | 1997 | Glutaraldehyde measurements at [redacted]<br>Non GLP, Unpublished | Yes | BASF |
| A6.14_04 | [redacted] | 2007 | Monitoring of laboratory personnel. [redacted]<br>Non GLP, Unpublished | Yes | BASF |
| A6.15.3_01_a | The Scientific Committee on Food of the European Commission, Health & Consumer Protection Directorate-General | 1999 | Opinion on an additional list of monomers and additives for food contact Annex VII to the minutes of the 119th Plenary meeting, 12 December 1999,<br>BPD ID A6.15.3_01_a<br>Non GLP, Published | No | Public |
| A6.15.3_01_b | The Codex Alimentarius Commission of the Food and Agriculture Organization of the United Nations, WHO | 2005 | Agenda Item 11(b), CX/RVDF 06/16/13 (Part 1), Report of the working group on residues of veterinary drugs without ADI/MRL,<br>BPD ID A6.15.3_01_b<br>Non GLP, Published | No | Public |
| A6.15.3_01_c | The European Medicines Agency | 2007 | Veterinary Medicines and Inspections, Status if MRL procedures, MRL assessments in the context of Council Regulation (EEC) No 2377/90, 21 March 2007,<br>BPD ID A6.15.3_01_c<br>Non GLP, Published | No | Public |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| A7.1.1.1.1_01 | [redacted] | 1991 | Hydrolysis of 14 C-Glutaraldehyde in aqueous solutions buffered at pH 5, 7 and 9.<br>[redacted] | Yes | BASF |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| | | | GLP, Unpublished | | |
| A7.1.1.2.1_01 | [redacted] | 1993 | Determination of the Biodegradability or the Elimination of [redacted] in the DOC Die Away (ISO 7827)-Test. [redacted]<br>GLP, Unpublished | Yes | BASF |
| A7.1.1.2.3_01 | [redacted] | 2002 | [redacted] Glutaraldehyde), Determination of the Biodegradability in the marine CO2-Evolution Test. [redacted]<br>GLP, Unpublished | Yes | BASF |
| A7.1.2.1.1_01 | [redacted] | 1998 | Determination of the Biodegradability of [redacted] in the Activated Sludge Simulation Test according to GLP, EN 45001 and ISO 9002.<br>GLP, Unpublished | Yes | BASF |
| A7.1.2.2.2_01 | [redacted] | 1994 | Aerobic Aquatic Metabolism of [$^{14}$C]-Glutaraldehyde in River Water and Sediment.<br>GLP, Unpublished | Yes | Dow<br>BASF |
| A7.1.2.2.2_02 | [redacted] | 1994 | Anaerobic Aquatic Metabolism of [$^{14}$C] – Glutaraldehyde.<br>GLP, Unpublished | Yes | Dow<br>BASF |
| A7.1.3_02 | [redacted] | 2001 | Determination of the Adsorption of Glutaraldehyde to Activated Sludge Using the ISO/CD 18749 Batch [redacted]<br>GLP, Unpublished | Yes | Dow<br>BASF |
| A7.2.3.1_01 | [redacted] | 1994 | Soil Adsorption/Desorption of [$^{14}$C] Glutaraldehyde by the Batch Equilibrium Method.<br>GLP, Unpublished | Yes | Dow<br>BASF |
| A7.3.1_01 | [redacted] | 2005 | Glutaraldehyde, SRC calculations. [redacted]<br>Non GLP, Unpublished | No | BASF |
| A7.4.1.1_01 | [redacted] | 1981 | Acute toxicity of Glutaraldehyde [redacted] to | Yes | BASF |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| | | | Rainbow trout (Salmo gairdneri).<br>[redacted]<br>Non GLP, Unpublished | | |
| A7.4.1.1_02 | [redacted] | 1981 | Acute toxicity of Glutaraldehyde [redacted] to Bluegill (Lepomis macrochirus).<br>[redacted]<br>Non GLP, Unpublished | Yes | BASF |
| A7.4.1.1_03 | [redacted] | 1981 | Acute toxicity of Glutaraldehyde to Sheepshead minnows (Cyprinodon variegatus).<br>[redacted]<br>Non GLP, Unpublished | Yes | BASF |
| A7.4.1.2_01 | [redacted] | 1988 | Determination of the acute toxicity of Glutardialdehyd [redacted] to the waterflea Daphnia magna [redacted]<br>[redacted]<br>Non GLP, Unpublished | Yes | BASF |
| A7.4.1.2_02 | [redacted] | 1981 | Acute toxicity of Glutaraldehyde [redacted] to the Water Flea (Daphnia magna).<br>[redacted]<br>Non GLP, Unpublished | Yes | BASF |
| A7.4.1.2_04 | [redacted] | 1995 | Glutaraldehyde - Acute toxicity to Mysids ([redacted]) under flow-through conditions.<br>[redacted]<br>GLP, Unpublished | Yes | BASF |
| A7.4.1.2._05 | [redacted] | 1993 | Glutaraldehyde - Acute Toxicity to Eastern Oysters ([redacted] Under Flow-Through Conditions.<br>[redacted]<br>GLP, Unpublished | Yes | Dow<br>BASF |
| A7.4.1.2_06 | [redacted] | 1997 | [redacted] Acute Toxicity to *Acartia Tonsa*.<br>[redacted]<br>GLP, Unpublished | Yes | Dow<br>BASF |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| A7.4.1.2_07 | [redacted] | 2013 | Acute toxicity of [redacted] to the marine species *Acartia tonsa.*<br>[redacted]<br>GLP, Unpublished | Yes | BASF<br>Dow |
| A7.4.1.2_08 | [redacted] | 2013 | Assessment of the toxicity (48h LC50) of [redacted] the marine copepod *Acartia tonsa.*<br>[redacted]<br>GLP, Unpublished | Yes | BASF<br>Dow |
| A7.4.1.3_01 | [redacted] | 1997 | Determination of the inhibitory effect of [redacted] on cell multiplication of unicellular green algae.<br>[redacted]<br>Non GLP, Unpublished | Yes | BASF |
| A7.4.1.3_02 | [redacted] | 1993 | Algal growth inhibition test.<br>[redacted] translation of a German report dated 1988),<br>[redacted]<br>Non GLP, Unpublished | Yes | BASF |
| A7.4.1.4_01 | [redacted] | 1998 | Determination of the inhibition of Oxygen Consumption by activated Sludge by [redacted] in the Respiration Inhibition Test.<br>[redacted]<br>GLP, Unpublished | Yes | BASF |
| A7.4.3.2_01 | [redacted] | 2000 | [redacted] Glutaraldehyde) - Early Life-Stage toxicity test on the Rainbow trout (Oncorhynchus mykiss).<br>[redacted]<br>GLP, Unpublished | Yes | BASF |
| A7.4.3.4_01 | [redacted] | 1993 | Determination of the chronic toxicity of [redacted] to Daphnia magna. [redacted]<br>[redacted]<br>GLP, Unpublished | Yes | BASF |
| A7.5.1.1_01 | [redacted] | 2006 | [redacted] Determination of the carbon transformation by the glucose induced soil respiration (Carbon Transformation Test).<br>[redacted] | Yes | BASF<br>Dow |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| | | | [redacted]<br>GLP, Unpublished | | |
| A7.5.1.1_02 | [redacted] | 2006 | [redacted], Determination of the nitrate production in soil (Nitrogen Transformation Test).<br>[redacted]<br>GLP, Unpublished | Yes | BASF<br>Dow |
| A7.5.1.2_01 | [redacted] | 2002 | [redacted] Glutaraldehyde)<br>Determination of the acute letal effect of chemicals on the earthworm [redacted]<br>[redacted]<br>GLP, Unpublished | Yes | BASF<br>Dow |
| A7.5.1.3._02 | [redacted] | 2010 | [redacted] Determination of the effect of chemicals on the emergence and growth of higher plants. [redacted]<br>[redacted]<br>GLP, Unpublished | Yes | BASF<br>Dow |

## Appendix V: List of Studies of Dow

Data protection is claimed by the applicant in accordance with Article 60 of Regulation (EU) No 528/2012.

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| A2_6 | [redacted] | 2003 | [redacted]<br>Manufacturing Description.<br>The Dow Chemical Company<br>Unpublished | Yes | Dow |
| A3_1_1 | [redacted] | 2000a | Freezing Point/Melting Point of [redacted]<br>GLP, Unpublished | Yes | Dow |
| A3_1_2 | [redacted] | 2000b | Boiling Point of [redacted]<br>GLP, Unpublished | Yes | Dow |
| A3_1_3 | [redacted] | 2000c | Density of [redacted]<br>GLP, Unpublished | Yes | Dow |
| A3_2 | [redacted] | 2006 | A Critical Evaluation of Vapor Pressure Measurements for Aqueous Glutaraldehyde Formulations.<br>[redacted]<br>Non GLP, Unpublished | Yes | Dow |
| A3_2 | Olson J.D. | 1998 | The vapor pressure of pure and aqueous glutaraldehyde.<br>Fluid Phase Equilibria<br>Vol. 150-151, p 713-720 | No | Public Domain |
| A3_3 | [redacted] | 2007 | Determination of pH, odour, colour, physical state and acidity of Glutaraldehyde.<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A3_4_1 | [redacted] | 2000 | Ultra Violet/Visible (UV/vis) Spectrometry of [redacted] Glutaraldehyde.<br>[redacted]<br>Non GLP, Unpublished | Yes | Dow |
| A3_4_2 | [redacted] | 2000 | Fourier Transform Infrared Spectrometry (FT-IR) of [redacted] Glutaraldehyde.<br>[redacted]<br>Non GLP, Unpublished | Yes | Dow |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| A3_4_3 | [redacted] | 1999 | [redacted]<br>Analytical Characterization.<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A3_4_4 | [redacted] | 1999 | [redacted]<br>Analytical Characterization.<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A3_5 | [redacted] | 1994 | [redacted]<br>Determination of the Solubility in Water and Selected Solvents.<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A3_7 | [redacted] | 1994 | [redacted]<br>Determination of the Solubility in Water and Selected Solvents.<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A3_9 | [redacted] | 1996 | Partition Coefficient (n-Octanol/Deionized Water) of [$^{14}$C]Glutaraldehyde.<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A3_10 | [redacted] | 1994 | Stability of Glutaraldehyde.<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A3_11 | [redacted] | 1989 | End-Use Product Chemistry:<br>[redacted]<br>Non GLP, Unpublished | Yes | Dow |
| A3_12 | [redacted] | 2009 | Flash Point of [redacted]<br>[redacted]<br>Non GLP, Unpublished | Yes | Dow |
| A3_13 | [redacted] | 2000 | Surface Tension of [redacted]<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A3_14 | [redacted] | 2000 | Viscosity of [redacted]<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A3_15 | [redacted] | 1989 | End-Use Product Chemistry:<br>[redacted] | Yes | Dow |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| | | | [redacted]<br>Non GLP, Unpublished | | |
| A3_16 | [redacted] | 1989 | End-Use Product Chemistry:<br>[redacted]<br>Non GLP, Unpublished | Yes | Dow |
| A3_17 | [redacted] | 2000 | Shipping and Storage Compatibility for [redacted] Glutaraldehyde.<br>[redacted]<br>Non GLP, Unpublished | Yes | Dow |
| A4_1/01 | [redacted] | 2001 | Development and Validation of an Analytical Method for Glutaraldehyde<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A4_1/02 | [redacted] | 2005 | Five Batch Analysis of [redacted]<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A4_1/03 | [redacted] | 2010 | Glutaraldehyde Concentration by Potentiometric Hydroxylamine Hydrochloride Titration.<br>[redacted]<br>Non GLP, unpublished | Yes | Dow |
| A4_1/04 | [redacted] | 2007 | Methanol in Glutaraldehyde.<br>[redacted]<br>Non GLP, unpublished | Yes | Dow |
| A4_2 (a) | [redacted] | 2008 | Glutaraldehyde: Development and Validation of an Analytical Method for the Determination of Glutaraldehyde in Soil.<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A4_2 (b) | OSHA | 1987, additional data 1998 | US Department of Labour, Occupational Safety and Health Administration (OSHA) Method 64 (Glutaraldehyde in Air), OSHA Analytical Methods Manual, 1987, Additional data 1998. | No | US Department of Labour, Occupational Safety and Health Administration |
| A4_2 (c)(1) | [redacted] | 2008 | Glutaraldehyde: Development and Validation of an Analytical Method for | Yes | Dow |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| | | | the Determination of Glutaraldehyde in Water.<br>[redacted]<br>GLP, Unpublished | | |
| A4_2(d) | [redacted] | 2004 | Glutaraldehyde: Pharmacokinetics in [redacted] Rats Following Oral Gavage or Dermal Application.<br>[redacted]<br>GLP, Unpublished | Yes | Dow BASF |
| A5_4 | Eager R.G.Jr, Leder J. and Theis A.B. | 1986 | Glutaraldehyde: Factors Important for Microbiocidal Efficacy.<br>Presentation at the Third Conference on Progress in Chemical Disinfection, Binghamton, NY, April 3-5, 1986.<br>Union Carbide Corporation, a fully-owned subsidiary of The Dow Chemical Company | No | Public Domain |
| A5_7/01 | Griffiths P.A., Babb J.R., Bradley C.R. and Fraise A.P. | 1997 | Glutaraldehyde-resistant *Mycobacterium chelonae* from endoscope washer disinfectors.<br>Journal of Applied Microbiology 82(4): 519-526. | No | Public Domain |
| A5_7/02 | Duarte R.S., Lourenço M.C.S., de Souza Fonseca L., Cardoso Leao S., de Lourdes E., Amorin T., Rocha I.L.L., Santana Coelho F., Viana-Niero C., Machado Gomes K., Gomes da Silva M., de Oliveira Lorena N.S., Bettini Bitombo M. Ferreira, R.M.C., de Oliveira Garcia M.H., Pinto de Oliveira G., Lupi O., Rios Vilaça B., Rodriques Serradas L., Chebabo A., Andrade Marques E., Martins Teixeira L. Dalcolmo M., Conçalves Senna S. and Mello Sampaio J.L. | 2009 | Epidemic of Postsurgical Infections Caused by *Mycobacterium massiliense*.<br>Journal of Clinical Microbiology 47(7): 2149-2155. | No | Public Domain |
| A5_7/03 | Gregory A.W., Schaalje G.B., Smart J.D. and Robison R.A. | 1999 | The Mycobactericidal Efficacy of Ortho-Phthalaldehyde and the Comparative Resistances of *Mycobacterium bovis*, *Mycobacterium terrae*, and *Mycobacterium chelonae*. | No | Public Domain |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| | | | Infection Control and Hospital Epidemiology<br>20(5): 324-330 | | |
| A5_7/04 | [redacted] | 2001 | Bacterial resistance to glutaraldehyde: is it a problem?<br>[redacted]<br>Non GLP , Unpublished | Yes | Dow |
| A6_1_1 | [redacted] | 1992 | [redacted]: Acute Peroral Toxicity Study in the Rat.<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A6_1_2 | [redacted] | 1981 | Glutaraldehyde Dilutions: Percutaneous Toxicity and Eye Irritation Studies.<br>[redacted]<br>Non GLP, Unpublished | Yes | Dow |
| A6_1_3/01 | [redacted] | 1982 | Glutaraldehyde: Four-Hour LC50 Inhalation Study on Rats.<br>[redacted]<br>Non GLP, Unpublished | Yes | Dow |
| A6_1_3/02 | [redacted] | 1994 | Acute inhalation toxicity LC50 4 hours (rat) of "glutaraldehyde [redacted]", liquid aerosol study ([redacted]).<br>[redacted] (original report in German dated 1982) | Yes | BASF<br>Dow |
| | [redacted] | 2012 | Addendum: [redacted] - Technical trial without animals.<br>[redacted]<br>Non GLP, Unpublished | Yes | BASF<br>Dow |
| A6_1_3/03 | [redacted] | 1995 | Glutaraldehyde: Acute Vapor Inhalation Toxicity Study in Rats.<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A6_1_4 (e) | [redacted] | 1987a | [redacted]:<br>Primary Eye Irritancy Study in the Rabbit.<br>[redacted] | Yes | Dow |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| | | | GLP, Unpublished | | |
| A6_1_4 (s) | [redacted] | 1988 | [redacted] Aqueous Glutaraldehyde Samples ([redacted]): Primary Dermal Irritancy Studies in the Rabbit.<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A6_1_5/01 | [redacted] | 1993 | Guinea Pig Maximisation Test with Glutaraldehyde (Method of Magnusson and Kligman).<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A6_1_5/02 | [redacted] | 1994 | Mouse Lymph Node Assay and Mouse IgE Test on Glutaraldehyde.<br>[redacted]<br>Non GLP, Unpublished | Yes | Dow |
| A6_2/01 | [redacted] | 2004 | $^{14}$C-GDA- Study of the Biokinetics in Rats.<br>[redacted]<br>GLP, Unpublished | Yes | Dow<br>BASF |
| A6_2/02 | [redacted] | 2004 | Glutaraldehyde: Pharmacokinetics in [redacted] Rats Following Oral Gavage or Dermal Application.<br>[redacted]<br>GLP, Unpublished | Yes | Dow<br>BASF |
| A6_2/03 | [redacted] | 2007 | Glutaraldehyde: Pharmacokinetics of Drinking Water Administered Glutaraldehyde In [redacted] Rats.<br>[redacted]<br>GLP, Unpublished | Yes | Dow<br>BASF |
| A6_2/04 | [redacted] | 1991 | Glutaraldehyde: Species Comparisons of *In Vitro* Skin Penetration Following a Single Application to the [redacted] Rats, [redacted] Mice, [redacted] Guinea Pigs, and [redacted] Rabbits.<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A6_2/05(a) | [redacted] | 2007 | Glutaraldehyde: Identification of Metabolites in the [redacted] Rat.<br>[redacted] | Yes | Dow<br>BASF |

| Section No / Reference No | Author(s) | Year | Title.<br>Source (where different from company)<br>Company, Report No.<br>GLP (where relevant) / (Un)Published | Data Protection Claimed (Yes/No) | Owner |
|---|---|---|---|---|---|
| | | | [redacted]<br>GLP, Unpublished | | |
| A6_2/05(b) | Migneault I., Dartiguenave C., Bertrand M. J. and Waldron K. C. | 2004 | Glutaraldehyde: behaviour in aqueous solution, reaction with proteins and application to enzyme crosslinking.<br>Biotechniques<br>37(5) 790-802 | No | Public domain |
| A6_2/06 | [redacted] | 1985 | Skin Penetration and Pharmacokinetics of Glutaraldehyde in Rats and Rabbits.<br>[redacted]<br>GLP, Unpublished | Yes | Dow |
| A6_2/07(a) | Reifenrath W.G., Prystowsky S.D., Nonomura J.H., Robinson P.B. | 1985 | Topical Glutaraldehyde-Percutaneous Penetration and Skin Irritation.<br>Archives of Dermatological Research<br>(1985) 277:242-244 | No | Public domain |
| A6_2/07(b) | Schechter I. | 1971 | Prolonged Survival of Glutaraldehyde-Treated Skin Homografts.<br>Proc. Nat. Acad. Sci. USA<br>68(7) 1590-1593 | No | Public domain |
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| A7_5_1_2 | [redacted] | 2002 | [redacted] Glutaraldehyde), Determination of the acute letal effect of chemicals on the earthworm [redacted]<br>[redacted]<br>GLP, Unpublished | Yes | BASF Dow |
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