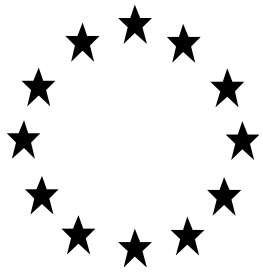
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



Propan-2-ol

Product-type 1
(Human hygiene biocidal products)

13 January 2015

Germany

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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 propan-2-ol as product-type 1 (Human hygiene), 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.

Propan-2-ol (CAS no. 67-63-0) was notified as an existing active substance, by Task Force "2-Propanol", hereafter referred to as the applicant, in product-type 1.

The Task Force "2-Propanol" consists of:
Bode Chemie GmbH
B. Braun Melsungen AG
Ecolab GmbH & Co. OHG
Lysoform Dr. Hans Rosemann GmbH
Schuelke & Mayr GmbH

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, Germany 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 propan-2-ol as an active substance in Product Type 1 was 31.07.2007, in accordance with Annex V of Regulation (EC) No 1451/2007.

On 31.07.2007, German competent authorities received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 29.01.2008.

On 05.11.2012, the Rapporteur Member State submitted to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report.

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 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 propan-2-ol for product-type 1, and, it should 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.

[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

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

Identity, Physico-chemical Properties and Method of Analysis of propan-2-ol

Propan-2-ol is a colourless liquid and has an initial diluted odour. It is indefinitely miscible with water (1000 g/L at 25°C) and miscible with many organic liquids, such as acetone, alcohol and ether. Propan-2-ol has a relatively high vapour pressure of 5780 Pa at 25°C. With its measured Henry's law constant of 0.80 Pa • m^3/mol at 25°C, the substance volatilizes from aqueous solutions under environmental conditions. Furthermore, propan-2-ol has a low log P_{OW} from 0.05 and no surface tension properties (70.7 mN/m; c = 1g/L; T = 22°C). An influence of the pH value to water solubility, Henry´s law constant and log P_{OW} is not expected.

For the detection a glass capillary gas chromatography method coupled with FID was developed.

Identity, Physico-chemical Properties and Method of Analysis of model formulation

The Task Force indicates only information of a dummy product. The dummy product is a model formulation and consists of the active substance and water. No further information about the Physico-chemical Properties and Method of Analysis are submitted, the Task Force refers to the active substance, which is acceptable in the frame of active substance approval but not for product authorisation.

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) bacteria including mycobacteria but excluding bacterial spores, fungi (yeast and moulds) and viruses 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 performed tests provide reliable results for efficacy assessment. The following study results can be used as information showing the basic efficacy of propan-2-ol against relevant target organisms, but are not suitable to prove the efficacy of a hand disinfectant in the field of use:

- Effectiveness of 70 % propan-2-ol against *Pseudomonas aeruginosa* and *Staphylococcus aureus* as well as *Escherichia coli* and *Enterococcus hirae* as representatives for gram negative and gram positive facultative pathogenic bacteria in the intended area of use of the product (PT 2: disinfectants for private and public health areas) was demonstrated (viability reduction >=10^5).

- Effectiveness of propan-2-ol in concentrations between 30 and 50 % against 3 gram positive (*S. aureus*, *E. faecium*, *M. terrae*), 2 gram negative bacterial species (*P. aeruginosa*, *P. mirabilis*) and one fungus (*C. albicans*) as representatives for gram negative, gram positive facultative pathogenic bacteria and fungi in the intended area of use was demonstrated (viability reduction >=10^5). For the fungus *Aspergillus niger*, a sufficient effectiveness of the substance according to the guideline could not be shown (viability reduction = 10E3.2 in 5 minutes using 80 % propan-2-ol).

- 70 % propan-2-ol fulfilled the efficacy criteria as required by the guideline EN 1650 against *Candida albicans* as a representative for yeasts and *Aspergillus niger* as a representative for a mould. A sufficient fungicidal activity of 70 % propan-2-ol could be shown (viability reduction >=10^4 in 15 minutes).

- Propan-2-ol at a concentration of 60 % or 70 % was effective against the virus *Herpes simplex* (log10 reduction value of at least 4) and at a concentration of 50 % and 70 % against the *feline calicivirus* (log10 reduction value of > 4). A general virucidal activity of propan-2-ol can not be deduced from the studies. In order to obtain the general label claim "virucidal", at least the non enveloped viruses, poliovirus and adenovirus, have to be tested.

The efficacy studies performed are regarded as sufficient at the active substance approval stage, even though the studies performed are not suitable to demonstrate the complete label claim bactericidal, fungicidal and virucidal. Additionally, propan-2-ol is generally known as an effective disinfectant, which implies the effectiveness of the substance in this field of use. Within the frame of product authorisation, essentially more efficacy data have to be provided: To support the full label claim virucidal, bactericidal and fungicidal, further laboratory tests would be necessary, this especially belongs to the label claim "virucidal". Additionally, further tests in the field of use have to be provided. At least the tests listed in EN 14885 for the respective field of use or comparable tests have to be provided in the frame of product authorisation. As not for all possible label claims an EN norm exists, further test will then be necessary depending on the specific label claim.

Mode of action
Propan-2-ol exhibits an unspecific mechanism of effect. It affects the cell membrane causing alteration of membrane fluidity and leakage, enters the cytoplasm and destroys the inner structure of the cell molecules and of the cytoplasm's proteins. It similarly interacts with corresponding viral structures. This process (referred to as denaturation) and the enzymes' coagulation leads to a loss of cellular activity resulting in the cell's death.

Occurrence of resistance
Due to the unspecific mode of action of 2-propanol, the development of resistance is not expected and not reported. A natural resistance against sporulated bacteria is known where 2-propanol is ineffective at any concentration. Likewise, 2-propanol is more effective against enveloped viruses compared to non-enveloped viruses. This is mainly due to the second layer of the enveloped viruses, which can be easily destroyed by alcoholic solutions leading to inactivation of the virus. The non-enveloped viruses have one protein-layer (capsid), which shows a pronounced natural resistance against chemical and physical disinfection methods.

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

Propan-2-ol (CAS-No. 67-63-0) is in Annex VI of Regulation (EC) No 1272/2008 (former Annex I of Directive 67/548/EEC) and its classification and labelling is as follows:

Table 2-1 Current classification of propan-2-ol based on Directive 67/548/EEC

	Classification	Wording
Hazard Symbols, Indications of danger	F Xi	Highly flammable Irritant
R-phrases	R11 R36 R67	Highly flammable Irritating to eyes Vapours may cause drowsiness and dizziness

Remark:
The content of this table is based on table 3.2 of Annex VI of Regulation (EC) No 1272/2008.

Table 2-2 Current classification of propan-2-ol based on Regulation (EC) No 1272/2008

	Classification	Wording
Hazard classes, Hazard categories	Flam. Liq. 2 Eye Irrit. 2 STOT SE 3	
Hazard statements	H225 H319 H336	Highly flammable liquid and vapour Causes serious eye irritation May cause drowsiness or dizziness

Remark:
The content of this table is based on table 3.1 of Annex VI of Regulation (EC) No 1272/2008.

Table 2-3 Current labelling of propan-2-ol based on Directive 67/548/EEC

	Labelling	Wording
Hazard Symbols, Indications of danger	F Xi	Highly flammable Irritant
R-phrases	R11 R36 R67	Highly flammable Irritating to eyes Vapours may cause drowsiness and dizziness
S-phrases	(S2) S7 S16 S24/25 S26	Keep out of the reach of children Keep container tightly closed Keep away from sources of ignition - No smoking Avoid contact with skin and eyes In case of contact with eyes, rinse immediately with plenty of water and seek medical advice

Remark:
The content of this table is based on table 3.2 of Annex VI of Regulation (EC) No 1272/2008.

Table 2-4 Current labelling of propan-2-ol based on Regulation (EC) No 1272/2008

	Labelling	Wording
Pictograms	GHS02 GHS07	
Signal Word	Danger	
Hazard statements	H225 H319 H336	Highly flammable liquid and vapour Causes serious eye irritation May cause drowsiness or dizziness
Precautionary statements		

Remark:
The content of this table is based on table 3.1 of Annex VI of Regulation (EC) No 1272/2008. In accordance with the entry there, Precautionary statements are not listed here either.

Table 2-5 Proposed classification of propan-2-ol based on Directive 67/548/EEC

	Classification	Wording
Hazard symbols, Indication of danger	F Xi	Highly flammable Irritant
R phrases	R11 R36 R66 R67	Highly flammable Irritating to eyes Repeated exposure may cause skin dryness or cracking Vapours may cause drowsiness and dizziness

Remark:
In addition to current classification/labelling, R66 is proposed, based on local skin effects and reactions that have been described for human individuals exposed to formulations containing propan-2-ol or to propan-2-ol dilutions.

Table 2-6 Proposed classification of propan-2-ol based on Regulation (EC) No 1272/2008

	Classification	Wording
Hazard classes, Hazard categories	Flam. Liq. 2 Eye Irrit. 2 STOT SE 3	
Hazard statements	H225 H319 H336 EUH066	Highly flammable liquid and vapour Causes serious eye irritation May cause drowsiness or dizziness Repeated exposure may cause skin dryness or cracking

Remark:
In addition to current classification/labelling, EUH066 is proposed, based on local skin effects and reactions that have been described for human individuals exposed to formulations containing propan-2-ol or to propan-2-ol dilutions.

Table 2-7 Proposed labelling of propan-2-ol based on Directive 67/548/EEC

	Labelling	Wording
Hazard Symbols, Indications of danger	F Xi	Highly flammable Irritant
R-phrases	R11 R36 R66 R67	Highly flammable Irritating to eyes Repeated exposure may cause skin dryness or cracking Vapours may cause drowsiness and dizziness
S-phrases	(S2) S7 S16 S24/25 S26	Keep out of the reach of children Keep container tightly closed Keep away from sources of ignition - No smoking Avoid contact with skin and eyes In case of contact with eyes, rinse immediately with plenty of water and seek medical advice

Remark:
Current labelling is based on table 3.2 of Annex VI of Regulation (EC) No 1272/2008. In addition to current labelling according to table 3.2 of Annex VI of Regulation (EC) No 1272/2008, R66 (Repeated exposure may cause skin dryness or cracking) is proposed by the RMS, based on local skin effects and reactions that have been described for human individuals exposed to formulations containing propan-2-ol or to propan-2-ol dilutions.

Table 2-8 Proposed labelling of propan-2-ol based on Regulation (EC) No 1272/2008

	Labelling	Wording
Pictograms	GHS02 GHS07	
Signal Word	Danger	
Hazard statements	H225 H319 H336 EUH066	Highly flammable liquid and vapour Causes serious eye irritation May cause drowsiness or dizziness Repeated exposure may cause skin dryness or cracking
Precautionary statements		

Remark:
Current labeling is based on table 3.1 of Annex VI of Regulation (EC) No 1272/2008. In accordance with the entry there Precautionary statements are not listed here either. In addition to current labelling according to table 3.1 of Annex VI of Regulation (EC) No 1272/2008, EUH066 (Repeated exposure may cause skin dryness or cracking) is proposed by the RMS, based on local skin effects and reactions that have been described for human individuals exposed to formulations containing propan-2-ol or to propan-2-ol dilutions.

Classification and Labelling of model formulation

As the biocidal product contains 70 % propan-2-ol it is suggested to classify and label it in almost the same way as the active substance.

Table 2-9 Proposed classification of model formulation based on Directive 1999/45/EC

	Classification	Wording
Hazard Symbols, Indications of danger	F Xi	Highly flammable Irritant
R-phrases	R11 R36 R66 R67	Highly flammable Irritating to eyes Repeated exposure may cause skin dryness or cracking Vapours may cause drowsiness and dizziness

Remark:
No environmental classification of the model formulation is required.

Table 2-10 Proposed classification of model formulation based on Regulation (EC) No 1272/2008

	Classification	Wording
Hazard classes, Hazard categories	Flam. Liq. 2 Eye Irrit. 2 STOT SE 3	Flammable liquids, Hazard Category 2
Hazard statements	H225 H319 H336 EUH066	Highly flammable liquid and vapour Causes serious eye irritation May cause drowsiness or dizziness Repeated exposure may cause skin dryness or cracking

Remark:
No environmental classification of the model formulation is required.

Table 2-11 Proposed labelling of model formulation__based on Directive 1999/45/EC

	Labelling	Wording
Hazard Symbols, Indications of danger	F Xi	Highly flammable Irritant
R-phrases	R11 R36 R66 R67	Highly flammable Irritating to eyes Repeated exposure may cause skin dryness or cracking Vapours may cause drowsiness and dizziness
S-phrases	(S2) S7 S16 S25 S26	Keep out of the reach of children Keep container tightly closed Keep away from sources of ignition - No smoking Avoid contact with eyes In case of contact with eyes, rinse immediately with plenty of water and seek medical advice

Remark:
The S-phrase 24 has been omitted because the biocidal product is used as a hand disinfectant.
No labelling according to environmental classification of the model formulation is required.

Table 2-12 Proposed labelling of model formulation based on Regulation (EC) No 1272/2008

	Labelling	Wording
Pictograms	GHS02 GHS07	
Signal Word	Danger	
Hazard statements	H225 H319 H336 EUH066	Highly flammable liquid and vapour Causes serious eye irritation May cause drowsiness or dizziness Repeated exposure may cause skin dryness or cracking
Precautionary statements	(P102) P210 P241 P243 P271 P304 + P340 P305 + P351 + P338 P337 + P313 P312 P403 + P233 P501	Keep out of reach of children Keep away from heat/sparks/open flames/hot surfaces. - No smoking Use explosion-proof electrical/ ventilating/ lighting/ …/equipment Take precautionary measures against static discharge Use only outdoors or in a well-ventilated area IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing If eye irritation persists: Get medical advice/ attention Call a POISON CENTER or doctor/physician if you feel unwell Store in a well-ventilated place. Keep container tightly closed Dispose of contents/container to …

Remark:

No labelling according to environmental classification of the model formulation is required. Based on the given hazard statements the number of the precautionary statements recommended in Annex I of the Regulation (EC) No 1272/2008 is quite big and could only partly be reduced , so to lose no essential information. The precautionary statement 280 has been omitted because the biocidal product is used as a hand disinfectant.

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1. Effects assessment

Absorption, Distribution, Excretion, and Metabolism

Oral absorption

In a toxicokinetics study with rats, animals received a mix of 2-^{14}C- and unlabelled propan-2-ol via oral gavage at 300 or 3000 mg/kg bw, and elimination of radiolabelled compounds was examined (Slauter et al. 1994). For the administered doses of 300 or 3000 mg/kg bw, a total of 88 and 94 % of the radioactivity, respectively, was found to be excreted within 72 hours, the major proportion being exhaled. The portion recovered with the faeces was below 1 % for both doses, supporting the conclusion that propan-2-ol is readily absorbed after oral exposure, and that near to 100 % absorption can be assumed.

Percutaneous absorption

In a well-documented study by Boatman et al. 1998, in vivo dermal absorption rates for male and female rats were investigated under occlusive conditions, using 70 % (w/w) propan-2-ol in aqueous solution, with 2-^{14}C-propan-2-ol as a tracer. Notably, deviations from OECD guideline conditions included shorter exposure duration (4 vs. at least 6 h) and a smaller area of application (4.3 vs. the recommended 10 cm²). Propan-2-ol levels in blood were shown to increase linearly within the 4 hours of dermal exposure without reaching a plateau. Total recovery of radioactivity within 48 h amounted to about 92 % of the applied dose. Based on recovered absorbed ^{14}C in relation to total recovery, the percutaneously absorbed portion of applied dose was calculated as amounting to about 7 % in 4 h for an application area of 4.3 cm². Assuming a linear relationship of absorption with the area of application and the duration of exposure, this corresponds to an absorption rate of about 0.85 mg/cm²/h or ca. 0.4 %/cm²/h. As a plateau in propan-2-ol blood levels had not been reached within 4 h of exposure, substance uptake appeared to not yet be at equilibrium with elimination.

Dermal absorption of propan-2-ol under non-occlusive conditions was also tested in human volunteers after repeated use of commercial hand rubs under different application regimens (Peschel et al. 1992; Turner et al. 2004; Bieber et al. 2006). In all of these three studies with humans, higher blood levels of propan-2-ol were detected as a result of exposure. The absorbed portion attributable to the recovered parent compound alone is estimated as roughly 0.2 % (Turner et al. 2004), 1.2 % (Bieber 2006) or 3.5 % (Peschel et al. 1992) of the applied dose. In the studies by Peschel et al. and Turner et al., propan-2-ol metabolites were not determined. In the study by Bieber 2006, acetone blood levels were followed, giving rise to AUC values for acetone that amounted to between roughly 40 and 70 % of the AUC values for propan-2-ol. The sum of absorbed propan-2-ol and acetone accounted for by the AUCs indicates propan-2-ol absorption of at least 2 %.

For none of the aforementioned three studies performed in human volunteers, a complete mass balance is available, since the rapid elimination of absorbed propan-2-ol, e.g. the portions converted to acetone or other metabolites, or eliminated by exhaled air were not or only partially taken into account. On the other hand, since the human studies were conducted under non-occlusive conditions, uptake via the inhalative in addition to the dermal route should be considered, although it is difficult to discern to which extent inhalation of vapours contributed to substance absorption. In a more recent dermal

absorption study (Kirschner et al., 2009) with male human volunteers, care was taken to minimise inhalative absorption by application of propan-2-ol-containing test solutions to skin areas of the back using a 200-cm² gauze swab. Each treatment was conducted with a total of 20 ml of either an aqueous solution containing 10 % propan-2-ol or a disinfectant containing 74.1 % ethanol and 10 % propan-2-ol (w/w), involving a total skin contact time of 10 minutes. Blood samples were collected before application (time 0), and subsequently, 15 and 60 minutes after commencement of application. Serum analysis for propan-2-ol and acetone revealed that propan-2-ol levels were below the limit of detection at all time points and that acetone levels were not significantly increased after substance application. These results were irrespective of whether aqueous propan-2-ol solution or a mixture of ethanol and propan-2-ol had been applied. Although it must be considered that the total amount of propan-2-ol applied was low (2 g) in comparison to other human studies, these data indicate that dermal absorption of propan-2-ol from application of 20 ml of a solution containing 10 % propan-2-ol over 10 minutes is negligible.

Thus, in overall consideration of the human data, the estimated total absorption value based on measurements of both propan-2-ol and acetone in blood in the study by Bieber (2 %) is likely to represent an overestimation of actual dermal absorption, since absorption via inhalation cannot be excluded.

Given the uncertainties associated with the human dermal absorption studies, it is proposed to employ the transdermal flux derived from the well-documented rat study (Boatman et al. 1998; 0.85 mg/cm²/h) for further calculation of systemic exposure via the dermal route. Even so, the rat dermal flux rate is assumed to provide a conservative assumption for the following reasons: Use of the results obtained in the rat study are probably more likely to overestimate dermal absorption for humans, since occlusive exposure conditions were used in the animal study, while in human exposure situations a significant degree of volatilisation can be expected, reducing the amount of substance available for absorption already during the period of exposure. Calculation of absorption for very short exposure durations (for less than time required for establishment of a steady-state in the flux rate) would be expected to result in an overestimation of the actually absorbed proportion. Finally, it is known that for many chemicals, rats show a higher dermal absorption rate in vivo as compared to humans.

In conclusion, in careful consideration of the available information on dermal absorption a transdermal flux rate of 0.85 mg/cm²/h would constitute a prudent assumption to be used in further risk characterisation for propan-2-ol.

Inhalative absorption

Non-pregnant female adult or immature rats were exposed to propan-2-ol in inhalation chambers for 7 h/d for 1, 10, or 19 days (adult rats) or for 1 day (immature rats), and propan-2-ol blood levels were determined via gas chromatography (Nelson et al. 1988). After 1 d of exposure, blood levels were found to be slightly higher in immature animals as compared to adult rats. Given the low number of animals examined, some doubts on the significance of this result remain, which otherwise may be tentatively interpreted as a consequence of the higher inhaled dose in relation to body weight in immature animals. Blood levels were slightly lower among adult animals that had been subjected to repeated exposure (for 10 or 19 days versus 1 day). These differences might reflect an adaptive response after repeated exposure, e.g. induction of enzymes of propan-2-ol metabolism.
Calculation of the percentage of inhalative absorption is impeded by the fact that the eliminated portion of absorbed propan-2-ol was not determined. However, from the calculated inhaled dose in mg/kg bw and the determined blood level for propan-2-ol, and further assuming a volume of distribution similar to that in humans (about 0.5 L/kg, Ernstgård et al. 2003), the recovery of propan-2-ol alone is estimated as corresponding to about 50 % of the inhaled dose for adult females exposed to 10000 ppm for 7 h. An earlier rat inhalation toxicity study (Laham et al. 1980) showed that blood acetone levels in rats exposed to 8000 ppm propan-2-ol for 4 h were at least as high as propan-2-ol levels. Thus, these data suggest that inhalative absorption of propan-2-ol amounts to roughly 100 %.

The rat inhalation studies in which animals had been exposed to radiolabelled propan-2-ol for 6 hours demonstrated excretion of up to 95 % of the inhaled radioactivity within 72 h (in breath, urine, and faeces; Slauter et al. 1994), and thus support the assumption of an inhalative absorption of about 100 %.

Metabolism and excretion

In a toxicokinetics study with rats and mice, animals were exposed to propan-2-ol containing ^{14}C radiolabelled propan-2-ol via different routes (i.v., oral, and inhalative for rats; i.v. and inhalative for mice; Slauter et al. 1994). In general, no significant differences in metabolism and elimination of radioactive compound were observed between sexes. Furthermore, the pharmacokinetic data obtained from i.v. and inhalative exposure experiments were similar for both species. Elimination was efficient, with 80-97 % of radioactivity in mice (88-95 % for rats) recovered within 72 h. The major proportion of radioactivity was exhaled with breath, the volatile fraction consisting of acetone, CO_2, and propan-2-ol. Only low amounts of administered dose were excreted with urine (≤ 8 %) and faeces (< 2 %), respectively. A fraction of radiolabelled substance was excreted as propan-2-ol (exhalation of up to 15 % of dose, excretion via urine < 1 %). Oxidation of propan-2-ol yielded acetone as the major metabolite, with up to roughly 60 % of the recovered dose in breath, and maximally 4 % in urine. Finally, glucuronidation of propan-2-ol appears to constitute a minor pathway of metabolism, as < 6 % of dose in urine were identified as propan-2-ol glucuronide. Thus, major routes of propan-2-ol elimination involve metabolism to acetone and ultimately CO_2, and exhalation (partly of unchanged propan-2-ol, but primarily of products of metabolism).
Elimination half-lives, derived from one-compartment modelling of propan-2-ol blood concentrations vs. time data, were similar for animals that had been subjected to low doses via different routes of exposure, ranging from 0.8 to 1.7 h for rats and from 0.6 to 0.9 h for mice.
Elimination of propan-2-ol after repeated dosing of rats with 300 mg/kg bw/d over 8 days did not markedly differ from elimination after single oral dosing (yielding half-lives of 1.7 as compared to 1.3 h, Slauter et al. 1994). Increasing the dose of exposure approximately 10-fold for inhalative and oral exposure led to a slight increase in elimination half-lives for inhalative exposure, and a substantial increase (to 4-6.8 h) for oral exposure (Slauter et al. 1994). These data suggest that at high doses, saturation of elimination, e.g. of metabolic processes, occurs. This was also supported by a higher amount of unmetabolised propan-2-ol found in breath in the high dose groups (Slauter et al. 1994).

Efficient elimination of propan-2-ol resulted in low residues in tissues and carcass after 96 h (1-5 %), regardless of the route of administration. Residual radioactivity found in individual tissues (adipose tissue, skeletal muscle, skin, liver, kidney) was below 2.4 % of dose (Slauter et al. 1994).
Propan-2-ol is metabolised to acetone mainly by cytosolic alcohol dehydrogenases (ADH, Enzyme Commission number 1.1.1.1), although it appears to be a poorer ADH substrate than ethanol (Dalziel and Dickinson 1966). Evidence from animal studies exists that the presence of ethanol retards elimination of propan-2-ol (WHO 1990), as oxidation by alcohol dehydrogenase appears to be the rate-limiting step in propan-2-ol metabolism. Biotransformation of propan-2-ol by hepatic microsomal oxidases (Cederbaum et al. 1981) appears to contribute only to a minor extent to overall oxidation. Microsomal oxidase induction has been suggested in studies involving treatment of rats with acetone or propan-2-ol (Snyderwine et al. 1988; Sipes et al. 1973), indicating that hepatotoxicity of compounds that are subject to metabolic activation may be potentiated by propan-2-ol.

Acute Toxicity

Propan-2-ol displayed only low acute toxicity in rats (resulting from oral or inhalative exposure) or in rabbits after oral or dermal administration. Acute oral toxicity was analysed in rats of different age groups by Kimura et al. 1971. Although newborn animals showed higher sensitivity towards propan-2-ol, the LD_{50} values established for immature (14 day-old), young adult (80-160 g), and older adult (300-470 g) rats were similar, given as 4400, 4710, and 5340 mg/kg bw, respectively. In addition, 3000 mg/kg bw was defined in young

adult rats as the dose eliciting first substance-related effects, but these effects were not specified. An earlier rat study by Smyth and Carpenter, although considerably lacking detail in description of materials and methods, reported an oral LD_{50} of 5840 mg/kg bw, apparently supporting the LD_{50} values established for adult rats in the study by Kimura et al. With rabbits administered propan-2-ol via oral gavage (Munch 1971), primarily neurological effects (stupor, loss of voluntary movements as well as disappearance of corneal reflex, nystagmus, dyspnoea and bradycardia) were described. The oral LD_{50} for rabbits was given as 7980 mg/kg bw.
From dermal exposure of rabbits to propan-2-ol for 24 h, a dermal LD_{50} was provided, amounting to about 12900 mg/kg bw (Smyth et al. 1948). However, due to a severe lack in reporting of experimental detail, e.g. regarding the area of dermal exposure, the reliability of the rabbit dermal toxicity study is limited.
In an acute inhalation toxicity study with rats (Laham et al. 1980), animals were exposed to a range of propan-2-ol concentrations for 8 hours. Adverse effects included irritation to mucous membranes and neurological effects (ataxia – prostration – narcosis, observed in time- and concentration-dependent order already during exposure), hypothermia, paralysis of hind legs, as well as organ toxicity affecting lung (congestion, pneumonia, oedema), liver (congestion, vacuolisation of hepatocytes), spleen (congestion) and brain (oedema). The LC_{50} values established were 22500 and 19000 ppm for males and females, respectively (about 56.2 and 47.5 mg/L). Based on default assumptions regarding inhalation volume according to the TGD on Human Risk Assessment, internal doses after 8 h exposure were calculated from inhaled external concentrations, yielding an estimated value of about 20200 mg/kg bw for males and 17100 mg/kg bw for females.

In conclusion, when comparing different routes of propan-2-ol administration to rats, oral gavage appears to be associated with lower LD_{50} values than following exposure via inhalation, which is likely to be due to rapid attainment of relevant internal peak concentrations following bolus administration.

Classification and labelling for acute toxicity according to Directive 67/548/EEC:

None

Classification and labelling according to Regulation (EC) No 1272/2008:

None

Irritation and corrosivity

Exposure of skin of rabbits, guinea pigs, or human volunteers for 4 h *in vivo* to undiluted propan-2-ol elicited only negligible or no irritation at all. Thus, propan-2-ol does not meet the criteria for classification as irritating to skin. Nevertheless, reports on human individuals exhibiting skin reactions to formulations containing propan-2-ol, but also to aqueous solutions containing up to 99 % propan-2-ol, exist (outlined in section 3.10).
In a compilation of results of eye irritation studies performed with different chemicals according to OECD guideline 405, eye irritating potential for propan-2-ol was defined via the maximum average score (MAS) of animals at 24 h or later after instillation (Bagley et al. 1999). The MAS provided for propan-2-ol was 30.5 (as compared to a maximum possible score of 110, calculated according to the weighted scoring scheme of Draize et al. 1944). An earlier study performed with the same volume (0.1 mL) of 70 % propan-2-ol yielded a similar maximal average score (37), and also documented reversibility of irritation (Griffith et al. 1980). The individual rabbit eye data of the studies performed by Bagley et al. were published in ECETOC 1998. Applying the criteria outlined in Annex VI of Directive 67/548/EEC, the mean average scores obtained for three observation days (24, 48, 72 h) were below the threshold for classification as irritating to eyes. However, propan-2-ol has been classified as eye irritating in other assessment procedures (WHO 1990, OECD 1997), in which further rabbit studies have been taken into account (e.g. the study by Exxon Biomedical Sciences Inc.: Document No. 86MRL272, 1986, which has not been submitted by the participant but is referred to in OECD 1997). Thus, classification of propan-2-ol as Xi; R36 (Irritant; irritating to eyes) is proposed, which is in line with the current classification listed in table 3.2 of Annex VI of Regulation (EC) No 1272/2008 (former Annex I of Directive

67/548/EEC).

Classification (labelling) for irritation/corrosivity according to Directive 67/548/EEC:

Xi; R36 (Irritant; irritating to eyes)

Classification (labelling) according to Regulation (EC) No 1272/2008:

Eye Irrit. 2; H319 (Eye irritation, hazard category 2;Causes serious eye irritation).

Sensitisation

In a mouse local lymph node assay, concentrations of 10, 25, and 50 % propan-2-ol yielded stimulation indices that were below the classification threshold for skin sensitisation.

Classification/labelling for sensitisation according to Directive 67/548/EEC:

None

Classification/labelling according to Regulation (EC) No 1272/2008:

None

Short-term Toxicity

Two subchronic inhalation tests and one drinking water study in rats were submitted for propan-2-ol. The inhalation study by Burleigh-Flayer et al. was selected as key study, because important result parameters were not assessed in the other two studies. In this experiment, the predominant systemic reaction to treatment with propan-2-ol was given by its narcotic effect, the intensity of which increased with dose, starting with hypoactivity at the mid dose, and then lack of startle reflex, ataxia, and narcosis at the high dose level. In general, these findings were only observed during or immediately following exposures and with LOAELs close to or clearly above the limit dose of 1000 mg/kg bw/d. The NOAEL was 286 mg/kg bw/d. In animals of the 2864 mg/kg bw/d group, narcosis was only observed during the first two study weeks, which was interpreted by the study authors to be in line with reports by other sources of habituation/development of a tolerance towards the narcotic effects of propan-2-ol. A mechanism for this process in rats involving interaction with ribosomal protein synthesis has been proposed by Muñoz and co-workers (Muñoz et al. 1991). Against this background, the increase in mean motor activity in female animals of the high dose group at the end of study wks 9 and 13 might be interpreted tentatively as a symptom of withdrawal, because the corresponding measurements were carried out 20 h after exposure.
Most likely as a local response to irritation (of the upper airways), females at 286 mg/kg bw/d and above displayed periocular swelling, while for males at these dose levels 'perinasal encrustation' was noted. The NOAEL for these observations was 57 mg/kg bw/d. It is considered whether these symptoms, in combination with histopathological observations in the chronic inhalation study in rats and with experience in humans, may warrant classification/labelling of propan-2-ol with Xi; R37 ('irrritating to respiratory system'). By contrast, no classification along specific target organ toxicity (irritation of the respiratory system) was proposed according to GHS. As the system of classification and labelling as detailed in Directive 67/548/EEC is to be replaced by the criteria laid down in Regulation (EC) No. 1272/2008, no classification/labelling as irritating to the respiratory system is proposed.
Due to reduced feed consumption, body weight gain was decreased in mid and high dose females after wk 1. However, this parameter returned to normal in the further course of the study and, in the high dose groups, was even significantly elevated as compared to controls upon study termination. Both the mechanism behind and the toxicological relevance of increased body weight gain are unclear. Water consumption was increased significantly in mid and high dose animals of both sexes beginning in study wk 1.
A number of haematological changes were noted in both male and female rats of the 859

and 2864 mg/kg bw/d groups. Many of these findings were, however, reversible over time. Noteworthy, such changes were not reported in the 2-yr study performed by the same laboratory in the same rat strain (cf. chronic toxicity section). Nevertheless, at 2864 mg/kg bw/d, increases in MCV (mean corpuscular erythrocyte volume) and MCH (mean corpuscular haemoglobin) were observed for males in both week 6 and 14, and an increase in MCV reported for females in week 14. This is consistent with elevated MCV and MCH values for female mice of the high dose group (cf. below, subchronic mouse inhalation study). Thus, haematological effects were observed in two rodent species. An increase in MCV and MCH values in combination with decreased RBC is typical of macrocytic hyperchromic anaemia; data regarding a possible mechanistic relationship to propan-2-ol exposure are however lacking.
Another noteworthy finding was the occurrence of hyaline droplets in the kidneys of male rats, which was consistent with observations made in the 12-wk drinking water (Pilegaard and Ladefoged 1993), the chronic inhalation (Burleigh-Flayer et al. 1997), and the multi-generation (Bevan et al. 1995) study in rats. The study authors reportedly suspected the droplets to consist of the protein 2µ-globulin, but after immunohistochemical staining of slides from male kidneys taken from a previous 9-d preliminary inhalation study in rats (in which the hyaline droplets were also noted), neither intensity nor distribution of this protein could be shown to be increased in treated vs. control animals (Burleigh-Flayer et al. 1994). 2µ-globulin nephropathy is a pathological condition, which can be caused *inter alia* by certain chemicals and is encountered exclusively in male rats, in which it eventually leads to chronic renal disease and – sometimes - occurrence of neoplastic lesions in the kidney. It has been established that 2µ-globulin nephropathy is not relevant for female rats or other species including humans (Meek et al. 2003; Doi et al. 2007). The adequacy of the staining method used for 2µ-globulin detection cannot be assessed due to lack of specific information. However, it was noted that the same external dose level of 500 ppm was not associated with adverse effects in the 2-yr inhalation study (cf. below, Burleigh-Flayer et al. 1997). The hyaline droplets, to the extent observed in the low dose group of the 13-wk study, were therefore rated as a clearly substance-related, but not toxicologically significant finding.
Reportedly, the liver was a further target organ in the 13-wk inhalation study in rats, as manifested by increased relative liver weight in the top dose group. However, neither was this finding accompanied by histopathological changes, nor was the extent of the change reported, therefore its toxicological relevance remains unclear.
No mortality was observed in the inhalation study up to and including a dose level of ca. 2864 mg/kg bw/d.
The NOAEL for acute systemic effects in rats (hypoactivity) after inhalation of propan-2-ol was 286 mg/kg bw/d (NOAEC: 500 ppm), while the NOAEL for non-acute, relevant medium-term systemic effects (elevation in MCV and MCH) was 859 mg/kg bw/d. The NOAEC for local reactions (irritation of the airways) was 100 ppm.
The results obtained in both non-key studies in rats were basically consistent with those of the Burleigh-Flayer study. In the drinking water experiment by Pilegaard and Ladefoged, increased relative kidney (at dose levels ≥ 1280 mg/kg bw/d) and testes weight (at 2520 mg/kg bw/d) was noted, again without further specification of the extent of these effects. One animal of the highest dose groups died in wk 1, with dehydration specified as the cause of death in the study report. The inhalation study by Nakaseko produced increased levels of liver enzymes in the serum at 4582 mg/kg bw/d. Both studies were performed using Wistar rats (in contrast to the Burleigh-Flayer study using animals of the Fischer strain).

Burleigh-Flayer et al. (1994) also exposed mice to the same air levels (in ppm) of propan-2-ol, corresponding to dose levels up to 3857 mg/kg bw/d. In this species, hypoactivity, narcosis and ataxia were observed during exposure to ≥ 1157 mg/kg bw/d (NOAEL = 386 mg/kg bw/d), and ataxia and/or hypoactivity at 3857 mg/kg bw/d also immediately after exposure. Signs of irritation were not reported. At 3857 mg/kg bw/d, female mice displayed haematological and clinical chemistry changes (NOAEL: 1157 mg/kg bw/d).

Classification (labelling) for repeated dose toxicity according to Directive 67/548/EEC:

Based on neurological effects observed in rats already at exposure to a propan-2-ol vapour concentration of 3.75 mg/L for 6 h, classification as R67 (Vapours may cause drowsiness and dizziness) is warranted.

Classification (labelling) according to Regulation (EC) No 1272/2008:

STOT SE 3; H336 (Specific target organ toxicity - single exposure, hazard category 3, narcosis; May cause drowsiness or dizziness).

Genotoxicity

In vitro tests:

Propan-2-ol was tested as negative with and without S9-mix in two bacterial and two mammalian *in vitro* systems (Ames mutagenicity assay, SOS (DNA damage) chromotest, mammalian cell HGPRT mutation assay and mammalian sister chromatid exchange test).

In vivo tests:

In an *in vivo* assay, propan-2-ol did not lead to an increase in micronuclei of bone marrow erythrocytes, and was thus judged to be non-mutagenic in this test.

It is concluded that propan-2-ol does not pose a genotoxic risk to humans.

Classification/labelling for genotoxicity according to Directive 67/548/EEC:

None

Classification/labelling for for genotoxicity according to Regulation (EC) No 1272/2008:

None

Chronic Toxicity/ Carcinogenicity

In principle, the combined chronic toxicity and oncogenicity study in rats and mice submitted by the applicant confirmed the effects and target organs of propan-2-ol toxicity already seen after repeated administration in the subchronic studies. Again, narcotic action of propan-2-ol was observed during exposure at dose levels of ≥ 1500 mg/kg bw/d (NOAEL: 300 mg/kg bw/d). Local irritation was mentioned for animals of the high dose group (females: periocular swelling) and substantiated by inflammatory/metaplastic changes within the nasal cavity of top dose animals. It is considered that these symptoms, in combination with the periocular swelling/perinasal encrustations in the subchronic rat study (Burleigh-Flayer et al. 1994) and with experience in humans, would basically support classification/labelling of propan-2-ol with Xi; R37 ('irrritating to respiratory system'). By contrast, no classification along specific target organ toxicity (irritation of the respiratory system) was proposed according to GHS. In conclusion, as the system of classification and labelling as detailed in Directive 67/548/EEC is to be replaced by the criteria laid down in Regulation (EC) No. 1272/2008, no classification/labelling as Xi; R37 is proposed.
As in the subchronic study, relative liver weight as well as body weight gain were increased at the mid and high dose levels, but no biological significance was attributed to these observations.
Both male and female rats of the mid and high dose groups displayed histopathological signs of exacerbation of progressive chronic nephropathy, which was further confirmed by the urinalysis findings obtained for the top dose group. These histopathological changes were observed at comparable incidences in males and females, but were in general more pronounced in males. Moreover, increased mortality and decreased mean survival time were noted in males, but not in females at the high-dose level. Chronic nephropathy reportedly was determined as the main cause of death for both females and males of the 5000 ppm (3000 mg/kg bw/d) groups and considered a major cause of death also for males of the 2500 ppm (1500 mg/kg bw/d) group. In males at 5000 ppm, atrophy of seminiferous tubules was noted upon histopathological examination.

Evaluation of mortality/survival data is limited by the fact that an unusually high mortality of ≥ 80 % was noted for treated as well as control groups of male rats at study termination. 100 % mortality was reached for males at the high dose level already in study wk 100. Before this time-point, emaciation and dehydration were noted in the animals of this group. In both sexes, dead animals or animals euthanised in a moribund state displayed a variety of histopathological lesions.
The only potentially significant neoplastic finding in rats consisted of an increase in interstitial (Leydig) cell adenomata. However, incidences in treated groups - although high and increasing with dose - were comparable to historical controls, while the control group displayed an unusually low incidence (64 %) of this observation. Historical incidences for Fischer control rats have been reported as being 86-91 % (Kapp et al. 1996). Evaluation of a tumourigenic potential of propan-2-ol in male rats was further impaired by the high mortality in all male groups and the clearly decreased life-span observed for males of the top dose group.

In mice, at the low dose of ca. 506 mg/kg bw/d, tubular proteinosis in the kidney and changes in relative organ weight (liver: up, testes: down) were noted, which were considered substance-related, but not necessarily adverse. At dose levels ≥ 2531 mg/kg bw/d, inhalation of propan-2-ol led to hypoactivity or narcosis. Furthermore, body weight gain was increased (but this increase was not rated toxicologically significant). At the top dose of 5063 mg/kg bw/d, relative liver weight was increased in both males and females. Upon microscopic inspection of the organs of females at this dose level, tubular dilation in the kidneys, congestion of the adrenals, and mucosal hyperplasia of the stomach as well as signs indicative of slight anaemia (extramedullary haematopoiesis and haemosiderosis in the spleen) were noted. Histopathological examination of the testes of male mice showed ectasia of the seminal vesicles, a finding whose origin or toxicological relevance could not be further elucidated.

In conclusion, in rats and mice, the NOAELs for acute narcotic effects in chronic toxicity studies were 300 and 506 mg/kg bw/d, respectively, with LOAELs clearly above the limit dose level of 1000 mg/kg bw/d. Aside from the narcotic effect of propan-2-ol on the central nervous system, long-term systemic toxicity was observed, the main target organ being the kidney, in which pathological changes could be linked to increased mortality and decreased mean survival time in male rats at the top dose level. The NOAELs for non-acute, long-term organ toxicity were 300 and 2531 mg/kg bw/d for rats and mice, respectively. No relevant substance-related neoplastic lesions were observed up to dose levels of 3000 and 5063 mg/kg bw/d in rats and mice, respectively.
With regard to the evaluation of carcinogenicity, the rat study showed some limitations, but taking into account the high dose levels administered, the absence of any substance-related neoplastic findings in mice, and the clearly negative genotoxicity database, overall, no indication for a relevant tumourigenic potential of propan-2-ol was found and no need for further investigation into this endpoint was identified.

Classification/labelling for carcinogenicity according to Directive 67/548/EEC:

None

Classification/labelling for carcinogenicity according to Regulation (EC) No 1272/2008:

None

Reproduction Toxicity

A developmental neurotoxicity study was conducted with maternal rats being exposed to propan-2-ol via gavage during gestation and lactation (Bates et al. 1994). One dam in the high dose group (1200 mg/kg bw/d) died on postnatal day 15. However, no other exposure-related adverse clinical signs or effects on body weight were observed in dams or offspring. In one female pup of the high dose group, retainment of vestiges of the cerebellar external germinal layer was documented for postnatal day 22 (Bates et al. 1994). However, this was

considered as being within the scope of normal cerebellar development, as disappearance of external germinal layer vestiges is regarded as being complete by day 30 (Altman 1987). Thus, there was no evidence of developmental toxicity associated with propan-2-ol exposure as high as 1200 mg/kg bw/d.
Developmental toxicity was further investigated in a detailed study with rats and rabbits (Tyl et al. 1994). Maternal animals received propan-2-ol by oral gavage during major embryonic organogenesis (from days 6-15 and 6-18 for rat and rabbit, respectively). Regarding maternal toxicity, rabbits were more susceptible than rats: mortalities occurred at 480 mg/kg bw/d for rabbits and at ≥ 800 mg/kg bw/d for rats. Further adverse effects on maternal animals included reduced body weight for both species, and reduced food consumption and clinical signs (cyanosis, lethargy, laboured respiration, diarrhoea) in rabbits. Thus, the NOAELs for maternal toxicity were established as 400 mg/kg bw/d for rats and 240 mg/kg bw/d for rabbits. There was no evidence for increased teratogenicity at any dose tested in rabbits and rats. However, foetal body weight per litter was significantly reduced at ≤ 800 mg/kg bw/d in rats. In the rabbit study, only a tendency towards lower female foetal body weight was observed at the highest dose, but this effect did not reach statistical significance (Tyl et al. 1994). Therefore, the oral NOAELs for developmental toxicity were similar for both species, namely 400 mg/kg bw/d for rats and 480 mg/kg bw/d for rabbits. The maternal and developmental oral NOAEL values were also supported by range-finding studies for both species that had been conducted by the authors of the main study (Tyl et al. 1994).
In the study by Nelson et al. 1988, pregnant rats were exposed to propan-2-ol via inhalation during days 1-19 of pregnancy, and thus during a period including preimplantation and organogenesis. In maternal animals, acute neurological effects (unsteady gait and narcosis) were observed at the end of daily exposure for concentrations ≥ 7000 ppm (Nelson et al. 1988). These acute effects were either not noticeable (at 7000 ppm) or diminished (at 10000 ppm) after 19 days. A possible explanation could lie in the assumption that after repeated exposure adaptation of animals, e.g. by enhanced metabolic elimination, might have occurred, which would be in line e.g. with the observation that propan-2-ol blood levels were slightly lower after repeated as compared to single exposure (Nelson et al. 1988). In addition, food consumption and body weight gain were decreased at ≥ 7000 mg/kg bw/d. No maternal mortality was reported. However, developmental toxicity was evident, comprising foetal growth retardation and increased incidence of malformations (skeletal and visceral) at ≥ 7000 ppm, and also pre- and postimplantation losses at 10000 ppm. Although a slight reduction in foetal weight was described already at 3500 ppm, this is not regarded as adverse, in relation to the larger litter size at this dose. Thus, NOAECs for maternal and developmental toxicity resulting from maternal inhalative exposure were both set at 3500 ppm (or ca. 2756 mg/kg bw/d). The decreased food consumption in maternal animals may be a factor contributing to unspecific developmental effects. However, considering the high rate of inhalative and oral absorption of propan-2-ol, it is assumed that propan-2-ol also easily distributes through the placenta. This is substantiated by a report concerning a newborn that displayed toxic propan-2-ol blood levels as a result of maternal propan-2-ol ingestion 1-2 days prior to delivery (Wood et al. 2007). Hence, an independent and specific nature of developmental effects (independent of maternal toxicity at the same exposure level) cannot be ruled out. However, the LOAEC for developmental effects (7000 ppm) corresponded to an estimated maternal internal dose of roughly 5000 mg/kg bw/d, and thus exceeded the limit dose level of 1000 mg/kg bw/d for developmental toxicity testing (OECD 414) by far. Therefore, no classification/labelling of propan-2-ol for developmental toxicity is proposed.

Fertility

In a two generation rat study (Bevan et al. 1995), propan-2-ol was administered to parental animals by oral gavage from at least 10 weeks prior to mating, until weaning (females) or birth of offspring (males). In parental generations, treatment-related increases in liver weight were observed. However, the only microscopic liver alteration was a centrilobular hepatocyte hypertrophy in a few (6 of 26) high dose P_2 male rats. This may be indicative of enzyme induction, which *per se* would not be regarded as adverse. Renal toxicity was observed in male animals (in P_1 at ≥ 500 mg/kg bw/d, in P_2 already at ≥ 100 mg/kg bw/d),

involving an increase in hyaline droplets in the epithelial cells of the proximal tubules, epithelial degeneration and hyperplasia, increased incidence of proteinaceous casts in renal tubules and focal interstitial mononuclear cell infiltration. An increase in hyaline droplet formation was also observed for rat males in other (subchronic) studies with propan-2-ol, i. e. in a 12-week drinking water study (Pilegaard and Ladefoged 1993) and in a 13-week inhalation study (Burleigh-Flayer et al. 1994). In addition, an increased incidence in severe kidney lesions (e.g. tubular proteinosis) was reported in a 2-yr inhalation experiment in rats, although at comparatively high internal exposure levels (≥ 1500 mg/kg bw/d, Burleigh-Flayer et al. 1997). Notably, hyaline droplet occurrence was described already at similarly low internal exposure levels for males in the 13-week inhalation study (at about 57 mg/kg bw/d) and for P_2 males in the reproduction toxicity study (100 mg/kg bw/d), but an association with other kidney alterations at such low dose levels was only reported in the multigeneration study, which may be due to bolus administration (oral gavage) in the latter. Exposure of male rats to certain xenobiotics has been related to α2μ-globulin nephropathy, a spectrum of kidney abnormalities typically comprising epithelial hyaline droplet increase, epithelial degeneration and hyperplasia, and proteinaceous casts. Alpha2μ-globulin nephropathy is attributed to an excessive accumulation of the rat male-specific low-molecular weight protein α2μ-globulin in phagolysosomes of renal proximal tubular cells. Alpha2μ-globulin accumulation is thought to result from binding of the xenobiotic or a metabolite to the globulin, rendering the protein resistant to degradation (US EPA 1991; Swenberg 1993; Doi et al. 2007). As α2μ-globulin is synthesised in large quantities exclusively by male rats and there is no evidence that any protein in the human kidney could function in an analogous manner, α2μ-globulin nephropathy is not regarded as being of relevance for human risk assessment (Meek et al. 2003). To date, however, it appears that results from binding studies involving a possible interaction of propan-2-ol or of acetone with α2μ-globulin are not available, and that the identity of hyaline droplet content has not been clarified, e.g. by immunohistochemistry (cf. section 3.5). Thus, a clear association of propan-2-ol exposure with an increase in renal α2μ-globulin deposits has not been proven.
Concerning reproduction, the male mating index was significantly decreased for the P_2 generation at the highest dose (1000 mg/kg bw/d). Histopathologicical findings in testes were absent and the female fecundity index (number of females pregnant/number of females mated) was comparable to controls in this generation, indicating that the ability of mated males to impregnate females was not impaired at the highest dose, although sperm parameters were not determined in the study. In summary, NOAELs of parental toxicity were established as < 100 mg/kg bw/d for males, based on male-specific kidney toxicity in the P_2 generation, and as 500 mg/kg bw/d for females, based on mortality at 1000 mg/kg bw/d in both P_1/P_2 generations. Considering offspring toxicity, the NOAEL of 500 mg/kg bw/d was deduced from the LOAEL based on 18 mortalities of the 1000 mg/kg bw/d treatment group in the F_1 generation during postnatal days 21-41. Finally, a reproductive NOAEL of 500 mg/kg bw/d was established, based on the significantly decreased mating index of P_2 males in the group receiving 1000 mg/kg bw/d. Considering that the dose associated with the decreased male mating index exceeded levels leading to other severe effects (nephrotoxicity) in males and that other abnormalities concerning fertility criteria were absent, no further classification regarding reproduction toxicity is proposed.

Classification/labelling for reproduction toxicity according to Directive 67/548/EEC:

None

Classification/labelling according to Regulation (EC) No 1272/2008:

None

Neurotoxicity

In an acute neurotoxicity study, rats were exposed to propan-2-ol vapours for 6 h. Evaluations were performed prior to and immediately after exposure (for motor activity) or prior to and 1, 6, and 24 h following exposure (behavioural observations). Concentration-

dependent reversible sedation of the central nervous system was observed in the exposed animals, with symptoms including ataxia, loss of reflex function and decreases in motor activity, in arousal, and in neuromuscular function. In addition, hypothermia was reported. Complete recovery even in the group exposed to the highest concentration (10000 ppm) occurred within 24 h, except for hind-leg splay (Gill et al. 1995). Thus, a NOAEC of 500 ppm (corresponding to an inhaled dose of about 340 mg/kg bw/d) was established for acute neurotoxic effects.
In female rats exposed to an atmospheric concentration of 5000 ppm for 6 h/d on 5 d/wk over 9 or 13 weeks, motor activity was assessed during exposure-free intervals. An increase in cumulative motor activity was observed already at the first evaluation time point 4 weeks after initiation of the test regimen. Although this effect prevailed beyond exposure, it was reversible within 2 d after the 9-week exposure, and within 14 d following the 13-week exposure. The authors hypothesised that the enhanced motor activity might represent a symptom of withdrawal from repeated exposure to propan-2-ol (Burleigh-Flayer et al. 1998).

Classification (labelling) for neurotoxicity according to Directive 67/548/EEC:

R67 (Vapours may cause drowsiness and dizziness), based on neurological effects observed in rats already at atmospheric exposure towards 3.75 mg/L x 6 h. (According to 67/548/EEC, Annex VI, criteria for R67 are met, if corresponding effects are observed at concentrations not exceeding 20 mg/L/4h). These effects were observed consistently in a number of single and repeated-dose studies in different animal species. Acute neurotoxicity (impaired postural balance) was also observed in a human volunteer study (Sethre et al. 2000a) involving inhalative exposure to 400 ppm for 8 hours (cf. 3.10, Medical Data).

Classification (labelling) according to Regulation (EC) No 1272/2008:

STOT SE 3; H336 (Specific target organ toxicity – single exposure, hazard category 3, narcosis; May cause drowsiness or dizziness).

Further Studies

No further mechanistic or other studies have been submitted by the applicant for the active substance.

Medical Data

Surveillance of manufacturing plant personnel

Epidemiological data obtained by medical surveillance of manufacturing plant personnel provide evidence that the manufacture of propan-2-ol by the strong-acid process is associated with an increase in upper respiratory tract cancer in humans. The suggested cancer hazard has been related to sulfuric acid and by-products (e.g. dialkyl sulfates) of this manufacturing process (B. Braun Melsungen AG 2006; OECD 1997).

Case reports

Intoxications have been reported after oral ingestion and inhalation. In addition, intoxications have been described for individuals exposed to rubbing alcohol, although it is unclear to which extent dermally absorbed propan-2-ol contributes to systemic toxicity. Symptoms of systemic intoxication include depression of the central nervous system, early gastrointestinal problems, hypothermia, cardiovascular effects (hypotension, cardiac arrest, secondary tachycardia) and hyperglycaemia. Severe intoxications may result in unconsciousness, coma, and death due to respiratory depression (WHO 1990).

Studies in human volunteers, case reports - Ingestion

No adverse effects were observed in healthy volunteers having ingested 2.6 or 6.4 mg/kg bw over 6 weeks (referred to in B. Braun Melsungen AG 2006, WHO 1990, and OECD 1997). Although a daily dose of about 180 mg/kg bw (16 mL) for 3 days was reported not to produce adverse effects, symptoms were evident after 280 mg/kg bw (B. Braun Melsungen

AG 2006). The majority of symptoms resulting from ingestion of large amounts of propan-2-ol are indicative of CNS toxicity/depression, and include headache, nausea, dizziness, vomiting, and incoordination. High exposures may result in unconsciousness and death. While fatalities among adults have been reported after ingestion of 400 mL propan-2-ol, the lowest amount documented to be life-threatening was an estimated dose of 170 mL (240 mL rubbing alcohol with 70 % propan-2-ol), that was ingested by an 18-month-old infant (WHO 1990).

Studies in human volunteers - Inhalation

In an inhalation study with human volunteers, the threshold for odour detection appeared to be as low as around 10 ppm (11/39 ppm, Smeets and Dalton 2002). Human exposure data demonstrate an irritating potential of propan-2-ol vapours to mucous membranes as a local effect: in a study with human volunteers, exposure to 400 ppm propan-2-ol vapours (0.98 mg/L) for 3-5 min was reported to cause mild irritation to eyes, nose, and throat. At 800 ppm, test subjects characterised the atmosphere as unbearable, although the effects were not severe from a toxicological point of view. 200 ppm (0.49 mg/L) has been judged by the study participants as being satisfactory for their own occupational exposure (Nelson et al. 1943). More recent evaluation of objective endpoints (nasal and ocular sensory irritation) indicated that the threshold for sensory irritation may actually be higher (Smeets and Dalton 2002, Smeets et al. 2002) and that subjective responses to concentrations below or around 400 ppm may be influenced by odour perception. Thus, in the study by Smeets et al. 2002, it was not possible to discern whether the reported increase in respiration frequency at an exposure level of 400 ppm reflected a response due to sensory irritation or a change in breathing in response to perception of an unpleasant odour.
Slight neurological symptoms in terms of impairment of postural balance were reported in a study involving exposure of human volunteers to 400 ppm for 8 hours, although no further effects could be established in other tests (Sethre et al., 2000a). In consideration of the available information for humans, it is proposed to set the LOAEC for acute systemic (neurological) effects in humans at 400 ppm (over 8 hours), based on the deterioration of postural balance. With respect to the setting of a relevant inhalation NOAEC in humans, exposure levels at which no adverse effects were reported in acute volunteer studies ranged from 150 to 360 ppm (Ernstgård et al. 2003; van Thriel et al. 2003; Muttray et al. 1998), although the volunteers were exposed for less than the equivalent of a working shift of 8 hours (for only 2 to 4 hours). However, investigations on occupational repeated exposure of women for 6 hours/working day yielded a median NOAEC value of 106 ppm with a range of 1 to 227 ppm (Triebig et al. 1989). To ensure an acceptable margin between the LOAEC of 400 ppm over 8 hours (based on neurological symptoms in the study by Sethre et al. 2000a) and a NOAEC for humans, it is proposed to apply a factor of 2 to derive an overall NOAEC of 200 ppm for exposure for 8 hours/day. The value of 200 ppm as an NOAEC for humans is also supported by experience with the German AGW/MAK value (German Occupational Safety value at the workplace) of 200 ppm. It is further suggested to use this overall NOAEC based on human data as the point of departure for derivation of systemic reference values (cf. 3.12, Overall Summary).

Studies in human volunteers - Eye contact

Propan-2-ol-dependent eye irritation has been described for humans, e.g. resulting from exposure of human volunteers to propan-2-ol vapours (Nelson et al. 1943). Supported by rabbit eye irritation studies (referred to in OECD 1997) and in accordance with Directive 67/548/EEC, classification of propan-2-ol as Xi; R36 (CLP: Eye Irrit. 2; H319) is proposed.

Dermal exposure

Recurrent case reports exist of individuals exhibiting signs of systemic toxicity following dermal exposure to propan-2-ol, e.g. by application of rubbing alcohol (WHO 1990; IPCS 1997). Most of the reports relating to intoxication from dermal exposure concern infants, which are likely to be more susceptible than adults. Although the rat study by Boatman et al. 1998 demonstrated absorption through skin under occlusive conditions and studies involving human volunteers provide evidence that absorption occurs also for humans, it is

difficult to discern to which extent systemic toxicity is attributed to absorption of propan-2-ol by the dermal route, as collateral uptake via inhalation and possibly by ingestion cannot always be ruled out.
No irritation was observed after application of 0.5 mL of undiluted propan-2-ol to skin of human volunteers for 4 hours (B. Braun Melsungen AG 2006 and 2007). However, local skin effects and reactions have been described for individuals exposed to formulations containing propan-2-ol and ethanol (redness, burning, itching, dry skin, contact eczema, skin fissures) or for individuals exposed to dilutions (aqueous solutions) of propan-2-ol (contact dermatitis, sensitivity reactions). Contact dermatitis has been reported in individuals treated with swabs impregnated with propan-2-ol for skin cleansing, giving rise to the suspicion that propan-2-ol may be responsible. Human patch tests, however, only yielded positive results for the swabs, but not for propan-2-ol in various dilutions or for other constituents (Leow and Freeman 1995). On the other hand, a human patch test performed on a female worker with dilutions of propan-2-ol from 2.5 to 99 % showed positive results (Ludwig & Hausen 1977; B. Braun Melsungen AG 2006) , and further reports on sensitivity reactions/contact dermatitis following exposure to propan-2-ol have been referred to in the literature (e.g. cited in Ludwig & Hausen.)
In summary, propan-2-ol does not meet the criteria for classification as irritating to skin (R38).
However, local skin effects and reactions have been observed for human individuals exposed to propan-2-ol-containing formulations or propan-2-ol dilutions. Although, the basis for sensitivity reactions or contact dermatitis in relation to propan-2-ol exposure is unclear. It appears plausible that cracking and dryness of skin, which were observed after topical application of formulations containing propan-2-ol, may contribute to such skin reactions. Based on the available information, classification/labelling as R66 (CLP: EUH066), Repeated exposure may cause skin dryness or cracking, is proposed.

Specific treatment in case of an accident or poisoning

Treatment includes prevention of further absorption (to be performed within minutes of oral ingestion) and symptom-oriented measures of life support (prevention of hypothermia, correction of fluid and electrolyte imbalance, respiratory support/mechanical ventilation). In severe cases, haemodialysis may be applied as a measure of detoxification. In case of eye contact with solution, rinsing with water for several minutes is advised (B. Braun Melsungen AG 2006).

Classification/labelling based on medical data, according to Directive 67/548/EEC:

Xi; R36 (Irritant; irritating to eyes), supported by rabbit eye irritation studies (referred to in OECD 1997) and observations of humans, and in accordance with Directive 67/548/EEC.
R66 (Repeated exposure may cause skin dryness or cracking) is proposed, based on local skin effects and reactions that have been described for human individuals exposed to formulations containing propan-2-ol and ethanol or to dilutions of propan-2-ol.

Classification/labelling based on medical data, according to Regulation (EC) No 1272/2008:

CLP: Eye Irrit. 2; H319 (Eye irritation hazard category 2; Causes serious eye irritation).
EUH066 (Repeated exposure may cause skin dryness or cracking) is proposed, based on local skin effects and reactions that have been described for human individuals exposed to formulations containing propan-2-ol and ethanol or to dilutions of propan-2-ol.

Summary & Conclusion:

It is noted that exposure of humans to propan-2-ol is expected to occur primarily via inhalation of vapours or by contact with skin.
In the rat, the lowest NOAELs/LOAELs for systemic effects in studies involving a relevant route of exposure (inhalation) were associated with signs of neurotoxicity. Acute neurological effects, e.g. decrease in motor activity, were consistently observed in acute, subchronic and chronic studies, with the acute neurotoxicity study and the subchronic study providing the lowest LOAEC (1500 ppm), but all time frames yielding an NOAEC of 500 ppm

over 6 h/d, equivalent to about 300 mg/kg bw/d. Thus, it is expected that the NOAEC/NOAEL of 500 ppm/300 mg/kg bw/d for acute systemic effects would also cover systemic medium- and long-term toxicity for the rat.

Several studies are available which involve acute intentional exposure of human volunteers to propan-2-ol via a relevant route of exposure (inhalation). Such studies would be expected to principally allow a more refined characterisation of possible acute neurological effects than the animal studies and therefore enable a more precise determination of relevant effect levels. In this context, the LOAEC of 400 ppm/8 h, based on the neurological effects of impairment of postural balance (Sethre et al. 2000a) was regarded as the relevant effect level for derivation of an overall NOAEC for humans of 200 ppm. A factor of 2 for extrapolation from LOAEC to NOAEC is proposed, since no effects were observed at 400 ppm on other neurological parameters tested in the same study (mood, neurobehavioural performance, olfactometry, spirometry; Sethre et al. 2000a). In addition, a NOAEC value of 200 ppm for 8 hours/day is also supported by experience with the German AGW/MAK value (German occupational safety value at the workplace) of 200 ppm for exposure for 8 hours/day. Thus, a derived NOAEC of 200 ppm/8 h was used as the point of departure for derivation of reference values. Based on the observation that medium and long-term NOAECs in inhalative rat studies were not lower than the NOAEC for acute systemic neurotoxicity, and on comparison between acute volunteer and occupational exposure studies, a single overall NOAEC/NOAEL is assumed to cover all time frames (acute-/medium-term/long-term) also for humans. Physiologically-based toxicokinetic modelling for propan-2-ol predicted average toxicokinetic dose metrics across different life stages (from birth to 75 years of age) that were within a factor of 2 compared to values for young adults. For individuals from 5-75 years of age, predicted average dose metrics were within a factor of 1.2 compared to young adults (Clewell et al. 2004). With respect to intraspecies (human) variability, it is therefore proposed to substitute the partial assessment factor for toxicokinetics of 3.2 by a chemical-specific assessment factor of 2 for the general population and by a chemical-specific assessment factor of 1.2 for professional workers, yielding overall intraspecies assessment factors of 6.4 (3.2 x 2) for the general population, and 3.8 (3.2 x 1.2) for professional workers.

In summary, the following Acceptable Exposure Levels (AELs) are derived from the toxicological data evaluated:

- **For the general population:**

  An AEC $_{\text{acute/medium-term/long-term}}$ of 31.25 ppm for an exposure for 8 hours/d, based on the derived NOAEC of 200 ppm for neurological effects in humans and applying an overall AF of 6.4 for intraspecies variability within the general population (from birth to 75 years of age). The AEC is assumed to also sufficiently cover local irritant effects in the eyes/airways.

  The AEC corresponds to the systemic/internal reference dose:
  AEL$_{\text{acute/medium-term/long-term}}$ of 10.7 mg/kg bw/d, assuming a human inhalation volume of 8.35 m^3/8 h for activity as described for volunteers in the study by Sethre et al. 2000a (between sedentary and light activity), and an average body weight of 60 kg.

- **For professional workers:**

  An **AEC $_{\text{acute/medium-term/long-term}}$ of 52.6 ppm** for an exposure for 8 hours/d, based on the derived NOAEC of 200 ppm for neurological effects in humans and applying an overall AF of 3.8 for intraspecies variability within the population (comprising age groups from 5 to 75 years of age). The AEC is assumed to also sufficiently cover local irritant effects in the eyes/airways.

  The AEC corresponds to the systemic/internal reference dose:
  AEL$_{\text{acute/medium-term/long-term}}$ of 17.9 mg/kg bw/d, assuming a human inhalation volume of 8.35 m^3/8 h for activity as described for volunteers in the study by Sethre et al. 2000a, and an average body weight of 60 kg.

As a result of the evaluation of the toxicological database for propan-2-ol, the following classification (labelling) according to Directive 67/548/EEC is proposed for the active substance propan-2-ol:

- Xi; R36 (Irritant; irritating to eyes), based on reversible eye irritation in rabbit studies reported in the secondary literature.
- R66 (Repeated exposure may cause skin dryness or cracking), based on local skin effects and reactions that have been described for human individuals exposed to formulations containing propan-2-ol and ethanol or to dilutions of propan-2-ol.
- R67 (Vapours may cause drowsiness and dizziness), based on neurological effects observed in rats already at atmospheric exposure to 3.75 mg/L for 6 h, and supported by an inhalation study with human volunteers (Sethre et al. 2000a).

Classification (labelling) according to Regulation (EC) No 1272/2008:

- Eye Irrit. 2; H319 (Eye irritation hazard category 2; Causes serious eye irritation)
- EUH066 (Repeated exposure may cause skin dryness or cracking)
- STOT SE 3; H336 (Specific target organ toxicity – single exposure, hazard category 3, narcosis; May cause drowsiness or dizziness).

2.2.1.2. Exposure assessment

Exposure of Professionals

The active substance propan-2-ol and the biocidal product, a disinfectant, are produced within the EU.

The following scenarios are covered by the exposure assessment in this report:
- Hand disinfection in hospitals (scenario 1)
- Secondary exposure to propan-2-ol (scenario 2)

For hand disinfection in hospitals a ready for use solution with 70 % w/w a.s. is used (scenario 1). The disinfectant is poured into the palms of one hand out of an automatic dispenser and the complete surface of both hands is moistened with the ready for use solution and let to dry.
Due to its physico-chemical properties, propan-2-ol evaporates during the application as hand disinfectant. The propan-2-ol concentration in air depends mainly on the applied dose, the room volume, the temperature (influence on vapour pressure), and the air exchange rate. Air exchange rates in hospitals depend on the use of the room.

The propan-2-ol concentrations of air are calculated with ConsExpo 4.1. For the reasonable worst case it is assumed that a nurse performs 4 hand disinfections in a patients room (3 patients per room) during half an hour. The last hand disinfection is performed before changing the room. During one shift 12 patient rooms are visited and after 90 minutes the nurse re-enters the first room. In total 48 disinfections are performed per shift. The concentration reaches a maximum during 4 hand disinfections in one room and it declines due to the air exchange in the room. At the end of the 90 minutes a certain proportion of propan-2-ol still remains in the air. For the reasonable worst case scenario the estimated 8-h time weighted average concentration (TWA) is **48 mg/m^3**.

Due to the evaporation of propan-2-ol the assessment of external dermal exposure is difficult to perform. The potential dermal exposure is limited to the time that propan-2-ol remains on hands. This time is calculated according to the formula presented in the TGD (EC 2003). According to these calculations the evaporation of 3 ml of 70 % propan-2-ol takes approx. 50 seconds. The exposed skin area is 840 cm^2 (palm and back of both hands). It is calculated that the applied volume of propan-2-ol (1806 mg / 840 cm²) totally evaporates within 50 sec. It is assumed that propan-2-ol with an area dose of **2.15 mg a.s./cm²** is available for dermal absorption for this short period of time respectively for one hand disinfection. A total amount of 3 ml biocidal product (2.58 g biocidal product) for one hand disinfection stays on both hands. The amount of 2580 mg biocidal product (corresponding to 1806 mg active substance) is multiplied by 48 disinfections per shift. The

resulting dermal exposure is estimated to be **86,688 mg a.s./person/day** for one working day (worst case assumption).

A secondary exposure to propan-2-ol using hand disinfectants cannot be excluded (scenario 2).
The inhalation exposure may occur to professional bystanders (e.g. nurse or cleaning staff) in patients' rooms where hand disinfection is performed. In a reasonable worst case it is assumed that the bystander stays in the room where 4 hand disinfections are performed. Taking into account the mean value of 40 mg/m^3 for 4 hand disinfections in one room for a duration of 30 min., the resulting 8-h time weighted average the inhalation exposure is **2.9 mg/m^3**. Dermal exposure is not expected since propan-2-ol evaporates within a short time during hand disinfection and a direct contact to the hand disinfection solution is not conceivable.

Exposure of Non-Professionals

Primary exposure
Intensive health care patient's visitors

Visitors of patients in intensive health care units have to disinfect their hands before entry. As proposed by the applicant it is assumed that up to 3 applications are performed per day. It was expected that the minimum room size for patients is about 25 m^3. This would be equivalent to an area of 10 m^2 and a height of 2.5 m, which is expected to be a minimum for patient rooms in hospitals. The air changing rate in normal intensive care units is about 3 h^{-1} according to German DIN 1946-4. It is assumed that application is a serial event performed every 2.5. h. After 2.5 h level of propan-2-ol is almost zero with the air change rates chosen above. It is assumed that exposure according to this scenario takes place on at most 30 subsequent days per year corresponding to medium-term exposure or to acute exposure if limited to one day. Additional uses of the same biocidal product by other persons are not considered.

Acute exposure	
Inhalation exposure:	0.5 mg/kg bw
Dermal exposure:	0.2 mg/kg bw
Total exposure:	0.7 mg/kg bw
Medium-term exposure	
Inhalation exposure:	1.7 mg/kg bw/d
Dermal exposure:	0.5 mg/kg bw/d
Total exposure:	2.2 mg/kg bw/d

Home dialysis
Patients performing home dialysis have to disinfect their hands before the operation. According to the applicant such a dialysis is performed in maximum once each day. Thus, patients are daily and therefore chronically exposed to the biocidal product and the active substance. The room volume is assumed as 25 m^3. This would be equivalent to a (small) room with an area of 10m^2 and 2.5 m height. The air exchange rate in private houses and the exposure duration are assumed to be 0.6 h^{-1} and 10 h, respectively. It is expected that persons performing home dialysis are of low activity and exercise level. Thus, for respiration rate the activity level "resting" is assumed.

Chronic exposure	
Inhalation exposure:	1.0 mg/kg bw/d
Dermal exposure:	0.2 mg/kg bw/d
Total exposure:	1.2 mg/kg bw/d

Secondary exposure
Visitors of home dialysis patients after primary exposure

Secondary non-professional exposure may occur if persons enter rooms after use of the biocidal product, for instance after home dialysis has been performed. Inhalation exposure may occur, whereas dermal exposure by contact to treated surfaces (hands) is considered negligible due to rapid evaporation. Secondary exposure estimates by inhalation should be in the same range as for primary exposure since uptake bases primarily on the vapour pressure of the active substance and secondarily exposed persons stay in the same room as the person that applies the biocidal product. Exposure might be acute or chronic depending on the frequency a person stays in rooms after use of the biocidal product. It is expected that persons performing home dialysis or which stay in such rooms are of low activity and exercise level.

Acute or chronic exposure
Adults
Inhalation exposure: 1.0 mg/kg bw(/d)
Total exposure: 1.0 mg/kg bw(/d)

Children
Inhalation exposure: 1.8 mg/kg bw(/d)
Total exposure: 1.8 mg/kg bw(/d)

Residues in food or feed from the intended use of propan-2-ol in PT 1, PT 2 or PT 4 biocidal products are not expected, as no direct or indirect contact with food or feed is intended. The representative biocidal product is an aqueous solution of 70 % propan-2-ol, that is not used directly on food or feed. Even so, use as a non-professional hand disinfectant or as surface disinfectant in food/feed processing areas could potentially lead to transfer of residues onto food. However, due to its high vapour pressure, the active substance evaporates completely within the time of application of the representative biocidal products, which are highly concentrated so that no transfer from treated hands or surfaces to food should occur. In the unlikely event that residue transfer does occur, the active substance will evaporate from the food before it is eaten. Therefore, dietary exposure to humans from the use of propan-2-ol as a biocide of PT 1, PT 2 or PT 4 can be excluded.

Cumulative/combined exposure

According to Article 10(1) cumulation effects from use of biocidal products containing the same active substance have to be taken into account. Since propan-2-ol is used for different product types cumulative exposure cannot be excluded.

Propan-2-ol is notified for the inclusion to Annex I of Directive 98/8/EC for PT1, 2, and 4. Primary exposure of professionals and non-professionals and secondary exposure of the general public and professionals is considered. For professional users it can be assumed that cumulative exposure to propan-2-ol from biocidal products of different product types is unlikely. Some product types are limited to specific professions. Thus, professional exposure to skin and hand disinfectants in PT1 is restricted to health care professions whereas professionals in the food area are only exposed to propan-2-ol from PT4. Thus, a person working in a restaurant or other similar institutions will not be exposed by disinfectants used by hospital staff for hand disinfection etc. and vice versa. However, professionals in hospitals may be exposed to biocidal products from PT1 and 2. Nevertheless, exposure to propan-2-ol is calculated on the basis of one shift. Thus, if exposure to both PT's is expected in one shift the time distribution of PT-specific uses in one shift has to be estimated. As a first assumption the PT with the highest exposure estimate is considered for cumulative exposure assessment.

<u>Accumulation of primary professional exposure</u>

An accumulation of professional exposure to non-professional and secondary exposure is not considered reasonable. Professional exposure is very regular frequent event compared to non-professional exposure. Thus, the fraction of non-professional exposure to total exposure is small, particularly if also the frequency of exposure is taken into account. For professional exposure assessment daily exposure is assumed, whereas non-professional and

secondary exposure is relatively rare.

Accumulation of primary non-professional exposure

Non-professional exposure to PT1 is restricted to visitors of hospital intensive health care units and to dialysis patients. Both exposure scenarios are relatively rare events. For the first scenario it is assumed that this is a medium-term scenario assuming that relatives visit hospital patients each day over a period of 30 days. However, if cumulative exposure is assessed this exposure scenario should be considered as acute scenario since it is unlikely that persons are exposed to all or even a few scenarios over a longer time period. The scenario for dialysis patients is not included into the acute exposure assessment because it is limited to very small and specific group. For PT2 and 4 only acute exposure scenarios have been identified as relevant for non-professional uses. For PT2 only the single application has been considered since multiple exposure is a very rare event. Other scenarios are unlikely if this scenario gets real. Thus, as a worst case it is assumed for non-professional exposure assessment:

1. All relevant exposure scenarios happen on the same day. Since this is a rare event it is considered as an acute cumulative scenario. Thus, estimates of all acute (medium-term) exposure scenarios are added and subsequent compared to the AEL_{acute} in section 2.1.1.3.

2. The exposure scenarios happen one after the other on subsequent days. This exposure is compared to the $AEL_{medium-term}$ or $AEL_{long-term}$ in in section 2.1.1.3. For exposure assessment the average is calculated from all acute and medium-/long-term exposure estimates.

Accumulation of secondary exposure

Secondary exposure of adults needs not to be accumulated to the non-professional primary exposure estimates since it is already integrated in the primary exposure assessment as discussed above. Thus, cumulative secondary exposure has only to be considered for children, which are unaccounted for primary exposure. Calculations are identical to adult exposure assessment. Professional secondary exposure is also covered by the primary professional exposure.

On the basis of the considerations above the following cumulative exposure estimates have been identified.

Exposure of professionals

Maximum exposure during one shift

Systemic inhalation exposure was calculated from the shift average concentration assuming a body weight of 60 kg, an inhalation rate of 10 m^3/ shift (default for light exercise according to Consexpo 4.1) and a shift duration of 8 h. For systemic dermal exposure a body weight of 60 kg was assumed. Professional secondary exposure is covered by the primary exposure.

Table 2-13 Cumulative exposure assessment for professional user

Exposure scenario	Exposure (mg/kg bw/[d])
Long-term exposure - internal dose	
PT1	**15.9**
PT2	**16.6**
PT4	**13.0**
Maximum Exposure	
PT2	**16.6**

Primary and secondary exposure of the general public

Table 2-14 Cumulative acute exposure assessment for the general public

Exposure scenario	Exposure (mg/kg bw/[d])
Acute exposure - internal dose	
Adults	
Intensive care unit visitors (PT1)	**2.2**
Household use (PT2)	**2.8**
Household use (PT4)	**4.6**
Total	**9.6**
Children	
Household use, secondary exposure (PT2)	**3.7**
Household use, secondary exposure (PT4)	**6.7**
Total	**10.4**

Table 2-15 Cumulative medium-/long-term exposure assessment for the general public

Exposure scenario	Exposure (mg/kg bw/[d])
Medium-term (long-term) exposure - internal dose	
Adults	
Average (PT1 intensive care unit visitors, PT1 Home dialysis, PT2, PT4)	**5.5**
Children	
Average (PT1, PT2, PT4)	**4.1**

2.2.1.3. Risk characterisation

Risk Assessment for Professionals

Propan-2-ol is used as 70 % (w/w) solution for hand disinfection by professionals. Dermal contact to the disinfection solution is the intended use and thus corresponding personal protective measures are simply not adequate. In a worst case assumption potential dermal exposure for the user is maximal 86688 mg/person/day. Due to the evaporation of dermally applied propan-2-ol, there is a potential inhalation exposure with an estimated 8-h time weighted average concentration (TWA) of 48 mg/m^3.

The calculation of the total internal body burden significantly depends on the methodology used for the calculation of dermal absorption. For the calculation of the internal body burden of propan-2-ol it is proposed to use data on dermal flux (0.85 mg/cm^2/h) instead of data on the percentage of dermal absorption. For inhalation route a 100% absorption percentage is estimated. The route-specific contributions of inhalation and dermal contact to the internal body burden are nearly identical values of 8 mg/kg bw/d for inhalation exposure and 7.9 mg/kg bw/d for dermal contact.

In the case of propan-2-ol, the AECs/AELs, based on the most sensitive systemic effect of acute CNS depression, were considered to cover reference values for other time frames, and thus common acute/medium-term/long-term reference values were established.

Taking the derived AEL of 17.9 mg/kg bw/d and the total internal body burden in scenario 1 (hand disinfection) of 15.9 mg/kg bw/d and scenario 2 (secondary exposure) of 0.48 mg/kg bw/d, the calculated exposure-to-AEL-ratios are below the value of 1 thus leading to no concern.

Relevant health risks to propan-2-ol are not anticipated to occur under the conditions specified.

Safety Measures for Professionals

Safety measures to prevent skin contact are *not* necessary according to risk assessment as well as compared to the German workplace limit value (AGW) of 200 ppm (resp. 500 mg/m^3). For a 'hand disinfection solution', personal protection measures (gloves) would be contradictory to the intended use. Reduction of respiratory exposure is desirable and, if necessary, possible by enhancing the air exchange rates.

Furthermore, contact with the eyes should be avoided because of eye irritation (Xi; R36) and measures to prevent a fire should be taken.

Risk Assessment for Non-Professionals

Table 2-16 Summary risk assessment for primary exposure to propan-2-ol

Exposure scenario	Exposure Adults (mg/kg bw/[d])	AEL (mg/kg bw/[d])	Exposure (% of AEL)
Acute exposure - internal dose Intensive care unit visitors	**Covered by medium-term exposure**		
Medium-term exposure - internal dose Intensive care units visitors			
Inhalation	**1.7**	**10.7**	**16**
Dermal	**0.5**	**10.7**	**5**
Total	**2.2**	**10.7**	**21**
Long-term (chronic) exposure - internal dose Home dialysis			
Inhalation	**1.0**	**10.7**	**9**
Dermal	**0.2**	**10.7**	**2**
Total	**1.2**	**10.7**	**11**

Table 2-17 Summary risk assessment for secondary exposure to propan-2-ol

Exposure scenario	Exposure Adults (mg/kg bw/[d])	AEL (mg/kg bw/[d])	Exposure (% of AEL)
Acute exposure - internal dose Home dialysis - Adults	**Covered by long-term exposure**		
Acute exposure - internal dose Home dialysis - Children	**Covered by long-term exposure**		
Long-term (chronic) exposure - internal dose Home dialysis - Adults			
Inhalation	**1.0**	**10.7**	**9**
Total	**1.0**	**10.7**	**9**
Long-term (chronic) exposure - internal dose Home dialysis - Children			
Inhalation	**1.8**	**10.7**	**17**
Total	**1.8**	**10.7**	**17**

Primary and secondary exposure to non-professionals and the general public is considered acceptable.

Safety Measures for Non-Professionals

Specific safety measures for non-professionals and the general public with respect to human health exposure assessment and risk characterisation are not required.

Cumulative/Combined Risk Assessment

On the basis of the considerations in 8.2.5 the following cumulative exposure estimates have been identified and compared to the relevant AEL

Professionals - Maximum exposure during one shift
Systemic inhalation exposure was calculated from the shift average concentration assuming a body weight of 60 kg, an inhalation rate of 10 m^3/ shift (default for light exercise according to Consexpo 4.1) and a shift duration of 8 h. For systemic dermal exposure a body weight of 60 kg was assumed. For details refer to 12.2.1.1. Professional secondary exposure is covered by the primary exposure.

Table 2-18 Summary cumulative risk assessment for professional users

Exposure scenario	Exposure (mg/kg bw/[d])	AEL (mg/kg bw/[d])	Exposure (% of AEL)
Maximum Exposure			
PT2	**15.9**	**17.9**	**89**

Primary non-professional and secondary exposure

Table 2-19 Summary cumulative acute risk assessment for the general public

Exposure scenario	Exposure (mg/kg bw/[d])	AEL (mg/kg bw/[d])	Exposure (% of AEL)
Acute exposure - internal dose			
Adults			
Total (PT1: Intensive care unit visitors PT2, PT4: Household use)	**9.6**	**10.7**	**90**
Children			
Total (PT2, PT4: Household use)	**10.4**	**10.7**	**97**

Table 2-20 Summary Cumulative medium-/long-term risk assessment for the general public

Exposure scenario	Exposure (mg/kg bw/[d])	AEL (mg/kg bw/[d])	Exposure (% of AEL)
Medium-term (long-term) exposure - internal dose			
Adults			
Average (PT1 intensive care unit visitors, PT1 Home dialysis, PT2, PT4)	**5.5**	**10.7**	**51**
Children			
Average (PT1, PT2, PT4)	**4.1**	**10.7**	**38**

The exposure estimates are up to 97% of the systemic AEL. Thus, it is concluded that cumulative exposure to propan-2-ol by application in PT1, 2 and 4 is acceptable for human health.

Aggregate exposure

Propan-2-ol may also occur in other biocidal product types as non-active substance. It is also used by consumers and workers in other fields that are not covered by biocide regulation (e.g. solvent in household cleaners or coatings).

Currently an aggregate exposure assessment for all sources of exposure is not possible. It can practically not be elucidated in detail at the moment, which kind of products will be authorised for all different areas of application and which influence may arise from exposure due to use in non-biocidal products. This lack of knowledge cannot be filled before the finalisation of active substance approval procedure and the REACH registration procedure. Propan-2-ol has been used for many years in various applications and graving non-accidental intoxications in this context has not been reported to our knowledge.
Therefore, the approval of propan-2-ol (PT1) is proposed.
Nevertheless, for national authorisation it is essential to consider whether exposure from all other sources than the foreseen biocidal use have a significant influence on risk assessment.

Overall conclusion

Acceptable exposure levels for acute, medium- and long-term exposure could be derived for propan-2-ol. Therefore, no risk to human health could be anticipated for the active

substance. All studies required by Directive 98/8/EC are available or statements for non-submission have been accepted. Different exposure scenarios or parameters might be relevant during product authorisation, therefore applicability of scenarios described in the report has to be evaluated and exposure should be re-assessed on a case-by-case basis.

2.2.2. Environmental Risk Assessment

The environmental risk characterisation is based on the concept of releases of active substance to the environment taking into account all relevant life cycle stages. The estimation of predicted environmental concentration (PEC) for the "dummy product" as well as the derivation of predicted no effect concentrations (PNECs) for different environmental compartments was performed according to the EU Technical Guidance Document (TGD) on Risk Assessment (2003) and to the Environmental Emission Scenarios for PT 1 (Royal Haskoning, 2004).

2.2.3. Fate and distribution in the environment

Biodegradation

Based on a test on ready biodegradability according to OECD 301 C ("modified MITI test (1)"), the a.s. propan-2-ol was shown to be readily biodegradable. Since according to the guideline the 10 day window criterion is not applicable to this test and the pass levels are met after 14 days, propan-2-ol is classified as "readily biodegradable.
Further studies on biodegradability in soil, water/sediment or sewage treatment plant were not deemed to be necessary.

Abiotic Degradation

Experimentally derived data on hydrolysis in water are not available. Propan-2-ol, as an alcohol, possesses no hydrolysable functional groups and therefore, is resistant to hydrolysis. For this reason, hydrolysis under environmental conditions is not expected.

Experimentally derived data on photolysis in water are not available. The molecular structure of propan-2-ol has no chromophore. In addition, for propan-2-ol a cut-off point of 210 nm is given in UV/VIS spectrophotometry. Therefore, no absorption between 290 nm and 750 nm takes place. Chemicals with UV/absorption maximum of < 290 cannot undergo direct photolysis in sunlight. Therefore, the substance is unaccessible for direct photodegradation in sunlight.

The vapour pressure of propan-2-ol at 25°C is 57.8 hPa and direct evaporation is expected, consequently. The Henry's law constant (0.82 $Pa \times m^3\ mol^{-1}$ at 25°C) indicates moderate volatility from water. Propan-2-ol present in the atmosphere will react with photo-chemically produced OH and NO_3 radicals. The half-life of propan-2-ol in the troposphere was estimated to be 3.1 days considering a global 24-hours mean OH-radical concentration of 5×10^5 OH radicals cm^{-3}.

Distribution and Mobility

Experimentally derived soil sorption coefficients are not available. A K_{OC} of 1.1 L/kg can be estimated based on the model PCKOCWIN v1.66. In addition, the K_{OC} was estimated according to a QSAR model described in EU TGD on Risk Assessment, Part III, chapter 4.3 (2003). Based on a log K_{OW} of 0.05 and the QSAR for alcohols, the K_{OC} was calculated to 3.3 L/kg. This K_{OC} is used for the environmental exposure assessment. Therefore, propan-2-ol is expected to exhibit only a weak adsorption in soils and sediments indicating a very high mobility of propan-2-ol in soil and a very low geoaccumulation potential. Adsorption of relevant amounts of propan-2-ol on soils and sediments is not expected.

The hydrosphere as well as the atmosphere is the target compartments due to calculations applying the fugacity model (Level 1) according to Mackay (1991). The results demonstrate that propan-2-ol is preferentially distributed to water (77.8 %) and air (22.1 %) in an

equilibrium atmosphere. The exact distribution between air and water in a non-equilibrium atmosphere is not known.
The distribution in the sewage treatment plant calculated by RMS using the SimpleTreat 3.0-model (a rate constant of 1 $h^{-1}$for STP was concluded since propan-2-ol is ready biodegradable) results in: release fractions to air 0.3 %, water 12.5 %, sludge 0 % and degraded fraction 87.1 %.

Bioaccumulation and Secondary Poisoning

Based on the physicochemical properties an approximate estimation of the bioconcentration factors (BCFs) can be calculated according to TGD (EC 2003). Applying the experimentally derived log K_{OW} of 0.05 results in a BCF_{Fish} of 0.22 L/kg ww and a $BCF_{Earthworm}$ of 0.85 L/kg ww. Consequently, the aquatic and terrestrial bioaccumulation potential of propan-2-ol can be assumed as low.

In consequence of the log K_{OW} < 3 and the low estimated BCF values, experimental studies are not required. Furthermore, no other indicators point to an intrinsic potential for bioconcentration. The surface tension, for instance, is 70.7 mN/m and thus, lies above the trigger value of ≤ 50 mN/m for surface active substances.

With regard to the low estimated BCF values in aquatic and terrestrial indicator species, propan-2-ol is not expected to accumulate in the environment. The risk of secondary poisoning is therefore assumed to be negligible via ingestion of contaminated food by birds or mammals.

2.2.4. Effects assessment

Aquatic Compartment including sediment

The active substance propan-2-ol is practically non-toxic to aquatic organisms. The lowest acute effect value for fish is the 96 h LC_{50} of 8692 mg a.s./L (*Pimephales promelas*) and for invertebrates an 48 h EC_{50} value of 2285 mg a.s./L for *Daphnia magna* was estimated. The toxicity to algae (*Pseudokirchneriella subspicata*) is also very low (E_rC_{50} = 10500 mg/L).

The estimation of long-term effects is limited to studies on invertebrates (*Daphnia magna*) and algae and the lowest chronic effect value is a 16 d NOEC of 141 mg/L determined for the endpoint growth. A $PNEC_{water}$ of 2.82 mg/L was derived from the available studies considering an assessment factor of 50.

Studies on sediment dwelling organisms are not provided by the applicant and are not necessary for the intended use. By using equilibrium partitioning method a $PNEC_{sediment}$ of 2.41 mg/kg ww could be estimated according to TGD on Risk Assessment (EC 2003), based on $PNEC_{water}$.

Inhibition of microbial activity (STP)

In a test on the respiration inhibition of activated sludge conducted according to OECD 209 guideline, the EC_{50} was calculated to be >1000 mg a.s./L nominal. For the risk assessment an EC_{50} value of 1000 mg/ L will be used as a worst case.

Since chemicals may cause adverse effects on microbial activity in STPs it is necessary to derive a $PNEC_{microorganisms,}$ STP. The $PNEC_{microorganisms,}$ STP is used for the calculation of the PEC/PNEC ratio concerning microbial activity in STPs. Considering an assessment factor of 100 to the EC_{50} of the respiration inhibition test a $PNEC_{microorganisms,}$ STP of 10 mg/L was derived.

Terrestrial Compartment

Direct exposure of the active substance to the soil compartment relating to the intended use does not occur and adsorption to soil is not expected. Therefore, tests on terrestrial organisms (inclusive inhibition to microbial activity) with propan-2-ol are scientifically not

justified.

Based on $PNEC_{water}$ and according to TGD on Risk Assessment (EC 2003) a $PNEC_{soil}$ of 0.496 mg/kg ww was derived by using equilibrium partitioning method.

Atmosphere

A $PNEC_{air}$ cannot be derived, but acute and subchronic inhalation studies with rats can be used as indication of adverse effects of chemicals on species arising from atmospheric contamination. Available results of these studies reveal that effect values are clearly above the environmental concentration in air. Therefore, no adverse effects on terrestrial organisms (mammals) are expected. As there are no studies on honeybees or terrestrial plants available, effects on these organisms cannot be assessed.

2.2.5. PBT and POP assessment

The PBT assessment for propan-2-ol was performed according to the guidance given in the TGD on risk assessment (2003) as described in part II, chapter 4.4 as well as following the REACH legislation.

P criterion: Half life > 40 d in freshwater or > 120 d in freshwater sediment or > 120 d in soil (according to the REACH legislation)
vP criterion: Half life > 60 d in freshwater or > 180 d in freshwater sediment or > 180 d in soil (according to the REACH legislation)

According to ready biodegradability tests, propan-2-ol is considered to be readily biodegradable. Generally, it is assumed that a chemical giving a positive result in a test of this type will rapidly biodegrade in the environment (Technical Guidance document, Guidance on Data Requirements for Active Substances and Biocidal products, 2000, chapter 7.0.2.2.1 Ready biodegradation). On the basis of this assumption, the P criterion as well as the vP criterion is not fulfilled.

B criterion: BCF > 2000 L/kg
vB criterion: BCF > 5000 L/kg

For propan-2-ol with a log K_{ow} less than three, the calculated bioconcentration factor for fish is 0.22 L/kg ww and for earthworm 0.85 L/kg ww. Therefore, the B criterion as well as the vB criterion is not fulfilled.

T criterion: Long-term NOEC for freshwater organism < 0.01 mg/L or CMR or endocrine disrupting effects

The lowest long-term NOEC is 141 mg/L for *Daphnia magna*, and thus clearly above the trigger value. There is no hint for CMR or endocrine disrupting effects. Therefore, the T criterion is not fulfilled.

Conclusion: The active substance **propan-2-ol is neither PBT - nor vP/vB** - candidate.

Assessment of Endocrine Disrupting Properties (ED)
There is no indication for endocrine disrupting properties of the active substance.

2.2.6. Exposure assessment

The biocidal product, a ready-to-use solution containing 70 % of propan-2-ol is used as hand and skin disinfectant in health care areas and other areas where hand disinfection is regarded appropriate to achieve desired levels of hygiene. It can be described as "leave-on" product. For the environmental exposure assessment of the biocidal product (b.p.) the following life cycle stages are selected as relevant:

- production of a.s.
- formulation of b.p.
- product used as "ready to use solution" for disinfections of skin and surfaces including subsequent cleaning of the treated areas.

The environmental release estimation for the life cycle stages "production" and "formulation" is not further considered for risk assessment. In general, PEC values for both life cycle stages are lower than the respective PNEC values for all environmental compartments.

For the use phase two approaches are calculated: (1) based on tonnage and (2) based on consumption. According to the EU-Report on the Workshop for PT 1-6 (2008) both approaches are presented. For the environmental risk assessment, the worst-case estimations are chosen to be relevant, respectively.

Aggregated Environmental Exposure Assessment

According to Article 10(1) of the BPD substances shall be included in Annex I, IA and IB also taking into account, **where relevant**, cumulation effects from the use of biocidal products containing the same active substances. This refers to environmental risk assessment of an active substance contained in different products of the same Product Type (PT) or of different PTs.

Propan-2-ol is notified for Annex I inclusion in PT 1, 2, and 4. The following uses are considered: PT 1 - skin and hand disinfectant in hospitals; PT 2 - disinfection of rooms, furniture and objects in the sanitary sector; PT 4 - assessment of small-scale applications (spraying of surfaces) / industrial kitchens / meat processing industry. As b.p. containing propan-2-ol are used in a wide dispersive way an aggregated environmental exposure assessment may be reasonable. According to the "Decision tree on the need for estimation of aggregated exposure" (BIP6.7 Decision Tree Agg Expo), the requirement for aggregated exposure estimations was checked for propan-2-ol. In summary, it has been concluded that no aggregated exposure assessment for propan-2-ol has to be performed as the biocidal uses of propan-2-ol is less than 10 % of the total tonnage produced and no specific biocidal emission patterns are identified.

2.2.7. Risk characterisation

Aquatic Compartment including Sediment

A $PNEC_{water}$ for the active substance propan-2-ol of 2.82 mg/L was derived from the lowest chronic effect value obtained with *Daphnia magna*. Further, a $PNEC_{sediment}$ of 2.41 mg/kg ww was determined by using equilibrium partitioning method based on the PNEC value for water. For the effect assessment of the sewage treatment plant a $PNEC_{microorganisms,}$ STP of 10 mg/L was derived.

During life cycle stage use a partial release of the b.p. via waste water - due to leakage or rinse-off and via cleaning of treated areas - to STP and subsequent to surface water and sediment can not be excluded. PEC values calculated for the application of the b.p. as skin and hand disinfection in hospitals based on consumption approach are higher compared to those ones based on the tonnage approach. Thus, the PECs based on consumption rates are selected for the environmental risk assessment.

Table 2-21 PEC/PNEC ratios for the use of the b.p. as skin and hand disinfectant in hospitals concerning STP, surface water and sediment

Compartment	PEC [µg/L]	PNEC [µg/L]	PEC / PNEC
STP	37.5	10000	3.75×10^{-3}
Surface water	3.75	2820	1.33×10^{-3}
Compartment	**PEC [µg/kg]**	**PNEC [µg/kg ww]**	**PEC / PNEC**
Sediment	3.21	2410	1.33×10^{-3}

The estimated PEC/PNEC values for sewage treatment plant, surface water as well as for sediment are below the trigger of 1. Thus, the use of the b.p. containing propan-2-ol indicates no unacceptable risk for the aquatic compartment.

Terrestrial Compartment including Groundwater

According to the intended use direct exposure to the soil compartment does not occur. Indirect release into the terrestrial compartment as a result of deposition from the atmosphere is possible. Propan-2-ol may also reach the soil compartment when sewage sludge is applied as fertilizer. However, it is not expected that soils are indirectly exposed as the active substance is highly volatile and will not adsorb to sewage sludge based on the low K_{oc} value. The $PNEC_{Soil}$ of 0.496 mg/kg ww was derived by using equilibrium partitioning method based on the $PNEC_{Water}$.

Table 2-22 PEC/PNEC ratio for the use of the b.p. as skin and hand disinfectant in hospitals concerning soil compartment and groundwater

Compartment	PEC [µg/kg]	PNEC [µg/kg ww]	PEC / PNEC
Soil	0.184	496	3.71 x 10-4
Compartment	**PEC [µg/L]**	**Trigger value [µg/L]***	**PEC / PNEC**
Groundwater	1.045 0.083#	0.1	10.45 0.83

*Quality standard for pesticides and biocidal products according to Directive 2006/118/EG (Annex I)
refined value of EU-location 'Chateaudun' (grassland) with FOCUS PEARL

The estimated PEC/PNEC value for soil is below the trigger of 1. Thus, the use of the b.p. containing propan-2-ol indicates no unacceptable risk for the soil compartment.

Since the legally admissible threshold for biocides in the groundwater is exceeded when propan-2-ol is applied as hand disinfectant, a refinement of the ground water assessment has been carried out using FOCUS PEARL. Four safe uses / scenarios could be identified. Therefore, the refined estimations with FOCUS PEARL revealed that the average concentration of propan-2-ol in groundwater (closest to the 80th percentile) remains below the threshold criteria 0.1 µg/L (according Drinking Water Directive as well as Groundwater Directive) but only for 4 EU-locations. According to the minutes of the 47th CA-Meeting (document: "CA-July12-Doc.6.1.b – Number of EU standard FOCUS-Scenarios which should demonstrate no risk for Annex I inclusion") it was agreed that FOCUS groundwater model PEARL should be used and that for active substance approval one safe use is sufficient. Thus, the use of the b.p. containing propan-2-ol indicates no unacceptable risk for the groundwater compartment.

Atmosphere

The main emission pathway during application step of the b.p. will be via air, because the substance evaporates completely within a short time due to the relatively high vapour pressure. Therefore, nearly the whole amount of substance applied is released to indoor air. For PEC estimation it was assumed that this air is emitted to the local outside air without deposition indoors. The exact distribution between air and waste water is not known, but as a reasonable worst-case it is assumed that 90 % of a.s. is emitted to air and 10 % to waste water.

The half-life of propan-2-ol in the troposphere was estimated to be 3.1 days. Therefore, the active substance propan-2-ol has a potential for long-range environmental transport referring to the Annex D of the Stockholm Convention on Persistent Organic Pollutants (17th May 2004): "… a chemical that migrates significantly through the air, its half-life in air should be greater than two days …". On the other hand, according to the EU TGD on Risk Assessment (Part II, chapter 3.7.2 (2003) effects on stratospheric ozone and acidification are not expected because propan-2-ol does not contain halogens, nitrogen or sulphur substituent and propan-2-ol is not listed as a substance of concern in the Regulation (EC) No 1005/2009 on substances that deplete the ozone layer.
The potential for global warming can not be characterised because there is no information available in the absorption spectrum in the range from 800 to 1200 nm.

As there are no ecotoxicological data on animal species for the air compartment available, no quantitative characterisation of risk by comparison of the PEC_{air} to $PNEC_{air}$ is possible. According to TGD on Risk Assessment (EC 2003, chapter 3.7) a chemical may be dangerous for the atmospheric environment at a low concentration, if it is classified as R48 ("Danger of serious damage to health by prolonged exposure"). This classification does not apply to propan-2-ol. Furthermore, inhalation studies with mammals can be used as indicators of adverse effects of volatile compounds on animals. The comparison of effect values obtained from inhalation studies with mammals (acute and subchronic studies with rats) with predicted environmental concentration for air indicate that there are no adverse effect of the volatile compound on terrestrial animals expected. Due to the intended use of the b.p. for product type 1 which is limited to indoor application and on basis of the available substance information the environmental risk of propan-2-ol for the atmosphere can be assumed as low.

Aggregated Risk Assessment

It has been concluded that no aggregated exposure assessment for propan-2-ol has to be performed. Therefore, no aggregated risk assessment is performed. Other uses beyond biocidal uses will mainly contribute to an aggregated exposure of propan-2-ol in the environment.

Overall Conclusion to the Environment

On basis of the risk assessment done for the different environmental compartments it can be concluded that the model formulation ("dummy product") containing the active substance propan-2-ol at a concentration of 70 % does not pose an unacceptable risk to the environment if used for skin and hand disinfection (product type 1, 'Human hygiene biocidal product').

Environmental Protection Measures

Animals are not expected to be exposed to the "dummy product" containing propan-2-ol or to the active substance during production, formulation, and use. No potential secondary poisoning of non-target animals towards propan-2-ol is anticipated. Therefore, special protection measures to protect animals are not required.

<u>General environmental precautions</u>:

No classification of the active substance and the model formulation ("dummy product")

containing 70 % of a.s. propan-2-ol due to environmental risks is proposed.

Because of the volatility of the a.s., the main exposure pathway to the environment is via air. As the intended use of the product is mainly indoors special precaution measures to air are not necessary.

A smaller amount of the biocidal product reaches the waste water system and propan-2-ol is classified to water contaminating class 1, which means slightly water contaminating according to the German "Administrative Regulation on the Classification of Substances Hazardous to Waters" (VwVwS). The product is miscible in water and decontamination is not possible. In general, discharge to water bodies is not allowed. Due to volatilisation potential and ready biodegradation of the active substance exposure to soil is negligible. Therefore, special measures or decontamination of soil is not necessary.

Instruction for safe disposal:

The a.s. propan-2-ol is highly flammable and is classified as hazardous waste according to the European Waste List 2001/118/EC. The Waste disposal code is 070604 and has to be given in the safety data sheet, the user manual and all documents for the waste management. The product and its container must be disposed of in a safe way, in compliance with any relevant legislation on the disposal of hazardous waste. Controlled disposal or incineration in accordance with the local registrations is recommended.
The requirements of the Regulation (EG) No. 1272/2008 (CLP-Regulation on Classification, Labelling and Packaging of substances and mixtures) has to be met.

2.2.8. Assessment of endocrine disruptor properties

Based on the provisional criteria specified in Article 5(3), second and third subparagraphs, of Regulation (EU) No 528/2012, propan-2-ol would not be considered as having endocrine disrupting properties.

Referring to environmental effect data there is no indication of endocrine disrupting properties of the active substance.

2.3. Overall conclusions

The outcome of the assessment for propan-2-ol in product-type 1 is specified in the BPC opinion following discussions at the 6th meeting of the Biocidal Products Committee (BPC). The BPC opinion is available from the ECHA web-site.

2.4. List of endpoints

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

3. SUMMARY TABLES

Human Health

Conclusion of risk characterisation for professional user, propan-2-ol, PT 1

Scenario	Relevant reference value [1] mg/kg bw/d	Estimated uptake [2] mg/kg bw/d	Estimated uptake/reference value (%)	Acceptable (yes/no)
1. Hand disinfection	17.9	15.9	89	yes

[1] AEL $_{acute/medium\text{-}term/long\text{-}term}$ = 17.9 mg/kg bw/d
[2] based on 100% absorption by inhalation, body weight 60 kg,
based on 0.85 mg/cm²/h dermal flux, exposed skin area 840 cm², exposure time 48 minutes

Conclusion of risk characterisation for indirect exposure, propan-2-ol, PT 1

Scenario	Relevant reference value [1] mg/kg bw/d	Estimated uptake [2] mg/kg bw/d	Estimated uptake/reference value (%)	Acceptable (yes/no)
2. Hand disinfection	17.9	0.48	3	yes

[1] AEL $_{acute/medium\text{-}term/long\text{-}term}$ = 17.9 mg/kg bw/d
[2] based on 100% absorption by inhalation, body weight 60 kg, dermal exposure not expected

Non-professional use - Summary of risk assessment for primary exposure

Scenario	Relevant reference value[2]	Estimated uptake mg/kg bw/d	Estimated uptake/reference value (%)	Acceptable (yes/no)
1a. Acute exposure Intensive care unit visitors	Covered by medium-term exposure			Yes
1b. Medium-term exposure Intensive care units visitors	$AEL_{acute/medium\text{-}term/long\text{-}term}$: 10.7 mg/kg bw/d	2.2 mg/kg bw/d	21	Yes
2. Long-term (chronic) exposure Home dialysis	$AEL_{acute/medium\text{-}term/long\text{-}term}$: 10.7 mg/kg bw/d	1.2	11	Yes

Non-professional use - Summary of risk assessment for secondary exposure

Scenario	Relevant reference value[2]	Estimated uptake mg/kg bw/d	Estimated uptake/reference value (%)	Acceptable (yes/no)
3a. + 4a. Acute exposure Intensive care units visitors	Covered by long-term exposure			Yes
3b. + 4b. Medium-term exposure Intensive care units visitors	Covered by long-term exposure			Yes

Scenario	Relevant reference value[2]	Estimated uptake mg/kg bw/d	Estimated uptake/reference value (%)	Acceptable (yes/no)
3c. Long-term (chronic) exposure Home dialysis - adults I	$AEL_{acute/medium-term/long-term}$: 10.7 mg/kg bw/d	1.0	9	Yes
4c. Long-term (chronic) exposure Home dialysis - children	$AEL_{acute/medium-term/long-term}$: 10.7 mg/kg bw/d	1.8	17	Yes

Summary cumulative acute risk assessment for the general public

Scenario	Relevant reference value[2]	Estimated uptake mg/kg bw/d	Estimated uptake/reference value (%)	Acceptable (yes/no)
Acute exposure				
Adults				
Total (PT1: Intensive care unit visitors PT2, PT4: Household use)	$AEL_{acute/medium-term/long-term}$: 10.7 mg/kg bw/d	9.6	90	Yes
Children				
Total (PT2, PT4: Household use)	$AEL_{acute/medium-term/long-term}$: 10.7 mg/kg bw/d	10.4	97	Yes

Summary cumulative medium-/long-term risk assessment for the general public

Scenario	Relevant reference value[2]	Estimated uptake mg/kg bw/d	Estimated uptake/reference value (%)	Acceptable (yes/no)
Medium-term (long-term) exposure				
Adults				
Average (PT1 intensive care unit visitors, PT1 Home dialysis, PT2, PT4)	$AEL_{acute/medium-term/long-term}$: 10.7 mg/kg bw/d	5.5	51	Yes
Children				
Average (PT1, PT2, PT4)	$AEL_{acute/medium-term/long-term}$: 10.7 mg/kg bw/d	4.1	38	Yes

Environment

Compartment	PNEC
Surface water	2.82 mg/L
Sediment	2.41 mg/kg ww
STP-microorganisms	10 mg/L
Soil	0.496 mg/kg ww

Summary table on calculated PEC/PNEC values					
Scenario	**PEC/PNECstp**	**PEC/PNECsw**	**PEC/PNECsed**	**PEC/PNECsoil**	**PEC/gw***
Skin and hand disinfectant	3.75×10^{-3}	1.33×10^{-3}	1.33×10^{-3}	3.71×10^{-4}	0.83

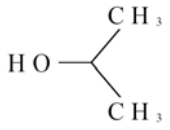
*Ground Water Quality Standard (0.1 µg/L) for pesticides and biocidal products according to Directive 2006/118/EG (Annex I)

Appendix I: List of endpoints

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

Active substance (ISO Common Name)	Propan-2-ol
Product-type	Bactericide, fungicide and virucide

Identity

Chemical name (IUPAC)	Propan-2-ol
Chemical name (CA)	2-Propanol
CAS No	67-63-0
EC No	200-661-7
Other substance No.	Index-Nr. 603-117-00-0 RTECS No.: NT8050000
Minimum purity of the active substance as manufactured (g/kg or g/l)	Min. 99 % (v/v)
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	Impurities other than water are volatile components as well as acid contents in variable compositions
Molecular formula	C_3H_8O
Molecular mass	60.09 g/mol
Structural formula	

Physical and chemical properties

Melting point (state purity)	-89.5 °C
Boiling point (state purity)	82.5 °C; 1013 hPa
Temperature of decomposition	No data
Appearance (state purity)	Colourless liquid with an initial diluted odour
Relative density (state purity)	0.78505 at 2 0°C
Surface tension	70.7 mN/m (c = 1g/L; T = 22 °C)
Vapour pressure (in Pa, state temperature)	5780 Pa; 25 °C
Henry's law constant (Pa m^3 mol^{-1})	0.80 Pa · m³/mol
Solubility in water (g/l or mg/l, state temperature)	Miscible with water
Solubility in organic solvents (in g/l or mg/l, state temperature)	miscible with acetone, alcohol and ether

Stability in organic solvents used in biocidal products including relevant breakdown products	Not applicable
Partition coefficient (log P_{OW}) (state temperature)	log P_{ow} = 0.05
Hydrolytic stability (DT_{50}) (state pH and temperature)	No hydrolysis
Dissociation constant	Not applicable
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	The UV/VIS spectra confirms to the molecular structure of Propan-2-ol. No absorption maximum >210 nm.
Photostability (DT_{50}) (aqueous, sunlight, state pH)	Not applicable
Quantum yield of direct phototransformation in water at Σ > 290 nm	Not applicable
Flammability	From the structural formula and composition of the substance it can be concluded that the substance does not evolve any flammable gases in contact with water or humid and that it is air substance stable at room temperature and is not pyrophoric.
Explosive properties	No explosive properties due to structural reason.

Classification and proposed labelling of the active substance

	Directive 67/548/EEC	**Regulation (EC) No 1272/2008**
with regard to physical/chemical data	F R11 (S2), S7, S16	GHS02 Danger Flam. Liq. 2 H225
with regard to toxicological data	Xi R36, R66*, R67 (S2), S24/25, S26	GHS07 Warning Eye Irrit. 2, STOT SE 3 H319, H336, EUH066*
with regard to fate and behaviour data	No classification is required	
with regard to ecotoxicological data	No classification is required	

*In addition to current classification/labelling of propan-2-ol, classification/labelling as R66 (EUH066) is proposed.

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	For the detection a glass capillary gas chromatography method coupled with FID was developed.
Impurities in technical active substance (principle of method)	For the detection a glass capillary gas chromatography method coupled with FID was developed. The method is described in Document III-A 4.1. The water content was determined with Karl Fischer Reagent Titration method.

Analytical methods for residues

Soil (principle of method and LOQ)	not required, no residues expected
Air (principle of method and LOQ)	residue definition: propan-2-ol GC-FID LOQ: 0.109 mg/m³ Open for validation data of GC-MS confirmatory method.
Water (principle of method and LOQ)	not required, no residues expected
Body fluids and tissues (principle of method and LOQ)	not required, not classified as T/T^+
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	not required, no residues expected
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	not required, no residues expected

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	Nearly 100 %,within 72 h (presumably much faster)
Rate and extent of dermal absorption for the active substance:	Absorption rate (transdermal flux) in rat study: 0.85 mg/cm²/h for aqueous solution containing 70 % propan-2-ol (by weight)
Rate and extent of dermal absorption for the representative product(s)[2]:	Since the biocidal product (dummy) consists only of the active substance and water toxicological properties can be derived from data provided for the active substance
Distribution:	Widely distributed. After 96 h, total ^{14}C tissue residues < 5 % of dose, < 2.4 % in individual tissues (based on data from i.v., oral, or inhalative exposure)
Potential for accumulation:	No evidence for accumulation
Rate and extent of excretion:	88-95 % of ^{14}C in 72 h: predominantly via exhalation (as CO_2, acetone, or propan-2-ol), up to 2 % in faeces, up to 8 % in urine, based on i.v., oral and inhalative administration
Toxicologically significant metabolite(s)	Acetone

Acute toxicity

Rat LD_{50} oral	4400 mg/kg bw
Rat LD_{50} dermal	No data for rat; rabbit: 12900 mg/kg bw
Rat LC_{50} inhalation	17100 mg/kg bw (47.5 mg/L air for 8 h; whole body, vapour)
Skin irritation	Not irritant
Eye irritation	Irritant **R36**
Skin sensitisation (test method used and result)	Non-sensitising (mouse, LLNA)

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

Repeated dose toxicity

Species/ target / critical effect	Rat: Systemic: CNS depression Local: Irritation of airways
Lowest relevant oral NOAEL / LOAEL	No suitable data, not required
Lowest relevant dermal NOAEL / LOAEL	No data
Lowest relevant inhalation NOAEL / LOAEL	Systemic (CNS depression): 500 ppm (1.25 mg/L air) or 286 mg/kg bw/d, 90-d rat Local: 100 ppm or 0.25 mg/L air at 6h/d, 5 d/wk, 90-d rat

Genotoxicity	No genotoxic potential

Carcinogenicity

Species/type of tumour	Rat: CNS depression, exacerbation of chronic nephropathy, no substance-related tumours Mouse: No increased frequencies of neoplastic lesions in males or females
lowest dose with tumours (rat, mouse)	5000 ppm or 12.5 mg/L air at 6 h/d, 5 d/wk (3000 mg/kg bw/d), 2-yr rat, highest dose tested

Reproductive toxicity

Species/ Reproduction target / critical effect	<u>Rat, oral, gavage:</u> *Parental (P_2 males, kidney):* nephrotoxicity *Reproductive:* mating index ↓ for P_2 males *Offspring:* bw↓ in early postnatal period (F1/F2), mortality during postnatal days 21-41 (F1)
Relevant parental NOAEL	< 100 mg/kg bw/d
Relevant reproductive NOAEL	500 mg/kg bw/d
Relevant offspring NOAEL	500 mg/kg bw/d
Species/Developmental target / critical effect	<u>Rat, oral:</u> *Maternal:* Mortality *Developmental:* Reduced foetal bw <u>Rabbit, oral:</u> *Maternal:* Reduced food consumption and bw, cyanosis, lethargy, laboured respiration, diarrhoea, mortality *Developmental:* No findings <u>Rat, inhalative:</u> *Maternal:* Unsteady gait, reduced food consumption and bw gain

	Developmental: Fetal growth retardation, increased incidence of malformations

Developmental toxicity

Lowest relevant developmental NOAEL / LOAEL	Rat, oral: 400 mg/kg bw/d Rabbit, oral: 480 mg/kg bw/d Rat, inhalative: ca. 2756 mg/kg bw/d (8.75 mg/L x 7 h/d)

Neurotoxicity / Delayed neurotoxicity

Species/ target/critical effect	Rat, oral gavage, developmental neurotoxcity study: *Maternal*: Mortality (1/35) *Developmental*: No findings Rat, acute, inhalative: Decrease in motor activity (M); further signs of CNS depression (sedation, ataxia, decreased arousal, decrease in neuromuscular function) observed at higher concentrations Rat, subchronic, inhalative: Hypoactivity; further signs of CNS depression (lack of startle reflex, ataxia, narcosis) observed at higher concentration; Mouse, subchronic, inhalative: Hypoactivity, narcosis, ataxia
Developmental neurotoxicity study NOAELs	*Maternal*: 700 mg/kg bw/d *Developmental*: 1200 mg/kg bw/d
Relevant acute neurotoxicity NOAEL	500 ppm or 1.25 mg/L air x 6 h (ca. 338 mg/kg bw) **R67** (R67 supported by results from subchronic and chronic inhalation studies in rats and mice)
Relevant subchronic neurotoxicity NOAEL	*13-week rat:* 500 ppm or 1.25 mg/L air x 6 h (ca. 286 mg/kg bw/d); : 500 ppm or 1.25 mg/L air x 6 h (ca. 386 mg/kg bw/d)

Other toxicological studies

.....	No data, not required

Medical data

Case reports	Ingestion (volunteers, case reports): 2.6-6.4 mg/kg bw/d for 6 wk: No adverse effects observed; 180 mg/kg bw/d for 3 d: No adverse effects observed; 280 mg/kg bw/d: Symptoms of toxicity
Study with human volunteers	Exposure to vapours: Exposure to ≥ 400 ppm for 3-5 min was reported to produce local effects (mild irritation of eyes, nose and throat); no irritation reported for 200 ppm. Exposure of volunteers to 400 ppm for 8 hours associated with neurological effects (disturbed postural balance; Sethre et al. 2000a)
Case reports	Dermal exposure: No irritation was observed after application of 0.5 ml undiluted propan-2-ol to volunteers for 4 h. However, local skin effects and reactions have been described in individuals exposed to formulations containing propan-2-ol and ethanol (redness, burning, itching, contact eczema, dry skin, skin fissures). There are some reports on reactions (positive patch test, contact dermatitis) resulting from exposure to propanol/propanol dilutions. It is considered plausible that cracking and dryness of skin may contribute to skin effects and reactions such as dermatitis. **R66**

Summary	**Value**	**Study**	**Safety factor**
Non-professional user			
ADI (acceptable daily intake, external long-term reference dose)	Not necessary, no residues in food expected		
$AEL_{acute/medium-term/long-term}$ General population	10.7 mg/kg bw/d (31.25 ppm for 8 hours/d)	Human volunteer study (Sethre et al. 2000a)	6.4
$AEL_{acute/medium-term/long-term}$ Professional workers	17.9 mg/kg bw/d (52.6 ppm for 8 hours/d)	Human volunteer study (Sethre et al. 2000a)	3.8

ADI (if residues in food or feed)	Not necessary, no residues in food expected
ARfD (acute reference dose)	Not necessary, no residues in food expected

Professional user

Reference value for inhalation (proposed OEL)	200 ppm	2-year inhalation rat	
Reference value for dermal absorption concerning the active substance:	Not determined		
Reference value for dermal absorption concerning the representative product(s)4:	Not determined		

Acceptable exposure scenarios (including method of calculation)

Professional users

Production of active substance:	Not assessed by the rapporteur under the requirements of the BPD	
Formulation of biocidal product	Not assessed by the rapporteur under the requirements of the BPD	
Intended uses	Hand disinfectant with 70 % active substance (ready for use solution)	
Mixing & Loading: No mixing & loading, ready for use product Application: The ready for use solution is poured into the palms of one hand out of an automatic dispenser. Form of exposure: Vapour of biocidal product (70 % a.s.) Duration: 50 seconds per application Frequency: 48 events per day, daily Model (inhalation): ConsExpo 4.1 Model (dermal): expert judgement Post-application: No post-application, the ready for use product itself is used up during the application process.	Potential inhalation exposure (all phases): Potential dermal exposure (all phases):	48 mg/m^3 86688 mg/person/day Area dose for one hand disinfection: 2.15 mg/cm^2

Secondary exposure Typical work in patients' rooms where hand disinfection is performed. Form of exposure: Vapour of b.p. Duration: 30 min. Model (inhalation): ConsExpo 4.1 Model (dermal): Expert judgement. Not expected since propan-2-ol evaporates within a short time during hand disinfection and a direct contact to the hand disinfection solution is not conceivable.	Potential inhalation exposure: 2,9 mg/m3
Non-professional users	Intensive health care units visitors, Consexpo 4.1, TGD on risk assessment (21% of AELmedium-term) Home dialysis, Consexpo 4.1, TGD on risk assessment (11% of AELlong-term)
Indirect exposure as a result of use	Exposure after use, e.g. home dialysis, Consexpo 4.1 (adults: 9 % of AELlong-term, children: 17 % of AELlong-term).
Cumulative/Combined Exposure	Acceptable for active substance approval (in maximum 97 % of AELacute for the general population).

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)	No hydrolysis
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	Not applicable, no absorption maximum >290 nm
Readily biodegradable (yes/no)	Readily biodegradable
Biodegradation in seawater	No data
Non-extractable residues	No data
Distribution in water / sediment systems (active substance)	No data
Distribution in water / sediment systems (metabolites)	No data

Route and rate of degradation in soil

Mineralization (aerobic)	No data
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50}lab (20°C, aerobic): No data

	DT_{90}lab (20°C, aerobic): No data DT_{50}lab (10°C, aerobic): No data DT_{50}lab (20°C, anaerobic): No data degradation in the saturated zone: No data
Field studies (state location, range or median with number of measurements)	DT_{50}f: No data
	DT_{90}f: No data
Anaerobic degradation	No data
Soil photolysis	No data
Non-extractable residues	No data
Relevant metabolites - name and/or code, % of applied active ingredient (range and maximum)	No data
Soil accumulation and plateau concentration	No data

Adsorption/desorption

Ka , Kd Ka_{oc} , Kd_{oc}	K_{OC} was estimated by QSAR-model for alcohols described in EU TGD (2003): K_{OC} = 3.3 L/kg
pH dependence (yes / no) (if yes type of dependence)	no

Fate and behaviour in air

Direct photolysis in air	No data
Quantum yield of direct photolysis	No data
Photo-oxidative degradation in air	tropospherical half-life of propan-2-ol: 3.1 d (according to Atkinson et al. (2006), reaction with OH radicals (global 24-hours-mean), concentration: 5 x 10^5 OH/cm^3)
Volatilization	Henry's law constant indicates moderate volatility.

Monitoring data, if available

Soil (indicate location and type of study)	---
Surface water (indicate location and type of study)	---
Ground water (indicate location and type of study)	---
Air (indicate location and type of study)	---

Chapter 5: Effects on Non-target Species

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

Species	Time-scale	Endpoint	Toxicity
Fish			
Pimephales promelas	96 h	Mortality	LC_{50} = 8692 mg/L (m) (calculated as geometric mean)
Invertebrates			
Daphnia magna	48 h	Immobility	EC_{50} = 2285 mg/L
Daphnia magna	16 d	Growth (length)	NOEC = 141 mg/L
Algae			
Pseudokirchneriella subspicata	48 h	Growth rate	E_rC_{50} = 10500 mg/L
Microorganisms			
Activated sludge (municipal sewage treatment plant)	3 h (static)	respiration inhibition	EC_{50} > 1000 mg a.s./L (nominal)

Effects on earthworms or other soil non-target organisms

Acute toxicity to	No data
Reproductive toxicity to	No data

Effects on soil micro-organisms

Nitrogen mineralization	No data
Carbon mineralization	No data

Effects on terrestrial vertebrates

Acute toxicity to mammals	No data
Acute toxicity to birds	No data
Dietary toxicity to birds	No data
Reproductive toxicity to birds	No data

Effects on honeybees

Acute oral toxicity	No data
Acute contact toxicity	No data

Effects on other beneficial arthropods

Acute oral toxicity	No data
Acute contact toxicity	No data
Acute toxicity to	No data

Bioconcentration

Bioconcentration factor (BCF)	Calculated BCF_{fish} = 0.22 L/kg ww Calculated $BCF_{earthworm}$ = 0.85 L/kg ww
Depuration time (DT_{50}) (DT_{90})	No data
Level of metabolites (%) in organisms accounting for > 10 % of residues	No data

Chapter 6: Other End Points

Residues in food or feed from the intended use of propan-2-ol in PT 1, PT 2, or PT 4 biocidal products are not expected, as no direct or indirect contact with food or feed is intended. The representative biocidal product is an aqueous solution of 70 % propan-2-ol, that is not used directly on food or feed. Even so, use as a non-professional hand disinfectant or as surface disinfectant in food/feed processing areas could potentially lead to transfer of residues onto food. However, due to its high vapour pressure, the active substance evaporates completely within the time of application of the representative biocidal products, which are highly concentrated, so that no transfer from treated hands or surfaces to food should occur. In the unlikely event that residue transfer does occur, the active substance will evaporate from the food before it is eaten. Therefore, dietary exposure to humans from the use of propan-2-ol as a biocide of PT 1, PT 2 or PT 4 can be excluded.

Appendix II: List of Intended Uses

Summary of intended uses

2-propanol is used as a broad-spectrum microbicide for hand disinfection in PT 1.

Object and/or situation	Product name	Organisms controlled	Formulation		Application				Applied amount per treatment			Remarks
(a)		(c)	Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	number		interval between applications (min)	g a.s./ml	Amount ml/treatment	g a.s./event	
						min	max		min max	min max	min max	
PT 1 (e.g. disinfect-tion of skin)	Propan-2-ol based disin-fectant	Obligate or facultative pathogenic bacteria (including mycobacteria, but excluding bacterial spores), fungi and viruses	Ready-to-use-solution	70 %	Hands rubbing	1	36/day	10	0.6	3/event	1.8/event	

(a) e.g. biting and suckling insects, fungi, molds; (b) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(c) GCPF Codes - GIFAP Technical Monograph No 2, 1989 ISBN 3-8263-3152-4); (d) All abbreviations used must be explained
(e) g/kg or g/l;(f) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench;
(g) Kind, e.g. overall, broadcast, aerial spraying, row, bait, crack and crevice equipment used must be indicated;
(h) Indicate the minimum and maximum number of application possible under practical conditions of use;
(i) Remarks may include: Extent of use/economic importance/restrictions

Appendix III: List of studies

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

LIST OF STUDIES FOR THE ACTIVE SUBSTANCE

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
III-A 2.7	[redacted]	[redacted]	Spectral data of 2-propanol: UV, MS and IR. [redacted]	No	-
III-A 2.7	[redacted]	[redacted]	Certificate of analysis. [redacted]	No	-
III-A 2.10	[redacted]	[redacted]	Ermittlung und Beurteilung von ausgewählten Aldehyden und Lösemitteln in der Luft am Arbeitsplatz im Arbeitsbereich, [redacted]	Yes	[redacted]
III-A 2.10	[redacted]	[redacted]	Ermittlung und Beurteilung von Isopropanol in der Luft und am Arbeitsplatz im Arbeitsbereich im Bereich Abfüllung Arzneimittel, [redacted]	Yes	[redacted]
III-A 2.10	[redacted]	[redacted]	Occupational exposure limits from: 2-Propanol [redacted]	No	-

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
III-A 2.10	[redacted]	[redacted]	Estimation of the environmental concentrations and the preliminary environmental risk assessment of 2-propanol in biocidal products [redacted]	Yes	[redacted]
III-A 2.10	[redacted]	[redacted]	Technical Guidance Document on Risk Assessment in support of Directive 93/67/EEC on risk assessment for new notified substances, Commission Regulation (EC) No. 1488/94 on risk assessment for existing substances (Parts I, II, III and IV) and Directive 98/8/EC of the European Parliament and the Council concerning the placing of biocidal products on the market. European Commission 2003 [redacted]	N	-
III-A 3.1.1/01	Merck	1996	The Merck Index, An encyclopedia of chemicals, drugs, and biologicals. Budavari S (Editor), 12th edition, Merck & Co, Inc Whitehouse station, NJ, USA, 889 [redacted] Published	No	-
III-A 3.1.1/02	CRC	2001	Data for 2-Propanol. Handbook of chemistry and physics. Lide DR (ed.), 82th ed.. CRC Press Boca Raton, USA, 31p [redacted] Published	No	-
III-A 3.1.2/01	Merck	1996	The Merck Index, An encyclopedia of chemicals, drugs, and biologicals. Budavari S (Editor), 12th edition, Merck & Co, Inc Whitehouse station, NJ, USA, 889 [redacted] Published	No	-
III-A 3.1.2/02	CRC	2001	Data for 2-Propanol. Handbook of chemistry and physics. Lide DR (ed.), 82th ed.. CRC Press Boca Raton, USA, 31p [redacted] Published	No	-

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
III-A 3.1.3/01	Merck	1996	The Merck Index, An encyclopedia of chemicals, drugs, and biologicals. Budavari S (Editor), 12th edition, Merck & Co, Inc Whitehouse station, NJ, USA, 889 [redacted] Published	No	-
III-A 3.1.3/02	Sax NI	1984	Dangerous properties of industrial materials. 6th ed.. Van Nostrand Reinhold Co., New York, USA, 1652 [redacted] Published	No	-
III-A 3.1.3/03	CRC	2001	Data for 2-Propanol. Handbook of chemistry and physics. Lide DR (ed.), 82th ed.. CRC Press Boca Raton, USA, 31p [redacted] Published	No	-
III-A 3.2/01	Riddick JA, Bunger WB, & Sakano TK	1986	Organic solvents – physical properties and methods of purification. Volume II, 4th Ed., John Wiley & Sons, New York, p 196-197 [redacted] Published	No	-
III-A 3.2/02	Daubert TE, & Danner RP	1989	Physical and thermodynamic properties of pure chemicals: data compilation. Design Inst Phys Prop Data, Amer Inst Chem Eng NY, NY, Hemisphere Pub Corp 5 Vol [redacted] Published	No	-
III-A 3.2/03	Yaws CL	1997	Vapor pressure. In: Handbook of chemical compound data for process safety: comprehensive safety and health-related data for hydrocarbons and organic chemicals: selected data for inorganic chemicals. Gulf. Publishing, Housten, Texas, pp 27-53 [redacted] Published	No	-
III-A 3.2.1/01	Snider JR, & Dawson GA	1985	Tropospheric light alcohols, carbonyls, and acetonitrile concentrations in the southwestern United States and Henry's Law Data. J Geophys Res 90, p 3797-3805 [redacted] Published	No	-

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
III-A 3.2.1/02	[redacted]	[redacted]	Estimation of the distribution behaviour in the environment and the bioconcentration factors of propan-2-ol. [redacted]	No	-
III-A 3.2.1/03	Howard PH	1990	Handbook of environmental fate and exposure data for Organic Chemicals. Lewis Publishers Inc., Chelsea, Michigan, USA, p. 304-309 [redacted] Published	No	-
III-A 3.2.1/04	Taft RW et al. [redacted]	1985	The molecular properties governing solubilities of organic nonelectrolytes in water. Nature 313, 384-386 [redacted]	No	-
III-A 3.2.1/05	[redacted]	[redacted]	Conversion of Henry's law constants for 2-propanol. [redacted]	Yes	[redacted]
III-A 3.3	Sax NI	1984	Dangerous properties of industrial materials. 6th ed.. Van Nostrand Reinhold Co., New York, USA, 1652 [redacted] Published	N	-
III-A 3.3	[redacted]	[redacted]	Certifcate of Analysis. [redacted]	No	-
III-A 3.4/01	CRC	2001	Data for 2-Propanol. Handbook of chemistry and physics. Lide DR (ed.), 82th ed.. CRC Press Boca Raton, USA, 31p [redacted] Published	No	-

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
III-A 3.4/02	SDBS	2007	SDBS No. 2149, 2-propanol (IR). SDBS Web : http://www.aist.go.jp/RIODB/SDBS/ (National Institute of Advanced Industrial Science and Technology) [redacted] Published	No	-
III-A 3.4/03	Gottlieb HE, Kotlyar V, & Nudelman A	1997	NMR Chemical shifts of common laboratory solvents as trace impurities. J Org Chem 62, p 7512-7515 [redacted] Published	No	-
III-A 3.4/04	CRC	2001	Data for 2-Propanol. Handbook of chemistry and physics. Lide DR (ed.), 82th ed.. CRC Press Boca Raton, USA, 31p [redacted] Published	No	-
III-A 3.4/05	[redacted]	[redacted]	Spectral data of 2-propanol: UV, MS and IR. [redacted]	No	-
III-A 3.4/06	[redacted]	[redacted]	Spectral data of 2-propanol: UV/Vis, GC-MS. [redacted]	No	-
III-A 3.4/07	[redacted]	[redacted]	Spectral data of 2-Propanol: UV/Vis and IR. [redacted]	No	-
III-A 3.4/08	[redacted]	[redacted]	Spectral data of 2-Propanol: MS and NMR (1H, 13C) [redacted]	No	-
III-A 3.4/09	[redacted]	[redacted]	Spectral data of 2-Propanol: NMR (1H) [redacted]	No	-

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
III-A 3.5	Riddick JA, Bunger WB, & Sakano TK	1986	Organic solvents – physical properties and methods of purification. Volume II, 4th Ed., John Wiley & Sons, New York, p 196-197 [redacted] Published	No	-
III-A 3.6	Riddick JA, Bunger WB, & Sakano TK	1986	Organic solvents – physical properties and methods of purification. Volume II, 4th Ed., John Wiley & Sons, New York, p 196-197 [redacted] Published	No	-
III-A 3.7	CRC	2001	Data for 2-Propanol. Handbook of chemistry and physics. Lide DR (ed.), 82th ed.. CRC Press Boca Raton, USA, 31p [redacted] Published	No	-
III-A 3.9/01	Dillingham EO, Mast RW, Bass GE, & Autian J	1973	Toxicity of methyl- and halogen-substituted alcohols in tissue culture relative to structure-activity models and acute toxicity in mice. J Pharm Sci 62, 22 [redacted] Published	No	-
III-A 3.9/02	Hansch C, Leo A, & Hoekman D	1995	Exploring QSAR. Hydrophobic, electronic, and steric constants. ACS Prof Ref Book. Heller SR, consult. ed., Washington, DC, Amer Chem Soc, p 7 [redacted] Published	No	-
III-A 3.11/01	Sax NI	1984	Dangerous properties of industrial materials, 6th ed.. Van Nostrand Reinhold Co., New York, USA, 1652 [redacted] Published	No	-
III-A 3.11/02	CRC	2001	Data for 2-Propanol. Handbook of chemistry and physics. Lide DR (ed.), 82th ed.. CRC Press Boca Raton, USA, 31p [redacted] Published	No	-
III-A 3.12/01	Sax NI	1984	Dangerous properties of industrial materials, 6th ed.. Van Nostrand Reinhold Co., New York, USA, 1652 [redacted] Published	No	-

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
III-A 3.12/02	Riddick JA, Bunger WB, & Sakano TK	1986	Organic solvents – physical properties and methods of purification. Volume II, 4th Ed., John Wiley & Sons, New York, p 196-197 [redacted] Published	No	-
III-A 3.13/01	CRC	2001	Data for 2-Propanol. Handbook of chemistry and physics. Lide DR (ed.), 82th ed.. CRC Press Boca Raton, USA, 31p [redacted] Published	No	-
III-A 3.13/02	Vazquez G, Alvarez E, & Navaza JM	1995	Surface tension of alcohol + water from 20 to 50 °C. J Chem Eng Data 40, 611-614, [redacted] Published	No	-
III-A 3.13/03	Kataoka S, & Cremer P	2006	Probing molecular structure at interfaces for comparison with bulk solution behavior: Water/2-Propanol mixtures monitored by vibrational sum frequency spectroscopy. J. Am. Chem. Soc. 2006, 128, p 5516-5522, [redacted] Published	No	-
III-A 3.13/04	Tahery R, & Modarress S	2005	A new and a simple model for surface tension prediction of water and organic liquid mixtures. Iran J. Sci. Technol., Transaction B, Engineering 29, B5, 501-509 [redacted] Published	No	-
III-A 3.13/05	[redacted]	[redacted]	Estimation of the surface tension of a 1g/L 2-Propanol solution in water. [redacted]	Yes	[redacted]
III-A 3.13/06	[redacted]	[redacted]	Isopropanol/2-Propanol, Partie-Nr.: 970, Determination of surface tension. [redacted]	Yes	[redacted]

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
III-A 3.14	CRC	2001	Data for 2-Propanol. Handbook of chemistry and physics. Lide DR (ed.), 82th ed.. CRC Press Boca Raton, USA, 31p [redacted] Published	No	-
III-A 3.15	CRC	2001	Data for 2-Propanol. Handbook of chemistry and physics. Lide DR (ed.), 82th ed.. CRC Press Boca Raton, USA, 31p [redacted] Published	No	-
III-A 4.1	Council of Europe	2005	EUROPEAN PHARMACOPOEIA 5.0 Monograph Isopropyl alcohol. 01/2005: 0970; p 1841-1842 [redacted] Published	No	-
III-A 4.2 Additional information	[redacted]	[redacted]	[redacted]	No	-
III-A 4.2b	NIOSH	1994	NIOSH Manual of Analytical Methods (NMAM), Fourth Edition, 8/15/94, Alcohols I, METHOD: 1400, Issue 2, 15 August 1994, 4p [redacted] Published	No	-
III-A 4.2b	OSHA	1997	Analytical Method No 109, 200 Constitution Avenue, NW Washington, DC 20210, 22p [redacted] Published	No	-
III-A 4.2c Justification for non-submission	[redacted]	[redacted]	[redacted]	No	-
III-A 4.2c Justification for non-submission	[redacted]	[redacted]	[redacted]	No	-
III-A 4.2d Justification for non-submission	[redacted]	[redacted]	[redacted]	No	-

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
III-A 5.3/01	[redacted]	[redacted]	BSEN1276 [redacted]	Yes	[redacted]
III-A 5.3/02	[redacted]	[redacted]	Vergelijkend onderzoek naar de desinfekterende werking van alcoholen in de Europese suspensie test. [redacted]	No	-
III-A 5.3/03	[redacted]	[redacted]	BSEN 1650 [redacted]	Yes	[redacted]
III-A 5.3/04	TylerR, & Ayliffe GAJ	1987	A surface test for virucidal activity of disinfectants: preliminary study with herpes virus. Journal of Hospital Infection 9:22-29 [redacted] Published	No	-
III-A 5.3/05	Gehrke C, Steinmann J, & Goroncy-Bermes P	2004	Inactivation of Feline Calicivirus, a surrogate of norovirus (formerly Norwalk-like viruses), by different types of alcohol in vitro and in vivo. Journal of Hospital Infection 56:49-55 [redacted] Published	No	-
III-A 6.1.1/01*	[redacted]	1971	Acute toxicity and limits of solvent residue for sixteen organic solvents. [redacted] Published	No	-
III-A 6.1.1/02	[redacted]	1972	Aliphatic alcohols and alky esters: narcotic and lethal potencies to tadpoles and to rabbits. [redacted] Published	No	-
III-A 6.1.1/03	[redacted]	1948	Further experience with the range finding test in the industrial toxicology laboratory. [redacted] Published	No	-

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
III-A 6.1.2/01	[redacted]	1948	Further experience with the range finding test in the industrial toxicology laboratory. [redacted] Published	No	-
III-A 6.1.3/01*	[redacted]	1980	Studies on inhalation toxicity of 2-propanol. [redacted] Published	No	-
III-A 6.1.3/02	[redacted]	1948	Further experience with the range finding test in the industrial toxicology laboratory. [redacted] Published	No	-
III-A6.1.4/01*	[redacted]	1999	Eye irritation: Updated reference chemicals data bank. [redacted] Published	No	-
III-A 6.1.4/02*	[redacted]	1996	Skin irritation: Reference chemicals data bank. [redacted] Published	No	-
III-A 6.1.4/03	Basketter DA, Chamberlain M, Griffiths HA, Rowson M, Whittle E, & York M	1997	The classification of skin irritants by human patch test. [redacted] Published	No	-
III-A 6.1.4/04	[redacted]	1980	Dose-response studies with chemical irritants in the albino rabbit eye as a basis for selecting optimum testing conditions for predicting hazard to the human eye. [redacted] Published	No	-
III-A 6.1.4/05	[redacted]	1975	Interspecies comparison of skin irritancy. [redacted] Published	No	-

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
III-A 6.1.5/01*	[redacted]	1998	Strategies for identifying false positive responses in predictive skin sensitization tests. [redacted] Published	No	-
III-A 6.2/01*	[redacted]	1998	Dermal absorption and pharmacokinetics of isopropanol in the male and female F-344 rat. [redacted] Published	No	-
III-A 6.2/02*	[redacted]	1988	Teratogenicity of n-propanol and isopropanol administered at high inhalation concentrations to rats. [redacted] Published	No	-
III-A 6.2/03	Turner P, Saeed B, & Kelsey MC	2004	Dermal absorption of isopropyl alcohol from a commercial hand rub: implications for its use in hand decontamination. J Hosp Infect 56, p 287 – 290 Published	No	-
III-A 6.2/04	Peschel O, Bauer MF, Gilg T, & von Meyer L	1992	Veraenderung von Begleitstoffanalysen durch perkutane Resorption propanolhaltiger Antiseptika. Blutalkohol 29, p 172 – 184 Published	No	-
III-A 6.2/05*	[redacted]	1994	Disposition and pharmacokinetics of isopropanol in F-344 rats and B6C3F1 mice. [redacted] Published	No	-
III-A 6.2/06	Bieber N.	2006	Absorption of alcohol from hand disinfection (Alkoholresorption nach Händedesinfektion) Dissertation Ernst-Moritz-Arndt-Universität Greifswald, Germany Published	No	-

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
III-A 6.4.1/01	[redacted]	1993	Toxic effects in rats of twelve weeks' dosing of 2-propanol, and neurotoxicity measured by densitometric measurement of glial fibrillary acidic protein in the dorsal hippocampus. [redacted] Published	No	-
III-A 6.4.3/01*	[redacted]	1994	Isopropanol 13-week vapor inhalation study in rats and mice with neurotoxicity evaluation in rats. [redacted] Published	No	-
III-A 6.4.3/02*	[redacted]	1994	Isopropanol 13-week vapor inhalation study in rats and mice with neurotoxicity evaluation in rats. [redacted] Published	No	-
III-A 6.4.3/03	[redacted]	1991	Toxicity of isopropyl alcohol (IPA). Part 2. Repeated inhalation exposures in rats. [redacted] Published	No	-
III-A 6.5/01*	[redacted]	1997	Isopropanol vapor inhalation oncogenicity study in Fischer 344 rats and CD-1 mice. [redacted] Published	No	-
III-A 6.5/02*	[redacted]	1997	Isopropanol vapor inhalation oncogenicity study in Fischer 344 rats and CD-1 mice. [redacted] Published	No	-
III-A 6.6.1/01*	Zeiger E, Anderson B, Haworth S, Lawlor T, & Mortelmans K	1992	Salmonella Mutagenicity Tests: V. Results from the testing of 311 chemicals. Environ Mol Mutagen 19 (Suppl 21), p 2 – 141 Published	No	-

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
III-A 6.6.1/02	von der Hude W, Behm C, Guertler R, & Basler A	1988	Evaluation of the SOS chromotest. Mutat Res 203, p 81 – 94 [redacted] Published	No	-
III-A 6.6.3/01*	[redacted]	1993	In vitro and in vivo assays of isopropanol for mutagenicity. [redacted] Published	No	-
III-A 6.6.3/02*	[redacted]	1987	Genotoxicity of three-carbon compounds evaluated in the SCE test in vitro. [redacted] Published	No	-
III-A 6.6.4/01*	[redacted]	1993	In vitro and in vivo assays of isopropanol for mutagenicity. [redacted] Published	No	-
III-A 6.7/01*	[redacted]	1997	Isopropanol vapor inhalation oncogenicity study in Fischer 344 rats and CD-1 mice. [redacted] Published	No	-
III-A 6.7/02*	[redacted]	1997	Isopropanol vapor inhalation oncogenicity study in Fischer 344 rats and CD-1 mice. [redacted] Published	No	-
III-A 6.8.1/01*	[redacted]	1994	Developmental neurotoxicity evaluation of orally administered isopropanol in rats. [redacted] Published	No	-

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
III-A 6.8.1/02*	[redacted]	1988	Teratogenicity of n-propanol and isopropanol administered at high inhalation concentrations to rats. [redacted] Published	No	-
III-A 6.8.1/03*	[redacted]	1994	Developmental toxicity evaluation of isopropanol by gavage in rats and rabbits. [redacted] Published	No	-
III-A 6.8.1/04*	[redacted]	1994	Developmental toxicity evaluation of isopropanol by gavage in rats and rabbits. [redacted] Published	No	-
III-A 6.8.2/01*	[redacted]	1995	Two-generation reproduction toxicity study with isopropanol in rats. [redacted] Published	No	-
III-A 6.9/01*	[redacted]	1995	Isopropanol: Acute vapor inhalation neurotoxicity study in rats. [redacted] Published	No	-
III-A 6.9/02	[redacted]	1998	Motor activity effects in female Fischer 344 rats exposed to isopropanol for 90 days. [redacted] Published	No	-
III-A 6.12/01	[redacted]	2003	5th Periodic Safety Update Report for: Alcohol solutions for disinfection of intact skin, [redacted] 40 pp.	Yes	[redacted]

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
III-A 6.12/01	[redacted]	2006	Isopropyl alcohol (CAS 67-63-0). Master file for a biocidal substance. [redacted] 37 p. [redacted] [redacted]	Yes	[redacted]
III-A 6.12/01	[redacted]	2007	Addendum Report 4 to 5th PSUR Periodica Safety Update Report for: Alcohol solutions for disinfection of intact skin [redacted] 41 pp. [redacted] [redacted]	Yes	[redacted]
III-A 6.12.2/01	Leow YH, & Freeman S	1995	Acute allergic contact dermatitis from Medi-Swabs®, with negative patch tests to the individual ingredients, including isopropyl alcohol. Contact Dermatitis 33, p 125 – 126 [redacted] Unpublished	No	-
III-A 7.1.1.1.1	Harris JC	1990	Rate of hydrolysis. In: Handbook of chemical property estimation methods (eds.: Lyman WJ, Reehl WF and Rosenblatt DH), American Chemical Society, Washington DC, 1990, pp. 7-1 – 7-48 [redacted] Published	No	-
III-A 7.1.1.1.2	U.S. EPA	1998	Fate, Transport and Transformation Test Guidelines OPPTS 835.2210 "Direct Photolysis Rate in Water by Sunlight". EPA 712-C-98-060, January 1998. [redacted] Published	No	-
III-A 7.1.1.2.1/01	Bridie AL, Wolff CJM, & Winter M	1979	BOD and COD of some petrochemicals. Water Res 13, p 627-630 [redacted] Published	No	-
III-A 7.1.1.2.1/02*	Gerike P, & Gode P	1990	The biodegradability and inhibitory threshold concentration of some disinfectants. Chemosphere 21(6), p 799-812 [redacted] Published	No	-

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
III-A 7.1.1.2.1/03	Price KS, Waggy GT, & Conway RA	1974	Brine shrimp bioassay and seawater BOD of petrochemicals. J Water Pollut Control Fed 46, p 63-77 [redacted] Published	No	-
III-A 7.1.1.2.1/05	[redacted]	2012	DOC Die-Away Test. Ready Biodegradability of Propanol-2 by Activated Sludge. [redacted]	Yes	[redacted]
III-A 7.1.1.2.1/06*	[redacted]	1993	Propyl alcohol [by using isopropyl alcohol, the number of the tested substanc:K-1085]'s biodegradability by microorganisms. [redacted]	No	-
III-A 7.1.1.2.3	Price KS, Waggy GT, & Conway RA	1974	Brine shrimp bioassay and seawater BOD of petrochemicals. J Water Pollut Control Fed 46, p 63-77 [redacted] Published	No	-
III-A 7.1.3	[redacted]	[redacted]	[redacted]	No	-
III-A 7.1.3	Technical Meeting	2005	Final Minutes of TM II 05: 4b. (general questions on environmental issues) Citric acid	No	-

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III-A 7.1.3	EC	2003	Technical Guidance Document on Risk Assessment in support of Directive 93/67/EEC on risk assessment for new notified substances, Commission Regulation (EC) No. 1488/94 on risk assessment for existing substances (Parts I, II, III and IV) and Directive 98/8/EC of the European Parliament and the Council concerning the placing of biocidal products on the market. European Commission 2003 [redacted] Published	No	-
III-A 7.3.1/01*	Atkinson R, Baulch DL, Cox RA, Crowley JN, Hampson RF, Hynes RG, Jenkin ME, Rossi MJ, & Troe J	2006	Evaluated kinetic and photochemical data for atmospheric chemistry: Volume II – Reactions of organic species, IUPAC Subcommittee on Gas Kinetic Data Evaluation for Atmospheric Chemistry. In: Atmos Chem Phy 6, pp. 3723-3729 & 3816-3820 of 3625-4055 [redacted] Published	No	-
III-A 7.3.1/01+02	EC	2003	Technical Guidance Document on Risk Assessment in support of Directive 93/67/EEC on risk assessment for new notified substances, Commission Regulation (EC) No. 1488/94 on risk assessment for existing substances (Parts I, II, III and IV) and Directive 98/8/EC of the European Parliament and the Council concerning the placing of biocidal products on the market. European Commission 2003 [redacted] Published	No	-
III-A 7.3.1/01+02	UNEP	2004	Stockholm Convention on Persistent Organic Pollutants (POP), entered into force 17 May 2004	No	-
III-A 7.3.1/02	Overend R, & Paraskevopoulos G	1978	Rates of OH radical reactions. 4. Reactions with methanol, ethanol, 1-propanol, and 2-propanol at 296K. J Phys Chem 82, p 1329-1333 [redacted] Published	No	-
III-A 7.3.1/03	Wallington TJ, Atkinson R, Winer AM, & Pitts JN jr	1987	A study of the reaction NO3 + NO2 + M $\rightarrow$ N2O5 + M (M=N2, O2). Int J Chem Kinet 19, p 243-249 [redacted] Published	No	-

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III-A 7.4.1.1/01*	[redacted]	1984	Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales promelas), [redacted] Published	No	-
III-A 7.4.1.1/02	[redacted]	1983	Estimating the acute toxicity of narcotic industrial chemicals to fathead minnows. [redacted] Published	No	-
III-A 7.4.1.1/03	[redacted]	1998	Acute toxicity test on Oryzias latipes to 2-Propanol. [redacted]	No	-
III-A 7.4.1.1/03	[redacted]	2007	Chemical Risk Information Platform (CHRIP) Total Search System for Chemical Substances: 2-Propanol; [redacted] Published	No	-
III-A 7.4.1.2/01	[redacted]	1998	Acute Immobilisation Test of 2-Propanol on Daphnia Magna. [redacted]	No	-
III-A 7.4.1.2/01	[redacted]	2007	Chemical Risk Information Platform (CHRIP) Total Search System for Chemical Substances: 2-Propanol; [redacted] Published	No	-

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
III-A 7.4.1.2/02	Bringmann G, & Kuehn R	1977	Befunde der Schadwirkung wasser-gefaehrdender Stoffe gegen Daphnia magna (The effects of water pollutants on Daphnia magna). Z Wasser Abwasser-Forsch 10, p 161-166 [redacted] Published	No	-
III-A 7.4.1.2/02	Bringmann G, & Kuehn R	1982	Ergebnisse der Schadwirkung wassergefährdender Stoffe gegen Daphnia magna in einem weiterentwickelten standardisierten Testverfahren. (Results of toxic action of water pollutants on Daphnia magna Straus tested by improved standardized procedure.) Z Wasser Abwasser Forsch 15, p 1-6 [redacted] Published	No	-
III-A 7.4.1.2/03	Calleja MC, Personne G, & Geladi P	1994	Comparative acute toxicity of the first 50 multicentre evaluation of In Vitro cytotoxicity chemicals to aquatic non-vertebrates. Arch Environ Contam Toxicol 26, p 69-78 [redacted] Published	No	-
III-A 7.4.1.2/03	Calleja MC, Personne G, & Geladi P	1993	The predictive potential of a battery of ecotoxicological test for human acute toxicity, as evaluated with the first 50 MEIC Chemicals. ATLA 21, p 330-349 [redacted] Published	No	-
III-A 7.4.1.2/03	Calleja MC, Personne G, & Geladi P	1994	Comparative acute toxicity of the first 50 multicentre evaluation of In Vitro cytotoxicity chemicals to aquatic non-vertebrates. Arch Environ Contam Toxicol 26, 69-78 [redacted] Published	No	-
III-A 7.4.1.2/04	Blackman RAA	1974	Toxicity of oil-sinking agents. Mar Pollut Bull 5, p 116-118 [redacted] Published	No	-

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III-A 7.4.1.2/05	Lilius H, Isomaa B, & Holmstrom T	1994	A comparison of the toxicity of 50 reference chemicals to freshly isolated rainbow trout hepatocytes and Daphnia magna. Aquat Toxicol 30 (1), p 47-60 [redacted] Published	No	-
III-A 7.4.1.2/05	Lilius H, Hästbacka T, & Isomaa B	1995	A comparison of the toxicity of 30 reference chemicals to Daphnia magna and Daphnia pulex. Environ Toxicol Chem 14(12), p 2085-2088 [redacted] Published	No	-
III-A 7.4.1.2/06*	Hermens J, Canton H, Janssen P, & De Jong R	1984	Quantitative structure-activity relationships and toxicity studies of mixtures of chemicals with anaesthetic potency: acute lethal and sublethal toxicity to Daphnia magna. Aquat Toxicol 5, p 143-154 [redacted] Published	No	-
III-A 7.4.1.3/01	[redacted]	1998	Growth inhibition test using Selenastrum caprocornutum to 2-Propanol. [redacted] Published	No	-
III-A 7.4.1.3/01	[redacted]	2007	Chemical Risk Information Platform (CHRIP) Total Search System for Chemical Substances: 2-Propanol; [redacted] Published	No	-
III-A 7.4.1.3/02	Bringmann G, & Kuehn R	1977	Grenzwerte der Schadwirkung wassergefährdender Stoffe gegen Bakterien (Pseudomonas putida) und Grünalgen (Scenedesmus quadricauda) im Zellvermehrungshemmtest. Z Wasser Abwasser Forsch 10, p 87-98 [redacted] Published	No	-

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III-A 7.4.1.3/02	Bringmann G, & Kuehn R	1978	Grenzwerte der Schadwirkung wassergefährdender Stoffe gegen Blaualgen (*Microcystis aeruginosa*) und Grünalgen (*Scenedesmus quadricauda*) im Zellvermehrungshemmtest. Vom Wasser 50, 45-60 [redacted] Published	No	-
III-A 7.4.1.3/02	Bringmann G, & Kuehn R	1980	Comparison of the toxicity thresholds of water pollutants to bacteria, algae, and protozoa in the cell multiplication inhibition test. Water Res 14, 231-241 [redacted] Published	No	-
III-A 7.4.1.3/03	Bringmann G, & Kuehn R	1978	Grenzwerte der Schadwirkung wassergefährdender Stoffe gegen Blaualgen (Microcystis aeruginosa) und Grünalgen (Scenedesmus quadricauda) im Zellvermehrungshemmtest. Vom Wasser 50, p 45-60 [redacted] Published	No	-
III-A 7.4.1.3/04*	Hsieh SH, Tsai KP, & Chen CY	2006	The combined toxic effects of nonpolar narcotic chemicals to Pseudokirchneriella subcapitata. Water Research 40, p 1957-1964 [redacted] Published	No	-
III-A 7.4.1.3/05	Calamari D, Galassi S, Setti F, & Vighi M	1983	Toxicity of selected chlorobenzenes to aquatic organisms. Chemosphere 12(2), p 253-262 [redacted] Published	No	-
III-A 7.4.1.3/05	EC	2003	Technical Guidance Document on Risk Assessment in support of Directive 93/67/EEC on risk assessment for new notified substances, Commission Regulation (EC) No. 1488/94 on risk assessment for existing substances (Parts I, II, III and IV) and Directive 98/8/EC of the European Parliament and the Council concerning the placing of biocidal products on the market. European Commission 2003 [redacted] Published	No	-

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III-A 7.4.1.3/05	ECOSAR	2004	ECOWin v0.99h: Ecosar Help-SAR neutral organics. 8p [redacted] Published	No	-
III-A 7.4.1.3/05	Galassi S, & Vighi M,	1981	Testing toxicity of volatile substances with algae. Chemosphere 10(10), 1123-1126 [redacted] Published	No	-
III-A 7.4.1.3/05	Verhaar HJM, Van Leeuwen CJ, Hermens JLM	1992	Classifying environmental pollutants. 1: Structure-activity relationships for prediction of aquatic toxicity. Chemosphere 25, p 471-491 [redacted] Published	No	-
III-A 7.4.1.3/06*	Cho CW, Jeon YC, Pham TP, Vijayaraghavan K, Yun YS	2008	The ecotoxicity of ionic liquids and traditional organic solvents on microalga Selenastrum capricornutum. Ecotoxicol. Environ Safety 71, p 166-171(1) [redacted] Published	No	-
III-A 7.4.1.3/06	[redacted]	2013	Estimation of the EC10 value from the algal test [redacted]		
III-A 7.4.1.4/01	Bringmann G, & Kuehn R	1977	Grenzwerte der Schadwirkung wassergefährdender Stoffe gegen Bakterien (Pseudomonas putida) und Grünalgen (Scenedesmus quadricauda) im Zell-vermehrungshemmtest. Z Wasser Abwasser Forsch 10, p 87-98 [redacted] Published	No	-
III-A 7.4.1.4/01	Bringmann G, & Kuehn R	1980	Comparison of the toxicity thresholds of water pollutants to bacteria, algae, and protozoa in the cell multiplication inhibition test. Water Res 14, p 231-241 [redacted] Published	No	-
III-A 7.4.1.4/02	Gerike P, & Gode P	1990	The biodegradability and inhibitory threshold concentration of some disinfectants. Chemosphere 21 (6), p 799-812 [redacted] Published	No	-

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III-A 7.4.1.4/03*	Klecka GM, Landi LP, & Rodner KM	1985	Evaluation of the OECD Activated Sludge, Respiration Inhibition Test. Chemosphere 14, p 1239-1251 [redacted] Published	No	-
III-A 7.4.2*	[redacted]	2006	Estimation of the distribution behaviour in the environment and the bioconcentration factors of propan-2-ol. [redacted] 15.11.2006, 9p [redacted]	No	-
III-A 7.4.3.1	[redacted]	1998	Prolongend toxicity test on Oryzias latipes to 2-Propanol. [redacted]	No	-
III-A 7.4.3.1	[redacted]	2007	Chemical Risk Information Platform (CHRIP) Total Search System for Chemical Substances: 2-Propanol; [redacted] Published	No	-
III-A 7.4.3.4/01	[redacted]	1998	Reproduction test of 2-Propanol on Daphnia magna. [redacted]	No	-
III-A 7.4.3.4/01	[redacted]	2007	Chemical Risk Information Platform (CHRIP) Total Search System for Chemical Substances: 2-Propanol; [redacted] Published	No	-

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
III-A 7.4.3.4/02*	Hermens J, Broekhuyzen E, Canton H, & Wegman R	1985	Quantitative-structure activity relationships and mixture toxicity studies of alcohols and chlorohydrocarbons: effects on growth of Daphnia magna. Aquat Toxicol 6, p 209-217 [redacted] Published	No	-
III-A 7.4.3.4/02*	Hermens J, Canton H, Janssen P, & De Jong R	1984	Quantitative structure-activity relationships and toxicity studies of mixtures of chemicals with anaesthetic potency: acute lethal and sublethal toxicity to Daphnia magna. Aquat Toxicol 5, p 143-154 [redacted] Published	No	-
III-A 7.4.3.4/03	Huels	1988	Huels-Bericht DL 106 (as cited in ECB IUCLID for propan-2-ol from 2000) [redacted] Unpublished	Yes	Huels
III-A 7.4.3.4/04	De Wolf W, Canton JH, Deneer JW, Wegman RCC, & Hermens JLM	1988	Quantitative structure-activity relationships and mixture-toxicity studies of alcohols and chlorohydrocarbons: reproducibility of effects on growth and reproduction of Daphnia magna. Aquat. Toxicol. 12, p 39-49 [redacted] Unpublished	No	-
III-A 7.5.1.3	Reynolds T	1979	An anomalous effect of isopropanol on lettuce germination. Plant Sci Lett 15, p 25-28 [redacted] Published	No	-
III-A 7.5.5	[redacted]	2006	Estimation of the distribution behaviour in the environment and the bioconcentration factors of propan-2-ol. [redacted] 15.11.2006, 9p [redacted] [redacted]	No	-

* key studies

LIST OF STUDIES FOR THE BIOCIDAL PRODUCT					
III-B 5.10	Wille B	1976	Possibility of the development of resistance to disinfectants in microorganisms. Zbl. Bakt. Hyg., 1. Abt. Orig. B, 162:217-220 [redacted] published	No	-
III-B 6.6	Brunner A	2004	Neue Krankenhausrichtlinien in der Schweiz und in Deutschland: SWKI-Richtlinie 99-3 und VDI 2167, Blatt1, 2004 [redacted] published	No	-
III-B 6.6	[redacted]	[redacted]	Occupational exposure limits from: 2-Propanol IUCLID-Dataset, 6 p. [redacted] [redacted]	No	-
III-B 6.6	TRGS 525	1998	Technische Regeln für Gefahrstoffe - Umgang mit Gefahrstoffen in Einrichtungen zur humanmedizinischen Versorgung Mai 1998 [redacted] published	No	-
III-B 6.6	Freijer JI, Cassee FR, van Bree L &	1997	Modelling of particulate matter deposition in the human airways. RIVM report 624029001, Bilthoven [redacted] published	No	-
III-B 6.6	DGKH	2002	Deutsche Gesellschaft für Krankenhaushygiene. Leitlinienentwurf: Ausführung und Betrieb von raumlufttechnischen Anlagen (RLT-Analgen) in Krankenhäusern Hyg. + Med. 27 (3) 106-113 [redacted] published	No	-
III-B 6.6	DIN 1946-4	2007	Raumlufttechnik- Teil 4: Raumlufttechnische Anlagen in Krankenhäusern. Deutschen Institut für Normung e.V. Berlin [redacted] published	No	-
III-B 6.6	Bremmer, H. J., Prud'homme de Lodder, L. C. H.;, van Engelen, & J. G. M.	2006	General Fact Sheet - Limiting conditions and reliability, ventilation, room size, body surface area. Updated version for ConsExpo 4. RIVM Report 320104002. [redacted] published	No	-
III-B 6.6	KlimaPartner	2007	Technisches Handbuch für Luft- und Klimatechnik (published) [redacted] published	No	-

III-B 6.6	The Engineering Tool Box	2005	Air Change Rates in some typical Rooms and Buildings (published) [redacted] published	No	-
III-B 7.1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
III-B 7.1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
III-B 7.1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
III-B 7.1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]