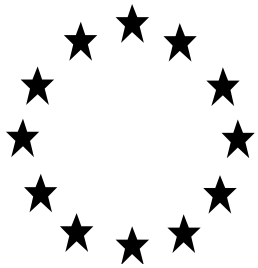
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



Biphenyl-2-ol

Product-type PT 1
(Qualysept Industrial)

March 2015

Spain

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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 [Biphenyl-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.

Biphenyl-2-ol (CAS no.90-43-7) was notified as an existing active substance, by LANXESS Deutschland GmbH and DOW Benelux B. V., hereafter referred to as the applicant, in Product-type 1.

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, Spain 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 Biphenyl-2-ol as an active substance in Product-type 1 was 31 July 2007, in accordance with Annex V of Regulation (EC) No 1451/2007.

On 12 July 2007, Spain competent authorities received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 31 October 2008.

On 2 June 2014, 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 Biphenyl-2-ol for Product-type 1, and, should it be approved, to facilitate the authorisation of individual biocidal products. In the evaluation of applications for product-authorisation, the provisions of Regulation (EU) No 528/2012 shall be applied, in particular the provisions of Chapter IV, as well as the common principles laid down in Annex VI.

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

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

[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

2. OVERALL SUMMARY AND CONCLUSIONS

2.1. Presentation of the Active Substance

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

This evaluation covers the use of Biphenyl-2-ol in Product-type 1, but it does not cover sodium 2-biphenylate. The most important mechanism is the interaction with bio-membranes. In the first step an adsorption of Biphenyl-2-ol to the cell membrane takes place. The greater the proportion of undissociated molecules of the biocide in the surrounding medium the stronger will be the adsorption. In further steps the function of membrane proteins is disturbed, substrate transport and ATP synthesis are inhibited. The cell membrane looses its semi-permeability and ions and organic molecules escape.

Specifications for the reference source are established.

The physico-chemical properties of the active substance and of the representative biocidal product have been evaluated and are deemed acceptable for the appropriate use, storage and transportation of the active substance and biocidal product.

Validated analytical methods are available for the determination of the Biphenyl-2-ol as manufactured and for the analysis of impurities. Validated analytical methods are also available for the determination of Biphenyl-2-ol in soil, water, air and food/feeding stuffs matrices. Other analytical methods are not required because Biphenyl-2-ol is not classified as toxic or highly toxic.

2.1.2. Intended Uses and Efficacy

The assessment of the biocidal activity of the active substance demonstrates that it has a sufficient level of efficacy against the target organism(s) and the evaluation of the summary data provided in support of the efficacy of the accompanying product, establishes that the product may be expected to be efficacious.

OPP is a multi-site bactericide and fungicide with basic activity at the cell wall, disruption of membrane potentials and general membrane permeability of cytoplasmic membrane.

Laboratory tests under a variety of use conditions have shown efficacy against potentially harmful germs as bacteria, fungi and yeasts), e.g. *Escherichia coli and Candida albicans.*The following tests were submitted:

EN1275 was performed against *Aspergillus niger*with the biocidal product after different exposure periods (1, 5 or 10 minutes). The results indicated that the number of colony-forming units (cfu) was reduced by 80%after 10 minutes.

Other test was performed according to Guidelines for the testing and evaluation of chemical disinfection procedures of the German Society of Hygiene and Microbiology and the results indicated that full efficacy was achieved with the test solution containing 80% of the intended use concentration after 1 minute residence time.

EN1650 was submitted to demonstrate the efficacy against the yeast *Candida albicans*. The results indicated that Qualysept Industrial was effective at 50 and 80% after 5min and 1min of contact time, respectively. Nevertheless, we know that this protocol is not appropriate to the intended use of this product type although the study demonstrates the efficacy of OPP as active substance against yeast.

EN1499 (hygienic hand washes: test methods – phase2/step2) was submitted to demonstrate

the efficacy against bacteria, *Escherichia coli* K12 with a contact time of 30 seconds. The results indicated that efficacy against bacteria is demonstrated at 30 seconds. This study was considered appropriate to the intended use of the product.

According to the data submitted, the efficacy against bacteria has been demonstrated appropriately. However, the efficacy against fungi and yeasts should be demonstrated at product authorization stage because the laboratory tests were not performed according to the protocol required for the intended use of the product.

Due to the unspecific mode of action (multi-site activity) a development of resistance against biocidal use of OPP is not expected.

The biocidal product is a ready-to-use formulation for hygienic hand disinfection and hand decontamination in hospitals and medical practice by professional users (Product-type 1). Likely in-use concentration is 2.0% w/v OPP. With the formulation Qualysept Industrial (OPP Hand Soap) hand washing and hand disinfection are achieved in one step.

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

2.1.3. Classification and Labelling

CURRENT CLASSIFICATION

Classification according to the CLP Regulation		
Hazard Class and Category Codes	Eye Irrit. 2 Skin Irrit. 2 STOT SE 3 Aquatic Acute 1	H319 H315 H335 H400
Labelling		
Pictograms	GHS07 GHS09 Wng	
Signal Word	Warning	
Hazard Statement Codes	H319: Causes serious eye irritation H315: Causes skin irritation H335: May cause respiratory irritation H400: Very toxic to aquatic life	
Specific Concentration limits, M-Factors		

PROPOSED CLASSIFICATION

The proposed classification and labelling for Biphenyl-2-ol according to Regulation (EC) No 1272/2008 (CLP Regulation) is:

Classification according to the CLP Regulation		
Hazard Class and Category Codes	Eye Irrit. 2 Skin Irrit. 2 STOT SE 3 Carc 2 Aquatic Acute 1 Aquatic Chronic 1	H319 H315 H335 H351 H400 H410

Labelling	
Pictograms	GHS07 GHS09 Wng
Signal Word	Warning
Hazard Statement Codes	H319: Causes serious eye irritation H315: Causes skin irritation H335: May cause respiratory irritation H351: Suspected of causing cancer H400: Very toxic to aquatic life H410: Very toxic to aquatic life with long lasting effects
Specific Concentration limits, M-Factors	

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

Hazard identification

Toxicokinetics and metabolism

A study was conducted in six human volunteers (males) to determine the degree of dermal absorption (Selim 6.2-03). The mean total absorption was 43.19. For the purpose of risk assessment in this dossier 43% dermal absorption of OPP through the skin will be applied. The mean total absorption, defined as the compound-related radioactivity present in the urine, feces (excluding tape strips) was 43.15% (concentration 0.4% ≅ 0.006 mg OPP/kg bw). This indicates that the ^{14}C-OPP derived radioactivity did not accumulate in the superficial layers of the skin.

A dermal study was conducted in six human volunteers (males) to obtain information on the metabolism of OPP (Bartels 6.2-01). Metabolites of OPP present in the urine samples from the study 6.2-03 were characterized. The major urinary metabolite was found to be the sulphate conjugate of OPP, accounting for 68.33% of the absorbed dose. Conjugation of OPP with glucuronic acid was less significant, accounting for only 3.46% of the absorbed dose. Hydroxylation of the phenol or phenyl ring, followed by conjugation was also shown to be significant, with phenylhydroquinoneglucuronide and 2,4'-dihydroxybiphenyl-sulfate representing 14.34% and 12.35% of the absorbed dose, respectively. Trace levels of unmetabolized parent compound (0.50% of absorbed dose) were found in early time interval samples only. No free phenylhydroquinone or phenylhydroquinone-sulphate were found in any of the urine samples (limit of detection = 0.25-0.59% absorbed dose). OPP, both free and conjugated, accounted for 73.0% of the total absorbed dose following dermal exposure to 0.4 mg test material for 8 h.

A study was conducted to determine the degree of oral absorption and to obtain information on the metabolism of ^{14}C-*ortho*-Phenylphenol (^{14}C-OPP) in the B6C3F1 mouse (McNett 6.2-02). The mean total absorption for the mice treatment groups, defined as the compound-related radioactivity present in the urine, faeces, tissues and carcass was 95-104% (concentration 25mg/kg and 1000 mg/kg). This suggests a low potential for bioaccumulation. The excretion of ^{14}C-OPP was rapid and complete by 12 - 24 h post-dosing with 74 - 98% of the recovered radioactivity in the urine and 6 - 13% in the faeces

An ADME study was conducted to obtain information on the metabolism of ^{14}C-*ortho*-Phenylphenol (^{14}C-OPP) in the B6C3F1 mouse and Fischer rats (McNett 6.2-02). In mice OPP was completely metabolized and rapidly eliminated via the urine predominantly as a sulphate and glucuronide conjugate of OPP. Qualitatively the extent of metabolism was comparable between mice and rats, although quantitative differences in the extent of OPP sulphation and glucuronidation were seen between these species. Binding to macromolecules or conjugation with intracellular glutathione occurs very rapidly thereby preventing the substance from being detectable or appearing free in the plasma.

No specific study of inhalation absorption of OPP is available.

Products of degradation (photolysis) in laboratory simulated ground waters

In laboratory experimental tests, it was observed that bisphenol-2-ol is degraded by photolysis in water (See Doc IIA, point 4.1.1.1.2 and 4.4) Two products of degradation are formed, benzoic acid and a diketohydroxy-compound, being this the higher proportion (maximum observes 13.7% of the OPP at day 1. The presence of these products is expected to be transiently as they are also quickly photodegraded.

In a QSAR evaluation, the environmental formation was predicted and also predicted lower toxicity than for OPP to aquatic media. Therefore, exposure and adverse effects in the aquatic media have been considered to be negligible and that the risk covered by the risk evaluated for the OPP. The risk of exposure for OPP and metabolites is considered negligible to aquatic media. Therefore it is still less likely the exposure to human to the product of transformation via the drinking water. In any case, the risk may be covered by the assessment of the OPP parent compound.

Therefore, additional toxicological information of this "products of transformation" (photolysis) is in principle not required as exposure to human via drinking water is expected to be negligible and risk may be covered from the assessment of parent compound. Nevertheless, it may be reasonable requiring performing an assessment for predicting the relative toxicity by read across from other similar substances in mammals, if enough information from similar substance is available.

Oral, dermal and inhalation absorption

A study was conducted in six human volunteers (males) to determine the degree of dermal absorption (Selim 6.2-03). The mean total absorption was 43.19. For the purpose of risk assessment in this dossier 43% dermal absorption of OPP through the skin will be applied.

A study was conducted to determine the degree of oral absorption and to obtain information on the metabolism of ^{14}C-*ortho*-Phenylphenol (^{14}C-OPP) in the B6C3F1 mouse ([redacted] 6.2-02). The mean total absorption for the mice treatment groups, defined as the compound-related radioactivity present in the urine, faeces, tissues and carcass was 95-104% (concentration 25 mg/kg and 1000 mg/kg). For the purpose of risk assessment in this dossier 100% oral absorption of OPP will be applied.

No specific study to determine the inhalation absorption of OPP is available. For inhalation application of OPP 100% absorption is assumed for risk characterization.

Acute toxicity

The oral acute toxicity was evaluated in the available document [redacted] 6.1.1-01. Under the conditions of this study, the acute oral LD_{50} of Dowicide 1 Antimicrobial (99.9% OPP) for male and female Fischer 344 rats was 2733 mg/kg (2730.3 mg OPP/kg), by nonlinear interpolation.

The dermal acute toxicity was evaluated in the available document [redacted] 6.1.2-01. The LD_{50} values for male and female rats were greater than 2000 mg/kg body weight and were not exactly determined.

The acute inhalation toxicity was evaluated in the available document Landry 6.1.3-01a. The LD_{50} values for male and female Fischer rats were greater than 36 mg/m^3 (0.036 mg/L) and were not exactly determined because the highest test atmosphere that could be generated was 0.036 mg/L, which is too low to provide an accurate determination (Landry 6.1.3-01b).

Irritation and Corrosivity

OPP is currently classified as Skin Irrit. 2 (H315: Causes skin irritation). The skin irritation was evaluated in the available document Gilbert 6.1.4-01/1981a in New Zealand White rabbits.

OPP is currently classified as Eye Irrit. 2 (H319: Causes serious eye irritation). To investigate eye irritation properties of OPP a test in the eye of albino rabbit was performed ([redacted] 6.1.4-01/1981b).

Based on the weight of evidence from existing information, it can be reasonably concluded that the substance is moderately irritant to the eye and because of its proven irritant effects on mucosa, it can be reasonably assumed that OPP is irritating to the airways when inhaled in high concentrations (e.g. pure substance dust) then it is classified as STOT SE 3 (H335: May cause respiratory irritation).

Sensitisation
OPP was tested for its skin sensitisation potential in Buehler test on Guinea pigs ([redacted] 6.1.5-01/1994b) with Dowicide 1 Antimicrobial (99.9% OPP). The animals were in apparent good health and gained weight over the study period. Therefore, under the conditions of this study, Dowicide 1 Antimicrobial (99.9% OPP) did not cause delayed contact hypersensitivity in guinea pigs.
A paper is submitted where OPP was tested for its skin sensitisation potential in Magnusson-Kligman test on Guinea pigs ([redacted] 6.1.5-02) with Preventol O Extra (OPP concentration ≥ 99.5 %). No animals were sensitized by Preventol O Extra.

In humans there are some case reports indicating positive patch test reactions in dermatological patients. Important data for humans is available from a volunteer study showing clearly negative results. See below section of "Human Data" and Table 2.2.1.1 1
The overall conclusion is that biphenyl-2-ol is not skin sensitizer in humans

Local effects
Based on the irritation effect of the assay dosing in the Screen Phase of the guinea pig sensitization study, a NOAEC of 7.5% is proposed.
No NOAEC/LOAEC may be deduced for medium or long term exposure. Therefore, only risk assessment may be performed for systemic effects for medium and long exposure.

Repeated dose toxicity
OPP was examined in a 21-day dermal study ([redacted] 6.3.2-01a) in Fischer 344 rats, in a 28-day oral study with Dog Beagle ([redacted] 6.3.1-01, 6.5-02), in a 91-day oral study [redacted] 6.4.1-01a) in male Fischer rats, in a 1-year oral study in dog ([redacted] 6.3.1-01, 6.5-02) and a 2-years oral study in Fischer rats ([redacted] 6.5-01a, 6.7-01a).
The NO(A)EL for dermal exposure in a 21-day dermal study in Fischer rat is 1000 mg/kg bw/day on the basis of the no systemic effects in any dose group.
The NO(A)EL for oral exposure in a 28-day oral study in dog Beagle is 300 mg/kg bw/day on the basis of the no adverse effects in any dose group.
The NO(A)EL for oral exposure in a 91-day oral study in male Fischer is 224 mg/kg/day (4000 ppm) on the basis of the urothelial hyperplasia and the necrotic foci in the bladders in the highest dose.
The NO(A)EL for oral exposure in a 1-year oral study in dog is 300 mg/kg/day on the basis of the no adverse effects in any dose group.
The NO(A)EL for oral exposure in a 2-year oral study in Fischer rats is 39 mg/kg/day on the basis of the increased incidence of simple urinary bladder hyperplasia in males and the increased incidence of urinary bladder transitional cell carcinoma in males.
No specific studies for subchronic and chronic dermal toxicity and for short, subchronic and chronic inhalation toxicity are available

Genotoxicity and carcinogenicity
Genotoxicity
In-vitro
The results of the Salmonella/Mammalian-Microsome Plate Incorporation Mutagenicity Assay (San 6.6.1-01) indicate that under the conditions of this study, a positive response was not observed with any of the tester strains either in the presence or absence of microsomal enzymes prepared from Aroclor induced rat and hamster liver.
The test substance Preventol O Extra (99.9 % OPP) is considered to be non mutagenic in the CHO-HGPRT Forward Mutation Assay, (Brendler 6.6.3-01) both with and without metabolic activation.
OPP was clastogenic in Chinese hamster ovary cells at cytotoxic concentrations. In the presence of S9 mix, phenylhydroquinone (metabolite produced from OPP) is formed which has a higher cytotoxic and clastogenic potential than OPP (Tayama 6.6.2-01).
In-vivo
Preventol O Extra (99.9 % OPP) was evaluated as non-genotoxic in the in vivo comet assay in hepatocytes and kidney cells of male mice ([redacted] 6.6.5-01).

Carcinogenicity
The carcinogenicity was examined in two combined chronic toxicity/oncogenicity testing studies:

- In the rat Fischer 344 ([redacted] 6.5-01a, 6.7-01a), where the urinary bladder showed evidence of a compound-induced neoplasia in the highest doses (male animals only). It was considered border-line at 4000 ppm (200 mg/kg body wt/day) as there was only a marginal and non-statistical increase in both urinary bladder hyperplasia and transitional cell carcinoma when compared to controls or 800-ppm males (39 mg/kg body wt/day). Evidence of a compound-induced neoplasia was not observed in female animals at any dose tested.
- In B6C3F1 mice ([redacted] 6.7-02a), where A statistically significant increased incidence of hepatocellular adenomas was observed in male mice of the 500 and 1000 mg/kgBW/day groups (in the middle and high dose groups) . There were no significant increases in tumours in female mice fed OPP.

For OPP there is convincing evidence that the carcinogenetic effects shown in rodents are threshold effects with an indirect and non-genotoxic mechanism and tumours observed in rodent species (liver tumours in mice and bladder tumours in rats) are not predictive of carcinogenicity for humans due to proven species differences. Based on the criteria for classification of Directive 2001/59/EC, liver tumours in sensitive strain of mice are not of relevance for classification.

In the WG and in the ad hoc follow up process for discussing the AF is was discused the relevant of tumours for humans. Th no relevant of the liver tumours in mice was agreed.
The bladder tumour observed in male rats has been discussed in deep in Doc IIA and considering the special studies related with the use of biphenol-2-ol in alkaline conditions.
There are evidences suggesting that these tumours in male rats are not relevant to human as the MOA is related with special sensitivity to alkaliniization in male rat bladder. However three ad hoc follow-up participants considered that the mechanisms of bladder tumour formation is not completely known and the relevance of these tumours for humans cannot be completely excluded. Therefore, biphenyl-2-ol may be classified as carcinogen Cat 2.

Reproductive and developmental toxicity
The teratogenicity of the OPP is examined in two studies:
(1) in Wistar rats ([redacted] 6.8.1- 01)
(2) in New Zealand White rabbits ([redacted] 6.8.1-02).

The relevant NOAEL for **maternal toxicity** adopted was **100 mg/kg bw/day** on the basis of the increased mortality (13%) in New Zealand White rabbits, gross pathologic alterations (ulceration and haemorrhage of the gastric mucosa, haemolysed blood in the intestinal tract and decreased ingesta) and histopathologic alterations (renal tubular degeneration and inflammation). The relevant NOAEL for **teratogenic toxicity** adopted was **250 mg/kg bw/day** (the highest assayed dose).on the basis of no adverse embryonal/fetal effects were observed at any dose level tested in New Zealand White rabbits
Two two-generation studies examined the impact of OPP in fertility in Sprague-Dawley rats ([redacted] 6.8.2-02a and [redacted] 6.8.2-01). The NOAEL for parental toxicity in rats is 35 mg/kg bw/d in males and females, based on the incidence of urothelial hyperplasia and calculi in the kidney and/or urinary bladder was increased in male rats. The NOAEL for development (F1) is 457 mg/kg bw/d in males and females, based on no adverse effects in any dose group
Neurotoxicity
OPP does not belong to a class of compounds for which a neurotoxic potential can be expected. In addition the available toxicity studies gave no indication of any relevant neurotoxic potential of the compound.
Human data
A short report entitled "Occupational medical experiences with *o*-Phenylphenol" is submitted (Heyne 6.12.1-01; no GLP). Occupational medical surveillance of workers exposed to *o*-Phenylphenol, performed every 3 years on a routine basis. The workers have been in the production of *o*-Phenylphenol in average for 13,9 years. During this period accidents with *o*-Phenylphenol or unwanted contamination with *o*-Phenylphenol haven't been recorded and

consultations of the Medical Department due to work or contact with *o*-Phenylphenol haven't been required. The Phenol-levels in urine have always been far below German biological tolerance level of 200 mg/L (formerly 300 mg/L). *o*-Phenylphenol did not reveal any unwanted effects in the workers. Especially no sensitization of airways or skin to *o*-Phenylphenol has occurred. The examinations have included the above laboratory parameters as well as clinical and technical examinations.
A short communication is submitted (Adams 6.12.6-01) where it is described two cases of allergic contact dermatitis due to occupational contact with OPP containing products. In both patients the dermatitis was extensive and severe. In the case 1, a 34-year-old medical laboratory assistant applied a common over-the-counter "medicated" cream to various parts of his body for "dry skin". Patch testing with the cream and *o*-Phenylphenol in 0.5% and 1% concentrations showed strong positive reactions at 72 h. In the case 2, a 57-year-old male machinist had experienced a recurring dermatitis on the hands, arms, trunk, thighs and feet for 25 years. A patch testing revealed a positive reaction to 1% *o*-Pheny1phenol in petrolatum, and a positive "provocative use test" from a suspected coolant which contained this preservative.
A short communication is submitted (Van Hecke 6.12.6-02) where it is described a case of allergic contact dermatitis due to occupational contact with OPP containing products. A 24-year-old machinist had had dermatitis of the hands for 10 months due to a coolant and a cleanser.
A paper is submitted (Schnuch 6.12.6-03) where it is examined the role of different preservatives in a large number of patients with suspected allergic contact dermatitis. Patch test data and data from the patients' history were collected from the 24 departments participating in the Information Network of Departments of Dermatology from 1 January 1990 to 31 December 1994. Patch test data from 28349 patients tested with preservatives of the standard series (SS), from 11485 patients tested additionally with a preservative series (PS), and from 1787 patients tested with an industrial biocide tray (IB) were evaluated. Nine of 24 centers applied patch tests for 24 h, the remainder (15 of 24) for 48 h. Readings were done at 72 h after application of the test chambers. The PS and IB contained OPP at a concentration of 1% in petrolatum. Of 11418 subjects tested, 59 showed an irritant or questionable result, 33 (0.3%) were positive in PS. Of 1785 subjects tested, 5 showed an irritant or questionable result, 5 (0.4%) were positive in IB.
A paper is submitted (Brasch 6.12.6-05) where the main purpose was to identify the most frequent contact allergens and reconsider the test concentrations. This study is a retrospective evaluation of patch test results with medical antimicrobials and preservatives, performed by eight centres of the IVDK (Informations verb und Dermatolocischer Kliniken) from 1989 to 1991. It was evaluated the patch test results and questionnaires of 2059 patients tested with a preliminary series of medical antimicrobials and preservatives where OPP was included. This series was tested in patients clinically suspected to suffer from contact allergy to preservatives. Of 2043 subjects tested with OPP (at a concentration of 1% in petrolatum), 6 showed a medium positive reaction, 8 an equivocal reaction and one an irritant reaction.
A paper is submitted (Geier 6.12.6-04) where 1132 patients were patch tested with a variety of "antiseptics/industrial chemicals". OPP was one of the test compounds. OPP was applied as a 1% solution in petrolatum. Of 1131 patients tested with OPP, 5 individuals (0.4%) showed positive reactions. One individual showed ambiguous results.
Other no critic studies with complementary information which does not contradict the results of the key studies are included in the next table.

Table 2.2.1.1-1: Effects of OPP in Humans

Doc IIIA Section No.	Type	Description	Results	Reference
6.12.1 Key study	Surveillance of manufacturing plant personnel	Medical surveillance of personnel involved in OPP production No. of workers exposed: 73 (2 ♀, 71 ♂) in average 13.9 years of medical supervision	No adverse effects. No airway or skin sensitisation towards OPP has occurred.	Heyne 6.12.1 (01)
6.12.6 Key study	Clinical cases	Two cases of allergic contact dermatitis due to occupational contact with OPP containing products (1) germicidal agent (2) coolant	allergic contact dermatitis in both cases due to OPP	Adams 6.12.6 (01)
6.12.6 Key study	Clinical case	One case of sensitivity to OPP due to occupational contact to a coolant containing OPP	Contact sensitivity to OPP in a coolant	Van Hecke 6.12.6 (02)
6.12.6 Key study	Multi-centre study	Patch tests on patients with suspected contact dermatitis. 11485 patients were tested additionally with a preservative series (PS) and 1785 were tested with an industrial biocide tray (IB). Occupational exposure was suspected in 17% of the cases	59 of 11418: irritative or questionable result in PS 33 of 11418: positive reaction in PS 5 of 1785: irritative or questionable result in IB 7 of 1785: positive reaction in IB	Schnuch 6.12.6 (03)
6.12.6 Key study	Study	retrospective study patch tests 1 % OPP was applied	6 of 2043: medium positive reaction 8 of 2043: equivocal reaction 1 of 2043: irritant reaction	Brasch 6.12.6 (05)
6.12.6 Key study	epidemiological study	1132 patients were patch tested with a variety of "antiseptics/industrial chemicals". OPP was one of the test compounds.	Of 1131 patients tested with OPP, 5 individuals (0.4%) showed positive reactions. One individual showed ambiguous results	Geier 6.12.6 (04)
6.12.6	Epidemiological study	Epidemiological study on metal workers. Patch tests with 1% OPP. 40 workers were tested. 39 of them presented with dermatitis of hands and/or forearms. 5 had incidences of dermatitis in the past.	OPP was not a contact allergen in any of the cases.	De Boer 6.12.6 (08)

Table 2.2.1.1-1: Effects of OPP in Humans

Doc IIIA Section No.	Type	Description	Results	Reference
6.12.6	epidemiological study	Epidemiological study on 424 metalworkers who were exposed to metal working fluid. Patch tests with 1% OPP on 277 patients.	2 of 277: positive reaction	Uter 6.12.6 (06)
6.12.1	Surveillance of manufacturing plant personnel	Regular medical examination and urine biomonitoring.	Medicinal surveillance and biomonitoring did not reveal findings of concern.	6.12.1 (02)

Other/special studies

A paper is submitted (Fukushima 6.10-01/AIII 6.10-1) where the effects of sodium *o*-phenylphenate (OPP-Na) and OPP on two-stage urinary bladder carcinogenesis in male F344 rats initiated with *N*-butyl-*N*-(4-hydroxybutyl)nitrosamine (BBN) were investigated. OPP-Na acts as a tumour promoter in the urinary bladder following initiation by BBN. OPP-Na alone also induced tumour formation in the urinary bladder and can therefore be considered a weak initiator in the two-stage model of carcinogenesis and a complete carcinogen. OPP had no significant tumour-promoting or initiating effects. The increase in urinary pH caused by OPP-Na but not by OPP might cause the difference in the carcinogenic potential of the two compounds.

A paper is submitted (Fujii 6.10-03/ AIII 6.10-2) where the effects of an alkalizer or an acidifier on bladder carcinogenesis induced by OPP or OPP-Na were examined. The results indicate that the administration of an alkalizer enhanced the carcinogenicity of OPP and the administration of an acidifier inhibited the carcinogenicity of OPP-Na to the rat urinary bladder. This suggests that the earlier finding that OPP-Na was more carcinogenic than OPP resulted from the higher alkalinity of OPP-Na.

A study is submitted ([redacted] 6.10-15/ AIII 6.10-3; no guideline; no GLP) where the possible role of prostaglandin-*H*-synthase (PGHS) in OPP-induced bladder tumour formation is investigated. OPP and phenylhydroquinone (PHQ) stimulate cyclooxygenase activity and are oxidised by PGHS. OPP, PHQ and 2-phenyl-1,4-benzo-quinone (PBQ) inhibit PGHS at higher concentrations.

Other no critic studies with complementary information which does not contradict the results of the key studies are included in the Table 2.2.1.1-2.

These effects of concern observed with Na/K salts (or OPP in alkaline condition) should be considered in the evaluation of the hazard and risk of products formulated or used in dilution in alkaline conditions.

Table 2.2.1.1-2: Other/special studies with OPP

Type of study	Dosage	Results	Reference
32-week, dietary, rats Key study	20000 ppm, with and without tumour initiator *ad libitum*	OPP had no significant tumour-promoting or -initiating effects in the urinary bladder.	[redacted]6.10 (01)/AIII 6.10 (1)
26-week, dietary, rats Key study	12500 ppm, with/without $NaHCO_3$ *ad libitum*	Urinary bladder tumourigenesis of OPP is enhanced by $NaHCO_3$.	[redacted]6.10 (03)/ AIII 6.10 (2)

Table 2.2.1.1-2: Other/special studies with OPP

Type of study	Dosage	Results	Reference
In-vitro interaction with PGHS Key study	OPP, PHQ, PBQ: 100 µM	OPP and PHQ stimulate cyclooxygenase activity and are oxidised by PGHS.OPP, PHQ and PBQ inhibit PGHS at higher concentrations.	[redacted] 6.10 (15)/ AIII 6.10 (3)
32-week, dietary, rats	12,500 ppm, with varying amounts of $NaHCO_3$ *ad libitum*	Morphological changes of the bladder epithelium, correlating with increased urinary pH.	[redacted] 6.10 (01)
32-week, dietary, rats	20,000 ppm, *ad libitum*	Reduced urinary osmolality. Increased pH and Na^+ correlate with tumourigenesis.	[redacted] 6.10 (04)
12-week, dietary, rats	0, 2500, 5000, 10,000, 20,000 ppm, *ad libitum*	At 20,000 ppm: morphological changes of the bladder luminal surface evident by SEM	[redacted] 6.10 (02)
90-day, dietary + acute DNA-binding study in rats	90-day study: OPP, SOPP: 2% in diet Acute assay: OPP, SOPP: 500 mg/kg	SOPP, but not OPP, caused regenerative hyperplasia of the urinary bladder. OPP-treated rats revealed renal damage. No interactions with DNA could be demonstrated for either compound.	[redacted] 6.10 (06)
8-week, dietary, rats	OPP: 1.25% with or without $NaHCO_3$ SOPP: 2% with or without NH_4Cl	Males are more sensitive to OPP than females under alkalinuric conditions with respect to bladder hyperplasia.	[redacted] 6.10 (07)
1-week, dietary, rats	OPP, SOPP: 0.1-2.0%	OPP and SOPP caused a dose-dependent increase in agglutinability of bladder epithelial cells by Con A which is an indication for carcinogenic potential.	[redacted] 6.10 (08)
Acute oral, rat	OPP, PHQ, PBQ: 700, 1400 mg/kg bw, single oral gavage, with or without inhibition of GSH synthesis	OPP treatment led to GSH depletion and eosinophilic degeneration of centrilobular hepatocytes. Inhibition of GSH synthesis aggravated hepatotoxicity of OPP.	[redacted] 6.10 (09)
Cytotoxicity test in primary rat hepato-	OPP, PHQ: 0–1 mM	OPP cytotoxicity is enhanced by monooxygenase inhibition and GSH depletion. PHQ-induced cell death can be inhibited by	[redacted] 6.10 (10)

Table 2.2.1.1-2: Other/special studies with OPP

Type of study	Dosage	Results	Reference
cytes		sulfhydryl compounds.	
In-vitro and in-vivo macro-molecular binding assay	^{14}C-OPP: 1 µCi In vivo: OPP, SOPP: 50-500 mg/kg, oral gavage, 16-18 h	A non-linear increase in macromolecular binding of OPP and SOPP was observed in vivo and in vitro. This may be caused by the saturation of detoxification pathways.	[redacted] 6.10 (11)
In-vitro metabolism of OPP	OPP: 1-100 µM	OPP is oxidised to PHQ and PHQ is oxidised to PBQ by cytochrome P-450. PBQ is reduced back to PHQ by cytochrome P-450 reductase (redox cycling).	[redacted] 6.10 (12)
In-vivo assay of DNA synthesis in bladder	OPP, SOPP: 2% in diet; 4–24 weeks	OPP and SOPP cause a proliferative response in renal pelvis and papilla when given at a dietary level of 2%.	[redacted] 6.10 (13)
In-vitro and in-vivo GSH conjugation	In-vitro study: 79 µg/mL In-vivo study: 1000 mg/kg, single oral dose	PHQ-GSH is excreted via the bile after OPP administration to rats. In vitro, PHQ-GSH can be formed non-enzymatically from PBQ and GSH or enzymatically from OPP and GSH.	[redacted] 6.10 (14)
In-vivo assay of DNA and protein adducts in rats	0, 15, 50, 125, 250, 500, 1000 mg/kg OPP, single oral gavage	OPP or its metabolites form protein, but not DNA, adducts in urinary bladder tissue.	[redacted] 6.10 (16)
Ten-week feeding study in rats	OPP: 1.25% in diet SOPP: 2.0% in diet 10 weeks	OPP and SOPP caused urothelial hyperplasia in rats as evident by histology and increased cell proliferation.	[redacted] 6.10 (17)
7 and 14 days feeding study in male B6C3F1 mice	0, 500, and 1000 mg/kg/day OPP in the diet for 7 and 14 days	The results indicate that OPP may be an agonist ligand for PPARα.	OPP_TOX_chronMaus_PPAR tumors_REPORT_2009-10

Effects assessment

The AELs were set as follows:

	Critical Study	Critical NOAEL	Assessment factor	AEL
Short exposure	teratogenicity oral study in New Zealand White rabbits	100 mg/kg bw/day	100	1 mg/kg bw/day
Mid exposure	2-years oral study	39 mg/kg/day for males	100	0.4 mg/kg bw/day
Long exposure	2-years oral study	39 mg/kg/day for males	100	0.4 mg/kg bw/day

Reasons for stablishing critical endpoints

The acute AEL for risk characterization was deduced from a teratogenicity oral study in New Zealand White rabbits ([redacted] 6.8.1-02). The relevant NOAEL for maternal toxicity adopted was 100 mg/kg bw/day on the basis of the increased mortality (13%), gross pathologic alterations and histopathologic alterations. Therefore, considering an assessment factor of 100, an AELacute of 1 mg/kg bw/day was calculated.

For mid and long term exposure, an Acceptable Exposure Level (AEL) value for repeated use is deduced from the NO(A)EL for chronic oral exposure in a 2-years oral study (Wahle 6.5-01a, 6.7-01a). The NOAEL is 39 mg/kg/day on the basis of the increased incidence of simple urinary bladder hyperplasia in males and the increased incidence of urinary bladder transitional cell carcinoma in males. . An AF=100 was stablished after a follow up discussion (See comment below). Therefore, considering an assessment factor of 100, an AELmedium and AELlong of 0.39 mg/kg bw/day was calculated.

Conclusion of the follow up discussion for stablishing AF

In the combined chronic toxicity and carcinogenicity study of [redacted] (1996), the transitional cell carcinoma occurred in rats treated with biphenyl-2-ol at 200 mg/kg bw/d, while the same effect was reported in rats at 270 mg/kg bw/d after life span administration of sodium biphenylate ([redacted] 1985). The NOAEL of 39 mg/kg bw/d from [redacted] study, to be used for the derivation of the reference values, would be 5-fold lower than the LOAEL of 200 mg/kg bw/d for transitional cell carcinoma. Overall, the rat seemed to be the most sensitive species, since the administration of biphenyl-2-ol to mice and dogs did not lead to adverse effects in the urinary bladder, and male rats appeared to be more susceptible to bladder tumours than the female rats. The male rat is in general considered much more susceptible to bladder changes including tumours related to local effects than other animal species and humans.

Three ad hoc follow-up participants considered that the mechanisms of bladder tumour formation is not completely known and the relevance of these tumours for humans cannot be excluded, therefore they proposed a margin of safety of 1000 from the LOAEL of 200 mg/kg bw/d, that would result in an additional assessment factor of 2.

However, given the bladder tumours species sensitivity, five participants agreed that an assessment factor of 100 applied to the conservative NOAEL of 39 mg/Kg bw/d would provide an adequate margin of safety for humans.

The eCA supported the majority view and an AF of 100 is applied.

The AELlong-term and AELmedium-term are rounded to 0.4 mg/kg bw/d

End points for Local effect assessment

For local effects, the NOAEC for short exposure is 7.5% on the basis of irritation effect of the assay dosing in the Screen Phase of the guinea pig sensitization study ([redacted] 6.1.5-01/1994b).

No NOAEC/LOAEC may be deduced for medium or long term exposure.

Conclusion of classification for carcinogenicity
There are evidences suggesting that these tumours in male rats are not relevant to human as the MOA is related with special sensitivity to alkalinisation in male rat bladder. However, the mechanisms of bladder tumour formation is not completely known and the relevance of these tumours for humans cannot be completely excluded. Therefore, biphenyl-2-ol may be classified as carcinogen Cat 2

Exposure assessment

The human exposure assessment towards the active substance, Biphenyl-2-ol or Qualysept Industrial (OPP Hand Soap) as biocidal group Product-type 1 (Human hygiene product) has been carried out considering the foreseen uses by the Applicant. Qualysept Industrial (OPP Hand Soap) is a product for hygienic hand disinfection (Product-type 1). After WGV2014 in ad hoc follow-up, it was decided that efficacy is only demonstrated against bacteria after 30 seconds contact time whereas efficacy against fungi and yeasts should be demonstrated at product authorisation stage.

The OPP representative formulation is presented as a 2% w/v concentration.It is intended for use in hospitals and medical practice by professional users. These users comprise adults only.

Non-professional exposure as well as secondary exposure is not foreseeable; the product is intended to be used by professionals in health care services only.

The assessment of human exposure was performed according to the TNsG on Human Exposure to Biocidal Products (2002, 2007, taking into account User Guidance to report 2002) and the exposure models contained in the computer programme ConsExpo 4.1.

Human exposure assessment for professional users

The application of biocidal products containing Biphenyl-2-ol as hand disinfection in health care units by professionals can result in direct exposure via skin contact or via inhalation, but the oral ingestion is not considered as a potential direct route for exposure. Professional exposure is assumed to be chronic.

For the purpose of the professional assessment for hand disinfection (PT 1), the hand washing /liquid soap scenario incorporated into ConsExpo 4.1 is used (RIVM report 320104001/2006). The model is adapted to the actual situation by accounting for the potential inhalation of Biphenyl-2-ol vapours during hand disinfection (using the exposure to vapours model in ConsExpo) as well as the recommended instructions for use applicable to professional users. For hand disinfection 3 mL of Qualysept Industrial is to be evenly spread in the hands, followed by foam with water and wash for 30 seconds total contact time. Exposure is terminated by rinsing with water.

Risk characterisation

Exposure levels for professional users are within acceptable margins of safety assuming a frequency of use of 10 events/day on a chronic basis.

Risk Assessment for Professionals

Chronic Exposure Scenario	Exposure Adults (mg/kg bw/[d])	AEL (mg/kg bw/[d])	Exposure % AEL
Hand disinfection using liquid soap, 30 seconds /event; 2%OPP, 20 events /day, Tier 1			
Inhalation	5.36E-04	0.4	0.13
Dermal	0.71	0.4	178
Total	0.71	0.4	178
Chronic Exposure Scenario	Exposure Adults (mg/kg bw/[d])	AEL (mg/kg bw/[d])	Exposure % AEL
Hand disinfection using liquid soap, 30 seconds /event; 2%OPP, 10 events /day, Tier 2			
Inhalation	2.68E-04	0.4	0.07
Dermal	0.35	0.4	87
Total	0.35	0.4	87

The biocidal product Qualysept Industrial (Biphenyl-2-ol Hand Soap) is classified as irritant to skin due to co-formulants. This is the current precautionary evaluation by the RMS due to the absence of an acceptable test with the product which may be overruled by submission of e.g. sound experimental data on product authorization level.

2.2.2. Environmental Risk Assessment

2.2.2.1. Fate and distribution in the environment

Considering the hydrolytic stability determined under stringent temperature conditions and at different pH values, it is not expected that hydrolytic processes will contribute to the degradation of OPP in the aquatic systems (estimated DT_{50}> 1 year).

OPP is rapidly photodegraded in sterile aqueous 0.01 M phosphate buffer (experimental DT_{50} = 0.3 days). Diketohydroxy-compound (maximum 13.6% AR) and benzoic acid (maximum 7.9% AR) were identified as the major transformation products, other 3 unidentified compounds were found to have a maximum between 1% and 10% of the AR. Innumerable minor phototransformation products (each < 1% AR) were formed. All transformation products occurred transiently and decreased to amounts of < 5% AR at the end of the study.In all cases the QSAR estimates were indicative of a significant potential for rapid degradation in the environment.

The tropospheric half-life of OPP was estimated using the AOPWIN program (v. 1.91, 2000). Using a mean daily OH concentration in air of 0.5 x 10^6 OH radicals per cm^3, a half-life in air of 0.59 days was assessed - corresponding to a chemical life-time in air of about 0.85 days - due to indirect photodegradation. It is not to be expected that it can be carried in the gaseous phase over long distances or can accumulate in air. Furthermore, OPP has a low vapour pressure.

OPP is concluded to be readily biodegradable (71-76% after 28 days and 100% after 16 days, respectively). Moreover, high overall removal rates in activated sludge wastewater treatment plants of 99 to 100% (complete mineralization) were observed in a monitoring study conducted by Körner *et al*. (2000) in a municipal sewage plant Steinhäule located on the Danube River in southern Germany. Several studies in different municipal sewage plants presented by the applicant (Ternes *et al*. (1998), and Lee *et al*. (2005)) confirm the data from [redacted], and a value of 99% elimination efficiency is used in the Tier 2 approach for the risk assessment.

The simple first order DT_{50} value of ortho-Phenylphenol in the test soil was 1 day (DT_{50} 2.7 hours) providing an appropriate margin of safety. The DT_{50} has been re-calculated considering a biphasic approach. A DT_{50} default value in soil of 30 days (according to the TGD for Risk Assessment Chapter 3, Table 8) is considered to be as worst case for the risk assessment and a DT_{50} of 15.08 days as a refinement.

Based on two reliable adsorption/desorption studies and the results obtained in the soil degradation study, no potential for translocation into deeper soil layers or even ground water is given. K_{oc} values were 346.7 in the HPLC screening test and 252-392 in the adsorption/desorption (batch equilibrium) study. Based on a classifications K_{oc} value of 347 $L \cdot kg^{-1}$, OPP can be classified as a moderately mobile substance.

Although a log Pow of 3.18 was determined, no indication for a possible bioaccumulative potential of OPP is given due to a calculated steady-state bioconcentration factor (BCF) of 21.7 (wet weight), 114-115 (lipid content). Taking into consideration these low bioconcentration factors and the low computed concentrations in surface water, a significant food chain concern does not exist.

2.2.2.2. Effects assessment

STP compartment

According to TGD for Risk Assessment (EC, 2003), and taking into account the test available with aquatic micro-organisms (according to OECD209 with activated sludge, EC_{50} = 56mg $OPP \cdot L^{-1}$), an assessment factor of 100 can be applied. Thus, a $PNEC_{microorganisms}$of0.56 mg a.i./L is derived.

Surface water compartment

The toxicity of OPP to aquatic organisms is well documented by acute and long-term studies. Three chronic NOEC values for the three trophic levels of the base set (fish, *Daphnia*, algae) are available for the aquatic compartment resulting in NOECs of 0.036 mg a.i./L (*Pimephales promelas*), 0.006 mg a.i./L (*Daphnia magna*) and 0.468 mg a.i./L (*Pseudokirchneriella subcapitata*). A sediment-water chironomid toxicity test using spiked water is available with *Chironomus riparius* with a NOEC of 1.85 mg a.i./L. Since concentrations declined during the test (34-55% present in the water phase after 7 days), initial concentrations in water are not adequate to express the NOEC.

The lowest NOEC value (*Daphnia magna*) of 0.006 mg a.s./L is considered for the PNEC calculation. Since long-term NOECs are available for all three trophic levels, an assessment factor of 10 was applied to the lowest long-term NOEC value. The $PNEC_{water}$ was thus calculated to be 0.0006 mg a.i./L.

Sediment

In two preliminary range finding test (non-GLP) with spiked sediment and spiked water, it was found that the test organisms exposed to spiked water were affected at considerably lower concentrations than the larvae exposed to spiked sediment, with a NOEC of 1.85 mg/L expressed as a concentration in water.

However, it is not agreed to use the NOEC for *C. riparius* because this NOEC is expressed on the basis of initial concentrations in the water phase and, actual concentrations during the 28-days were much lower because of distribution to sediment. For this reason,the equilibrium partitioning on the $PNEC_{water}$ has been used. For this, the Foc in suspended matter (0.1) should be used instead of the Foc sediment resulting in a $PNEC_{sediment}$ of 0.0049 mg/kg_{wwt} (0.02254 mg/kg_{dwt}).

$PNEC_{sed}$ = ($K_{susp-water}$/RHO_{susp}) * $PNEC_{water}$ * 1000 (page 113 of TGD)
$K_{susp-water}$ = $Fwater_{susp}$ + ($Fsolid_{susp}$ * (Kp_{susp}/1000) * RHO_{solid}) (page 47 of TGD)
= 0.9 + (0.1 * (34.7/1000) * 2500) = 9.575 m^3/m^3

$PNEC_{sed}$ = (9.575/1150) * 0.0006 * 1000 = 0.0049 mg/kg
$PNEC_{sed}$ = 0.0049 mg/kg OPP/kg wet sediment

Terrestrial compartment

For the effects assessment of the soil, compartment tests are available for three trophic levels (terrestrial microorganisms, earthworms, and plants):

- Terrestrial microorganisms (C- and N-cycle):

EC_{50} (28 days) = 633.5 mg a.s.·kg_{dw}^{-1} soil

- Earthworms (*Eisenia fetida*):

LC_{50} (14 days) = 198.2 mg a.i.·kg^{-1} soil

NOEC (14 days) = 125 mg a.i.·kg_{dw}^{-1} soil

- Terrestrial plants (*Avena sativa*):

LC_{50} (14 days) = 53.9 mg a.i.·kg^{-1} soil

NOEC (14 days) = 12.5 mg a.i.·kg_{dw}^{-1} soil

The lowest result was obtained in the study with plants. A $PNEC_{soil}$ was calculated on basis of the lowest LC_{50} of three trophic levels using an assessment factor of 1000 (TGD, Table 20).

$PNEC_{soil}$ = 53.9 mg OPP·kg^{-1} dry weight soil·10^{-3}
= 0.054 mg OPP·kg^{-1} dry weight soil
= 0.054 * 1.13
$PNEC_{soil}$ = 0.061 mg OPP·kg^{-1} wet weight soil

Non-compartment specific effects relevant to the food chain (secondary poisoning)

A flow-through study was conducted to evaluate the bioconcentration of OPP in zebra fish (*Danio rerio*). The arithmetic means of five consecutive steady-state BCF were 21.7(wet weight), 114-115 (lipid content), indicating a negligible potential of the test substance to bioaccumulate. The achievement of steady-state conditions during the uptake (53 h exposure) phase as well as the consecutive depuration (19 h) were rapid processes.

A risk due to the proposed uses of OPP can be ruled out, since these data show that OPP does not accumulate in the environment. There is no need to assess this exposure route further.

The summary of ecotoxicity data used for the risk assessment are summarised in the Table 2.2.2.2-1.

Table 2.2.2.2-1: Summary of toxicity data used for the risk assessment

Species	Endpoint /Type of test	Results [mg a.i./L]
Oncorhynchus mykiss	Fish acute 96 h - LC_{50} Mortality	1
Daphnia magna	Aquatic invertebrates acute 48 h - LC_{50} Mortality	2.7
Pseudo-kirchneriella subcapitata	Algae growth inhibition 72 h – NOEC Growth inhibition	0.468
Activated sludge	Microorganisms 3 h - respiration inhibition	56
Pimephales promelas (Fathead minnow)	Fish chronic 21 d - NOEC Reproduction (Egg hatch F1) 21 d - LOEC Reproduction (Egg hatch F1)	36 293
Daphnia magna	Aquatic invertebrates chronic 21 d – NOEC Reproduction	0.006
Avena sativa	14 d – EC_{50} Germination rate, mortality and phytotoxicity	53.9
Eisenia fetida	Earthworms 14 d –LC_{50} Mortality, weight, abnormal behaviour	198.2
Soil microorganisms	28 d – EC_{50} nitrification	633.5
Mallard duck	Birds 14 d – LC_{50}	>2250
Mallard duck	Birds 5 d – LD_{50}	>5620
Rat Fischer 344	Mammals acute LD_{50} 1 dose + 2weeks of observation	2733 mg/kg
Beagle Dogs	Mammals chronic NOAEL 1 year	300 mg/kg/day

2.2.2.3. PBT and POP assessment

Assessment of PBT criteria

OPP can be considered readily biodegradable. Monitoring and laboratory studies have also shown that OPP is easily removed in STP systems. Based on literature studies, OPP is also not persistent water-sediment systems, and a soil biodegradation study also has shown that OPP is removed either by sorption or by biodegradation process. Considering the hydrolytic stability determined under stringent temperature conditions and at different pH values it is not expected that hydrolytic processes will contribute to the degradation of OPP in the aquatic systems (estimated DT_{50}> 1 year), however, from the photolysis study in water, it has been shown that OPP is photolytically unstable in the aqueous medium.Therefore, it is unlikely that OPP persists in the water, sediment or soil compartments.

The assessment of the (potential for) bioaccumulation in the context of PBT or vPvB evaluation makes use of measured bioconcentration factor. When not available, BCF value may be estimated from the octanol/water partition coefficient (Kow) by using (Q)SAR models. The calculated steady-state bioconcentration factor (BCF) for fish of 21.7 L/kg(wet weight), 114-115 (lipid content), indicates a negligible potential of OPP to bioaccumulate. Therefore, OPP does not fulfil the B criterion since its BCF is under the cut-off values proposed in the TGD (BCF > 2,000 for PBT assessment and > 5,000 for vPvB assessment).

The lowest NOEC obtained for OPP was 0.006 mg/L (*Daphnia magna* test). Since the cut off value given by the TGD corresponds to 0.01 mg/L, the substance meets the T criterion.

Assessment of POPs criteria

The vapour pressure of OPP is 0.906 Pa at 25°C, the half-life in air is of 0.587 days, indicating that the criteria for long-range transport potential (vapour pressure <1000 Pa andhalf-life in air > 2 days)is not fulfilled. In soil, biodegradation and sorption study was performed to understand the persistence of OPP in this compartment, indicating that OPP is relatively low mobile in soil, although a biodegradation character can also be attributed.

The calculated steady-state bioconcentration factor (BCF) for fish is 21.7 L/kg(wet weight), 114-115 (lipid content), and hence <5000. Thus, the bioaccumulation criterion is not fulfilled for OPP.

In conclusion, considering the above rationale, it can be concluded that OPP does not fulfil the POPs criteria.

Conclusion:

OPP must not be regarded as a Persistent or Bioaccumulative, Toxic, POP or ED substance because it does not fulfil the criteria. Therefore, OPP is not PBT/vPvB.

2.2.2.4. Exposure assessment

Sewage water treatment plants are regarded as the only pathway of direct OPP emissions after use as hand disinfectant in hospitals or at home.

For the environmental risk assessment, only the application approach has been presented, the tonnage approach has not been evaluated. Emissions from the hand wash of nurses are assessed. The standard scenario (400 beds) provided in the ESD for PT 1 has been used. However, due to the fact that no default values for the active substance are provided in the pick list in the ESD for $Qsubst_{pres\_bed}$, the agreed default values in the WG-V-2014 has been used (item 7.5a of the WG-V-2014 agenda). Already agreed values of the TOX WG have also been taken over (10 applications per shift for liquid soaps, using 3 g of soap/application).

Predicted Environmental Concentration (PEC) values were determined for different environmental compartments in Doc. II-B.

2.2.2.5. Risk characterisation

Aquatic compartment (incl. sewage treatment plant)

The following risk quotients were derived for the aquatic compartment from the calculated/measured exposure and effect data for OPP (see Table 2.2.2.5-1).

Table 2.2.2.5-1: PEC/PNEC ratios for OPP (aquatic compartment)

Compartments		PEC	PEC/PNEC
STP effluent [mg/L]	**Tier 1**	1.66E-03	0.003
	Tier 2	1.35E-04	0.0004
Local concentration in surface water during emission episode [mg/L]	**Tier 1**	1.66E-04	0.277
	Tier 2	1.35E-05	0.02
Sediment [mg/kg]	**Tier 1**	1.38E-03	0.282
	Tier 2	1.12E-04	0.02

Tier 1: 12.31% of the influent residues being present in the STP effluent water phase
Tier 2: 1% of the influent residues being present in the STP effluent water phase

Sewage treatment plant: the derived risk quotients are clearly < 1, even using the worst-case assumption (Tier 1) of 12.3% of the influent residues being present in the STP effluent water phase for the calculation. At Tier 2, the more realistic scenario of 1% of the influent residues being present in the STP effluent water phase, the risk is by far < 1. Thus, it is considered that there is no risk for microorganisms in a STP caused by OPP used as liquid hand disinfecting soap in hospitals.

Surface water: As PEC/PNEC ratios are < 1 at Tier 1 and Tier 2. Therefore, there is no relevant risk to aquatic organisms in surface waters exposed to OPP used as liquid hand disinfecting soap in hospitals even using the worst-case assumption (Tier 1) of 12.3% of the influent residues being present in the STP effluent water phase for the calculation and when 99% degradation of OPP in STP is considered.

Sediment: The PEC/PNEC ratio is < 1 at Tier 1 and Tier 2 for sediment dwelling organisms. Therefore, sediment dwelling organisms are not at risk by the intended uses of OPP as an antimicrobial component of liquid hand disinfecting soap in hospitals even considering the worst-case assumption (Tier 1) of 12.3% of the influent residues being present in the STP effluent water phase for the calculation.

All derived risk quotients for the aquatic compartment are clearly < 1, even using conservative worst-case assumptions for the calculation. Thus, it is considered that there is no relevant risk for the aquatic environment caused by OPP used as an antimicrobial component of liquid hand soaps.

Terrestrial compartment (soil)

To assess the risk for the environmental compartment soil regarding the exposure via sludge, the $PNEC_{soil}$ is compared with the PEC_{soil} (see Table 2.2.2.5-2).

Table 2.2.2.5-2: PEC/PNEC ratios for OPP (terrestrial compartment)

	PEC_{soil} values Concentration in agricultural soil over 30 days **[mg/kg_{wwt}]**		**PEC/PNEC**	
	DT_{50} = 30 d	**DT_{50} = 15.08 d**	**DT_{50} = 30 d**	**DT_{50} = 15.08 d**
Tier 1[1]	1.44E-03	1.08E-03	0.024	0.018
Tier 2[2]	4.73E-04	3.49E-04	0.008	0.006

[1]Tier 1: 3.13% of the STP influent residues being present in STP sludge
[2]Tier 2: 1% of the STP influent residues being present in STP sludge

As the PEC/PNEC ratios are < 1, no relevant risk for soil organisms is indicated due to the use of OPP as an antimicrobial component of liquid hand soaps.

Groundwater compartment

According the EU TGD (European Commission, 2003), the predicted concentration of the active substance in soil pore water is taken as a surrogate estimate of the potential concentration in groundwater. No accepted ecological endpoints have been established to enable characterisation of risk to the groundwater compartment (European Commission, 2003). However, the groundwater directive (Directive 2006/118/EC) stipulates a maximum acceptable concentration for pesticides in groundwater of 0.1 $\mu g \cdot L^{-1}$. The PEC values are given in Table 2.2.2.5-3.

Table 2.2.2.5-3: PEC values for OPP (groundwater)

	PEC_{gw} values [$mg \cdot L^{-1}$]		**PEC_{gw}values [$\mu g \cdot L^{-1}$]**	
	DT_{50} = 30 d	**DT_{50} = 15.08 d**	**DT_{50} = 30 d**	**DT_{50} = 15.08 d**
Tier 1[1]	7.60E-05	3.85E-05	0.08	0.04
Tier 2[2]	2.49E-05	1.25E-05	0.02	0.01

[1]Tier 1: 3.13% of the STP influent residues being present in STP sludge
[2]Tier 2: 1% of the STP influent residues being present in STP sludge

From the values presented above it can be seen that emissions associated with the use of OPP as hand soap (Qualysept Industrial) do not result in pore water concentrations exceeding this threshold. It is therefore concluded that OPP no represent a risk to groundwater following the application of sewage sludge to land.

Non compartment specific effects relevant to the food chain(secondary poisoning)

A flow-through study was conducted to evaluate the bioconcentration of OPP in zebra fish (*Danio rerio*). The arithmetic means of five consecutive steady-state BCF were 21.7 (wet weight), 114-115 (lipid content), indicating a negligible potential of the test substance to bioaccumulate. The achievement of steady-state conditions during the uptake (53 h exposure) phase as well as the consecutive depuration (19 h) were rapid processes.

A risk due to the proposed uses of OPP can be ruled out, since these data show that OPP does

not accumulate in the environment. There is no need to assess this exposure route further.

A secondary exposure of OPP to man via the food chain can be excluded due to low tonnage of the biocidal product used in whole Europe, rapid degradation in water and minimum amounts which reach the environmental compartments. A risk due to the proposed uses of OPP can be ruled out, since these data show that OPP does not accumulate in the environment. There is no need to assess this exposure route further.

2.2.2.6. Assessment of endocrine disruptor properties

In relation to the potential of OPP to interfere with the hormone system, OPP is present in one of the documents-lists of the Commission staff working document on implementation of the Community Strategy for Endocrine Disrupters - a range of substances suspected of interfering with the hormone systems of humans and wildlife (COM(2004) 1372), and cited as "candidate substance" for a first-in depth study. No endocrine disruption effect was reported in this document or in the following (COM(2007) 1635).

In addition, the prolonged toxicity of OPP to fathead minnow (*Pimephales promelas*) was tested in a reproductive performance test by Caunter& Williams (2002). In the test, measures of fecundity were assessed daily. Viability of resultant embryos was assessed in animals held in the same treatment regime to which the adults were exposed. A suite of histological and biological endpoints, that potentially are directly reflective of effects associated with endocrine disrupting chemicals, was also evaluated. The results of the study show that OPP does not indicate any adverse effects on reproductive parameters of pair-breeding fathead minnows up to a nominal test concentration of 50 µg a.i./L. With regard to the induction of the biomarker vitellogenin as an early indicator of possible endocrine modulation, no substance-related effects were noted compared to the positive control 17α-ethynylestradiol.

Result of the first EU evaluation project on potential endocrine substances (EUROPEAN COMMISSION, STUDY ON THE SCIENTIFIC EVALUATION OF 12 SUBSTANCES IN THE CONTEXT OF ENDOCRINE DISRUPTER PRIORITY LIST OF ACTIONS, 2002).

From the summary for humans: "The available data from in vivo studies in laboratory mammals (using oral or dermal exposure routes) indicates that *o*-Phenylphenol does not cause adverse effects on reproductive and developmental endpoints (which may be endocrine mediated) at exposure levels where general systemic toxic effects are observed. The lowest NOEL in the in vivo studies was 250 $mg \cdot kg_{bw}^{-1} \cdot day^{-1}$ for foetotoxic and developmental effects. Limited exposure data for workers and consumers has been located."

For wildlife: "The available aquatic effects data shows that the threshold exposure concentrations of *o*-Phenylphenol above which reproduction of the invertebrate *Daphnia magna* and fish (fathead minnow) are reduced (NOECs = 0.036 $mg \cdot L^{-1}$ and 0.009 $mg \cdot L^{-1}$ respectively) are lower than the threshold levels for general toxic effects (i.e. lethality). The effects observed on reproduction in fish were evidently not oestrogen mediated. However, there is no information on the mechanism of action for the effects on reproduction observed in *Daphnia magna*."

The results of this EU evaluation project were also confirmed in a peer evaluation done by the CSTEE (2003)

Thus, it can be stated that, to date, no evidence of endocrine disruption activity can be attributed to OPP.

2.3. Overall conclusions

The outcome of the assessment for Biphenyl-2-ol in Product-type 1 is specified in the BPC opinion following discussions at the BPC 9 meeting of the Biocidal Products Committee (BPC). The BPC opinion is available from the ECHA website.

Further information STP simulation tests will be required six months before the approval of the active substance to support the degradation rate.

2.4. List of endpoints

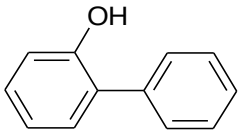
The most important endpoints, as identified during the evaluation process, are listed in Appendix I.

Appendix I: List of endpoints

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

Active substance (ISO Name)	2-Phenylphenol
Product-type	human hygiene biocidal products

Identity

Chemical name (IUPAC)	2-Phenylphenol
Chemical name (CA)	[1,1'-Biphenyl]-2-ol
CAS No	90-43-7
EC No	201-993-5
Other substance No.	CIPAC No. 246
Minimum purity of the active substance as manufactured (g/kg or g/l)	≥ 995 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	None
Molecular formula	$C_{12}H_{10}O$
Molecular mass	170.2 g/mol
Structural formula	

Physical and chemical properties

Melting point (state purity)	56.7 ºC (purity: 99.9%)
Boiling point (state purity)	287 ºC (purity: 99.9%)
Thermal stability / Temperature of decomposition	Exothermal decomposition starts at 290 °C. As no decomposition of the test substance could be observed below 150 °C, Biphenyl-2-ol is considered to be stable at room temperature.
Appearance (state purity)	Colourless solid flakes with slight phenolic odour (purity: 99.9%)
Relative density (state purity)	1.237 at 20 °C (purity: 99.9%)
Surface tension (state temperature and concentration of the test solution)	58.72mN/m at 20.1 ºC (0.558 g/L)
Vapour pressure (in Pa, state temperature)	0.474Pa at 20 °C, 0.906 Pa at 25 °C
Henry's law constant (Pa m^3mol^{-1})	Ratio between vapour pressure and water solubility: 0.15 Pa×m^3×mol^{-1} at 20 °C and pH 5 0.14 Pa×m^3×mol^{-1} at 20 °C and pH 7 0.13 Pa×m^3×mol^{-1} at 20 °C and pH 9

Solubility in water (g/L or mg/L, state temperature)	Results at pH 5: 0.43 g/L at 10°C 0.53 g/L at 20°C 0.70 g/L at 30°C Results at pH 7: 0.45 g/L at 10°C 0.56 g/L at 20°C 0.73 g/L at 30°C Results at pH 9: 0.52 g/L at 10°C 0.64 g/L at 20°C 0.84 g/L at 30°C
Solubility in organic solvents (in g/L or mg/L, state temperature)	Results at 20 °C: *n*-heptane: 50.3 g/L acetone, 1,2-dichloroethane, ethyl acetate, methanol, *p*-xylene: > 250 g/L No significant temperature dependence is expected.
Stability in organic solvents used in biocidal products including relevant breakdown products	Biphenyl-2-ol as manufactured does not include an organic solvent in PT 2, 3, 4, 6, 7, 10 and 13. Therefore a study regarding stability in organic solvents does not apply. The b. p. for PT 1 and 9 contains an organic solvent.
Partition coefficient (log P_{OW}) (state temperature)	Log P_{OW}: 3.18 at 22.51 °C. (more accurate value which is to be used exclusively) "the log P_{OW} of Biphenyl-2-ol is nearly independent from pH value when investigated at pH 5, pH 7 and pH 9."
Dissociation constant	pK = 9.5 at 20 °C
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	Molar absorptivity: 12800 at 245 nm 8200 at 267 nm The UV-visible spectrum show a band with a maximum at 285 nm and a bandwidth of 40 nm, therefore a short absorption appears above 290 nm.
Flammability or flash point	Biphenyl-2-ol is not highly flammable, does not liberate gases in hazardous amounts when contact with water, does not deliver indications of pyrophoric properties and does not undergo spontaneous combustion.
Explosive properties	Based on scientific judgement it is certified that due to the structural formula Biphenyl-2-ol contains neither oxidising groups nor other chemically instable functional groups. Thus Biphenyl-2-ol is incapable of rapid decomposition with evolution of gases or release of heat, i.e. the solid material does not present any risk for explosion.

Oxidising properties	Based on scientific judgement it is certified that due to the structural formula Biphenyl-2-ol does not contain oxidising groups in its molecular backbone and thus may not react exothermically with a combustible material. Therefore Biphenyl-2-ol does not have oxidising properties.
Auto-ignition or relative self ignition temperature	Biphenyl-2-ol does not undergo spontaneous combustion

Classification and proposed labelling

with regard to physical hazards	None
with regard to human health hazards	Carc 2: H351; Eye Irrit. 2: H319; Skin Irrit. 2: H315; STOT SE 3: H335
with regard to environmental hazards	Aquatic Acute 1:H400; Aquatic Chronic 1; H410

Chapter 2:Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	Biphenyl-2-olis separated by means of gas chromatography using flame ionisation detection. The quantitative evaluation is carried out by area normalisation with consideration of water content and non-volatile components.
Impurities in technical active substance (principle of method)	The analytical method for the determination of impurities in the active substance is confidential. This information is provided separately in the confidential part of the dossier.

Analytical methods for residues

Soil (principle of method and LOQ)	HPLC-MS/MS; LOQ = 5 µg/kg
Air (principle of method and LOQ)	GC-MS; LOQ = 0.35 µg/m^3.
Water (principle of method and LOQ)	Surface and drinking water: HPLC-MS/MS; LOQ = 0.1µg/L
Body fluids and tissues (principle of method and LOQ)	Not applicable since OPP is not classified as toxic or highly toxic.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Citrus Fruit: GC-MS; LOQ = 0.1 µg/kg QuEChERS Method: EN155662:2008
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Meat: GC-MS/MS; LOQ = 0.01 µg/kg

Chapter 3:Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	100% is assumed
Rate and extent of dermal absorption*:	43% is assumed
Distribution:	Extensively metabolized. Poorly distributed.
Potential for accumulation:	Low potential for bioaccumulation.
Rate and extent of excretion:	Quickly excreted (12 - 24 h post-dosing).
Toxicologically significant metabolite(s)	phenylhydroquinoneglucuronide and 2,4'-dihydroxybiphenyl-sulfate

* the dermal absorption value is applicable for the active substance and might not be usable in product authorization

Acute toxicity

Rat LD_{50} oral	2730 mg/kg bw
Rat LD_{50} dermal	>2000 mg/kg bw
Rat LC_{50} inhalation	>36 mg/m^3 (0.036 mg/L)

Skin corrosion/irritation	Skin Irrit. 2 (H315: Causes skin irritation)
Eye irritation	Eye Irrit. 2 (H319: Causes serious eye irritation)
Respiratory tract irritation	No data
Skin sensitisation (test method used and result)	Non Sensitizer (Buehler test on Guinea pigs; 0/10 Number of animals sensitised/total number of animals) Non Sensitizer (Magnusson-Kligman test on Guinea pigs; 0/20 Number of animals sensitised/total number of animals)
Respiratory sensitisation (test method used and result)	No data

Repeated dose toxicity

Short term

Species/ target / critical effect	Oral: New Zealand White rabbits / increased mortality (13%), gross pathologic alterations and histopathologic alterations Dermal: Fischer 344 rats/ no systemic effects in any dose group

Relevant oral NOAEL / LOAEL	NOAEL = 100 mg/kg bw/day (teratogenicity oral study) LOAEL = 250 mg/kg bw/day (teratogenicity oral study)
Relevant dermal NOAEL / LOAEL	NOAEL = 1000 mg/kg bw/day (21-day dermal study)
Relevant inhalation NOAEL / LOAEL	No data
Relevant NOAEC (local effects)	7.5%

Subchronic

Species/ target / critical effect	Rats /urinary blader/ increased incidence of simple urinary bladder hyperplasia in males and the increased incidence of urinary bladder transitional cell carcinoma in males
Relevant oral NOAEL / LOAEL	NOAEL = 39 mg/kg bw/day (2-years oral study) LOAEL = 250 mg/kg bw/day (2-years oral study)
Relevant dermal NOAEL / LOAEL	No Data
Relevant inhalation NOAEL / LOAEL	No Data
Relevant NOAEC (local effects)	No Data

Long term

Species/ target / critical effect	Rats /urinary blader/ increased incidence of simple urinary bladder hyperplasia in males and the increased incidence of urinary bladder transitional cell carcinoma in males
Relevant oral NOAEL / LOAEL	NOAEL = 39 mg/kg bw/day (2-years oral study) LOAEL = 250 mg/kg bw/day (2-years oral study)
Relevant dermal NOAEL / LOAEL	No Data
Relevant inhalation NOAEL / LOAEL	No Data
Relevant NOAEC (local effects)	No Data

Genotoxicity	*In vitro* Biphenyl-2-ol is considered to be nonmutagenic but it was clastogenic in Chinese hamster ovary cells at cytotoxic concentrations *In vivo* Biphenyl-2-ol is not genotoxic or mutagenic in vivo.

Carcinogenicity

Species/type of tumour	Fischer 344 rat/ neoplasia in urinary bladder (male animals only) B6C3F1 mice/ hepatocellular adenomas(male animals only) The tumours found in mice are not predictive of carcinogenicity for humans. The relevance of urinary bladder tumours in male rats cannot be completely excluded
Relevant NOAEL/LOAEL	200 mg/kg body wt/day 500 mg/kgBW/day

Reproductive toxicity

Developmental toxicity

Species/ Developmental target / critical effect	New Zealand White rabbits/ No recorded effect on development parameters/ No effects on foetal development
Relevant maternal NOAEL	NOAEL = 100 mg/kg/day
Relevant developmental NOAEL	NOAEL = 250 mg/kg/day

Fertility

Species/critical effect	RatCD Sprague-Dawley/ No recorded effect on reproductive parameters/ bladder calculi, urothelial hyperplasia
Relevant parental NOAEL	NOAEL = 35 mg / kg bw / day
Relevant offspring NOAEL	NOAEL = 125 mg / kg bw / day
Relevant fertility NOAEL	NOAEL = 457 mg / kg bw / day

Neurotoxicity

Species/ target/critical effect	No data

Developmental Neurotoxicity

Species/ target/critical effect	No Data

Immunotoxicity

Species/ target/critical effect	No Data

Developmental Immunotoxicity

Species/ target/critical effect	No Data

Other toxicological studies

Human data:
allergic contact dermatitis or contact sensitivity to Biphenyl-2-ol
Other/special studies:
Biphenyl-2-ol is carcinogenic in urinary bladder in alkaline conditions in rats

Medical data

No data

Summary

	Value	Study	Safety factor
$AEL_{long\text{-}term}$	0.4 mg/kg bw/day	2-years oral study	100
$AEL_{medium\text{-}term}$	0.4 mg/kg bw/day	2-years oral study	100
$AEL_{short\text{-}term}$	1 mg/kg bw/day	teratogenicity oral study in New Zealand White rabbits	100
ADI[2]	No relevant		
ARfD	No relevant		

MRLs

Relevant commodities	

Reference value for groundwater

According to BPR Annex VI, point 68	

Dermal absorption

Study (*in vitro/vivo*), species tested	Dermal absorption, excretion in vivo, humans.
Formulation (formulation type and including concentration(s) tested, vehicle)	0.4% (w/v) OPP solution in isopropyl alcohol
Dermal absorption values used in risk assessment	43% (100% in corrosive products)

Acceptable exposure scenarios (including method of calculation)

Formulation of biocidal product	Likely in-use concentration is 2.0% w/v Biphenyl-2-ol.
Intended uses	The biocidal product is a ready-to-use formulation for hygienic hand disinfection and hand decontamination in hospitals and medical practice by professional users (Product-type 1 of the EU Biocidal Product Directive).
Industrial users	Not applicable

[2]If residues in food or feed.

Professional users	Chronic exposure: maximum of 10 uses per day, 30 seconds contact time (Hand washing /liquid soap scenario&exposure to vapours model ConsExpo 4.1) No risk.
Non professional users	Not applicable
General public	Not applicable
Exposure via residue in food	exposure of Biphenyl-2-ol to food and feedstuffs can be excluded when the product is applied according to the recommended use

Chapter 4:Fate and Behaviour in the Environment

Route and rate of degradation in water

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	pH 5: stable at 50 °C pH 7: stable at 50 °C pH 9: stable at 50 °C Estimated $t_{1/2}$> 1 year
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	Biphenyl-2-ol: Experimental DT_{50}: 0.3 days (pure water) Environmental DT_{50} [Phoenix, AZ, USA]: 1.7 days Environmental DT_{50} [Athens, Greece]: 2.6 days Diketohydroxy-compound (max. 13.6% at day 1, < 5% after 7 days): Experimental DT_{50}: 1.3 days (pure water) Environmental DT_{50} [Phoenix, AZ, USA]: 7.2 days Environmental DT_{50} [Athens, Greece]: 11.1 days
Readily biodegradable (yes/no)	Yes; 71-76% biodegradation after 28 d 100% biodegradation after 14 d 100% biodegradation after 10 d (inherent test)
Inherent biodegradable (yes/no)	
Biodegradation in freshwater	
Biodegradation in seawater	Not relevant since Biphenyl-2-ol is not used or released in the marine environment at considerable amounts. Therefore, a seawater biodegradation test is not required.
Non-extractable residues	Not relevant due to indoor use.
Distribution in water / sediment systems (active substance)	Not relevant due to indoor use. Estimation from screening experiments: <14 d
Distribution in water / sediment systems (metabolites)	Not relevant due to indoor use.

Route and rate of degradation in soil

Mineralization (aerobic)	Results are given as mean value of duplicate test of [phenyl-UL-^{14}C]-labelled Biphenyl-2-ol in % of the applied radioactivity for day 127 of incubation under aerobic conditions: 9.6% (n = 2, 20 ± 1 °C)
Laboratory studies (range or median, with number of measurements, with regression coefficient)	$DT_{50\ lab}$ (20 °C, aerobic): 2.7 hours* (n = 1), r^2 = 0.994 DT_{90lab} (20 °C, aerobic): 8.81 hours* (n = 1), r^2 = 0.994
degradation in the saturated zone:	
Field studies(state location, range or median with number of measurements)	Not relevant due to indoor use
Anaerobic degradation	Not relevant due to indoor use.
Soil photolysis	Not relevant due to indoor use.
Non-extractable residues	77.4% at day 127 (n = 2, 20 ± 1 °C)
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	No relevant metabolites
Soil accumulation and plateau concentration	Not relevant due to indoor use

Adsorption/desorption

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	Adsorption, OECD Guideline 106: K_f: 7.04 , 7.47, 8.53, 11.66 (n = 4) K_{oc}: 252, 355, 389, 393 (n = 4, mean: 347) Desorption 1: K_{fdes}: 9.36, 16.42, 16.78, 18.62 (n = 4) K_{ocdes}: 334, 621, 699, 864 (n = 4) Adsorption, OECD Guideline 121: estimated mean K_{oc} value: 346.7 K_d was not reported pH dependence was not apparent

Fate and behaviour in air

Direct photolysis in air	Not relevant because there is no relevant release of the compound to the air compartment
Quantum yield of direct photolysis	
Photo-oxidative degradation in air	DT_{50} = 0.59 days
Volatilization	Not relevant because there is no relevant release of the compound to the air compartment

Reference value for groundwater

According to BPR Annex VI, point 68	

Monitoring data, if available

Soil (indicate location and type of study)	No data presented
Surface water (indicate location and type of study)	**Municipal sewage plant Steinhäule located on the Danube River in southern Germany.** The plant has mechanical purification devices (primary clarification), actived sludge treatment, biological nitrate removal (nitrification/denitrifcation), biological phosphate removal and final settlement tanks as main cleaning steps. Concentrations of Biphenyl-2-ol in 24 h influent and effluent samples from 10/11 March 1998
Ground water (indicate location and type of study)	No data presented
Air (indicate location and type of study)	No data presented

Substance (µg/L)	**Influent 10/11 March (8 a.m.-8a.m.)**	**Effluent 10/11 March (4 p.m.-4 p.m.)**
Biphenyl-2-ol	1.54 ± 0.349	< 0.015

Chapter 5:Effects on Non-target Species

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

Species	Time-scale	Endpoint	Toxicity
Fish			
Oncorhynchus mykiss	96 hours	Mortality	LC_{50} = 4.0 mg/L Dill *et al*. (1985)
Pimephales promelas	21 days	Reproduction	NOEC = 0.036 mg/L [redacted] (2002)
Invertebrates			

Daphnia magna	48 hours	Mortality	LC_{50}= 2.7 mg/L Dill *et al.* (1985)
Daphnia magna	21 days	Survival & repro-duction	NOEC = 0.006 mg/L Bruns (2001)
Algae			
Pseudokirchneriella subcapitata	72 hours	Growth inhibition	E_rC_{50} = 3.57 mg/L E_bC_{50} = 1.35 mg/L NOEC = 0.468 mg/L Hicks (2001)
Microorganisms			
Activated sludge	3 hours	Inhibition of respiratory rate	EC_{50} = 56 mg/L Klecka, Landi, and Bodner (1985)

Effects on earthworms or other soil non-target organisms

Acute toxicity to earthworms ..	LC_{50} (14 days) = 198.2 mg/kg Moser &Scheffczyk (2004)
Reproductive toxicity to earthworms	No study available

Effects on soil micro-organisms

Nitrogen mineralization	EC_{50} (28days) = 633.5 mg a.s./kg d.wt. soil Schulz.L (2012)
Carbon mineralization	

Effects on terrestrial vertebrates

Acute toxicity to mammals	LD_{50} = 2733 mg/kg bw (♂+♀) [redacted] (1994)
Chronic toxicity to mammals (Annex IIA, point VI.6.5)	NOAEL=300 mg/kg diet (1year) Cosse *et al*. (1990)
Acute toxicity to birds	LC_{50}> 2250 mg/kg bw [redacted] (1986)
Dietary toxicity to birds	LD_{50}> 5620 mg/kg diet [redacted] (1986)
Reproductive toxicity to birds	No study available

Effects on honeybees

Acute oral toxicity	No study available
Acute contact toxicity	No study available

Effects on other beneficial arthropods

Acute oral toxicity	No study available
Acute contact toxicity	No study available
Acute toxicity to ……..	No study available

Bioconcentration

Bioconcentration factor (BCF)	BCF = 21.7 (whole fish), 114-115 (lipid content) Caspers (1999)
Depuration time(DT_{50})	< 1 h (5 µg/L) / < 19 h (50 µg/L)
Depuration time(DT_{90})	2 h (5 µg/L) / < 6 h (50 µg/L)
Level of metabolites (%) in organisms accounting for > 10 % of residues	No metabolites identified

Chapter 6:Other End Points

Appendix II: List of Intended Uses

Object and/or situation	Product name	Organisms controlled	Formulation		Application			Applied amount per treatment			Remarks:
			Type (d-f)	Conc. of a.s.(i)	method kind (f-h)	number min max	interval between applications (min)	g a.s./L min max	water L/m^2 min max	g a.s./m^2 min max	
Personal hygiene PT 1	Qualysept Industrial(Biphenyl-2-ol Hand Soap)	Bacteria, fungi and yeasts	AL Liquid soap	20 g/L	hand washing	1 - 8 per day	?	20 g/L	–	–	–

Appendix III: List of studies

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

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A2.6(01) IIA, II 2.6	Stroech, K.D.	1991	Preventol O Extra (2-Phenylphenol) Synthesis. Date: 1991-02-19 **CONFIDENTIAL**	Bayer AG, Leverkusen, Germany	--	No	No	Yes	LANXESS Deutschland GmbH
A2.7(01) IIA, II 2.7	Anonymous	2000	Preventol O Extra in flakes. Date: 2000-02-11	BU, Material Protection Products, Leverkusen, Germany	--	No	No	Yes	LANXESS Deutschland GmbH
A2.7(01) IIA, II 2.7 also filed: A2.8(01)	Erstling, K.	2005	Determination of main and minor components in Preventol O Extra, 5-batch analysis. Date: 2005-02-16 **CONFIDENTIAL**	Bayer Industry Services GmbH & Co. OHG, BIS-SUA-Analytics, Leverkusen, Germany	Study No.: G 05/0009/00 LEV	Yes	No	Yes	LANXESS Deutschland GmbH

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A2.7(02) IIA, II 2.7	Stroech, K.	2014	Quality Control Data from the production plant covering approximately 68 months (Jan. 2009 to Sept. 2014) to derive a specification limit for OPP. **CONFIDENTIAL**	LANXESS Deutschland GmbH Köln, Germany	--	Yes	--	--	LANXESS Deutschland GmbH
A2.8(02) IIA, II 2.8	Feldhues, E.	2006	Additional information on study report No. 2005/0009/00, Determination of main and minor components in Preventol O extra 5-Batch-Analysis. Date: 2006-05-12 **CONFIDENTIAL**	Bayer Industry Services GmbH & Co KG, BIS-SUA-PUA I, Leverkusen, Germany	--	No	No	Yes	LANXESS Deutschland GmbH

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A3.1.1(01) IIA, III 3.1 also filed: A3.1.2(01) also filed: A3.1.3(01) also filed A3.10(01)	Erstling, K.	2001 a	Physicochemical properties. Date: 2001-09-13 Amended: 2004-12-02, 2006-03-02, 2006-04-24, 2007-06-26	Bayer AG, Leverkusen, Germany	A 00/0068/01 LEV	Yes	No	Yes	LANXESS Deutschland GmbH
A3.1.3(02) IIA, III 3.1	Erstling, K.	2007	Physicochemical properties of Preventol O Extra	Bayer Industry Services, Leverkusen, Germany	2007/0045/02	Yes	No	Yes	LANXESS Deutschland GmbH
A3.2(01) IIA, III 3.2	Olf, G.	2003	Vapour pressure, Physical-Chemical properties. Date: 2003-02-11 Amended: 2003-02-24 2007-06-29	Bayer AG, Leverkusen, Germany	03/003/01	Yes	No	Yes	LANXESS Deutschland GmbH
A3.2(02) IIA, III 3.2 also filed: A7.3.1(01)	Beiell, U.	2004	Preventol O Extra (*o*-Phenylphenol) Calculation of Henry's Law Constant and Photodegradation. Date: 2004-09-27	Dr. Knoell Consult GmbH, Mannheim, Germany	--	No	No	Yes	LANXESS Deutschland GmbH

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A3.3(01) IIA, III 3.3	Stroech, K.	2006	*o*-Phenylphenol / Appearance. Date: 2006-04-11	LANXESS Deutschland GmbH, Leverkusen, Germany	--	No	No	Yes	LANXESS Deutschland GmbH
A3.4(01) IIA, III 3.4	Erstling, K.	2004	Spectral Data of Preventol O Extra. Date: 2004-07-16 Amended: 2004-12-01	Bayer Industry Services, Leverkusen, Germany	A 02/0162/03 LEV	Yes	No	Yes	LANXESS Deutschland GmbH
A3.5(01) IIA, III 3.5	Erstling, K.	2002	Water solubility. Date: 2002-02-15	Bayer AG, Leverkusen, Germany	A 00/0068/02 LEV	Yes	No	Yes	LANXESS Deutschland GmbH
A3.6(01) – also filed: A3.9(01)	Kausler	1991	Partition coefficient, dissociation constant, pH value. Date: 1991-01-09 Amended: 2005-02-03 2007-06-26	Bayer AG, Leverkusen, Germany	A 89/0062/06 LEV	Yes	No	Yes	LANXESS Deutschland GmbH

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A3.6(02) – also filed: A3.9(02)	Erstling, K.	2001 b	Partition coefficient (*n*-octanol/water) / Dissociation constant. Date: 2001-10-23 Amended: 2001-11-14, 2004-12-03 and 2005-01-14 2007-06-28	Bayer AG, Leverkusen, Germany	A 00/0068/03 LEV	Yes	No	Yes	LANXESS Deutschland GmbH
A3.7(01) IIIA, III.1	Jungheim, R.	2004	Solubility of Preventol O Extra in organic solvents. Date: 2004-07-26	Bayer Industry Services, Leverkusen, Germany	A 02/0162/04 LEV	Yes	No	Yes	LANXESS Deutschland GmbH
A3.7(02) IIIA, III.1	Feldhues, E.	2006 a	Statement Solubility of Preventol O Extra in organic solvents, Temperature dependence. Date: 2006-11-20	Bayer Industry Services, BIS-SUA-PUA I, Leverkusen, Germany	--	No	No	Yes	LANXESS Deutschland GmbH

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A3.9(03) IIA, III 3.6	Feldhues, E.	2006 b	Statement Partition coefficient n-octanol/water of Preventol O Extra, Temperature and pH dependence. Date: 2006-11-20	Bayer Industry Services, BIS-SUA-PUA I, Leverkusen, Germany	--	No	No	Yes	LANXESS Deutschland GmbH
A3.11(01) IIA, III 3.8	Heinz, U.	2004	Determination of safety relevant data of Preventol O Extra. Date: 2004-07-12 Amended: 2005-01-14	Bayer Industry Services, Leverkusen, Germany	04/00223	Yes	No	Yes	LANXESS Deutschland GmbH
A3.13(01) IIA, III 3.10	Olf, G.	2004	Surface tension of Preventol O Extra. Date: 2004-09-16	Bayer Technology Services, Leverkusen, Germany	04006/03	Yes	No	Yes	LANXESS Deutschland GmbH
A3.15(01) IIA, III 3.11	Stroech, K.	2004 a	*o*-Phenylphenol / Explosive properties. Date: 2004-07-29	Bayer Chemicals AG, Leverkusen, Germany	--	No	No	Yes	LANXESS Deutschland GmbH
A3.16(01) IIA, III 3.12	Stroech, K.	2004 b	*o*-Phenylphenol / Oxidising properties. Date: 2004-07-29	Bayer Chemicals AG, Leverkusen, Germany	--	No	No	Yes	LANXESS Deutschland GmbH

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A3.17(01) IIA, III 3.13 also filed A8.1(02)	Kraus, H.	2006	*o*-Phenylphenol (OPP) / Reactivity towards container material. Date: 2006-05-30	LANXESS Deutschland GmbH, Leverkusen, Germany	--	No	No	Yes	LANXESS Deutschland GmbH
A4.1(01) IIA, IV 4.1	Feldhues, E.	2005	Validation of analytical methods for the determination of main and minor components in Preventol O Extra. Date: 2005-02-04 Amended: 2006-04-24 **CONFIDENTIAL**	Bayer Industry Services GmbH & Co. OHG, BIS-SUA-Analytics, Leverkusen, Germany	A 02/0162/08 LEV	Yes	No	Yes	LANXESS Deutschland GmbH
A4.1(02) IIA, IV 4.1	Dick, W.	1990 a	Water – Volumetric method. Date: 1990-12-18 **CONFIDENTIAL**	ZF-DZA/Analytik LEV/OAL, Leverkusen, Germany	2011-0131301-90	No	No	Yes	LANXESS Deutschland GmbH

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A4.1(03) IIA, IV 4.1	Dick, W.	1990 b	Karl Fischer titrant (KF-T) – Equivalent water concentration-Volumetric method. Date: 1990-12-18 **CONFIDENTIAL**	ZF-DZA/Analytik LEV/OAL, Leverkusen, Germany	2011-0131401-90	No	No	Yes	LANXESS Deutschland GmbH
A4.2(01) IIA, IV 4.2	Brumhard, B.	2004	Method 00829 for the determination of residues of Preventol O Extra in soil by HPLC-MS/MS. Date: 2004-01-05	Bayer Crop Science AG, Monheim am Rhein, Germany	Bayer Method No.: 00829; Report No.: MR- 107/03	Yes	No	Yes	LANXESS Deutschland GmbH
A4.2(02) IIA, IV 4.2	Feldhues, E.	2005 b	Validation of an analytical method for the determination of Preventol O Extra in air samples. Date:2005-02-21 Amended: 2007-06-20 2010-01-22	Bayer Industry Services GmbH & Co. OHG, BIS-SUA-Analytics, Leverkusen, Germany	A 02/0162/05 LEV	Yes	No	Yes	LANXESS Deutschland GmbH

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A4.2(03) IIA, IV 4.2	Kóniger, A.	2010	Validation of a GC method for the determination of Preventol O Extra in air. Date: 2010-01-22	CURRENTA GmbH &Co. OHG Services Analytik Leverkusen Germany	2009/0013/01	Yes	--	--	LANXESS Deutschland GmbH
A4.2(04) IIA, IV 4.2	Brumhard, B.	2003	Enforcement method 00828 (MR-100/03) for the determination of Preventol O Extra in surface and drinking water by HPLC-MS/MS. Date: 2003-12-17 Amended: 2005-03-14 2007-07-02	Bayer Crop Science AG, Monheim am Rhein, Germany	Report No.: MR-100/03; Method No.: 00828	Yes	No	Yes	LANXESS Deutschland GmbH
A4.3(01) IIA, IV 4.3	Stroech, K.	2014	Residue determination of 2-phenylphenol in meat via GC/MS/MS measurement. 2014-06-16, amended 2014-10-23	Lanxess Deutschland GmbH, Köln, Germany		No	No	Yes	LANXESS Deutschland GmbH

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A4.3(02) IIA, IV 4.3	Semrau, J	2011	Determination of residues of orthophenylphenol (OPP) and phenylhydroquinone (PHQ) and their conjugates after a single postharvest application of AGF/1-04 in oranges, Southern Europe 2011.	Eurofins Agroscience Services GmbH, Stade, Germany, (), 2011-12-12	Report No.: S11-01940	Yes	No	Yes	Agrupost, Valencia, Spain
A5 IIA 5.4	Russell, A.D., Hugo, W.B. and Ayliffe, G.A.J.	1990	Principles and practice of disinfection, preservation and sterilisation.	--	--	--	Yes	No	Second Edition, Blackwell Scientific Public
A5.3.1(01) IIA, V 5.3	Bomblies, L. and Wedde, A.	2000	Preventol O Extra (active substance. Determination of the "Minimal Inhibitory Concentration (MIC) against various test microorganisms. Date: 2000-09-16	Labor L+S, Bad-Bocklet-Großenbrach, Germany	01020940	No	No	Yes	LANXESS Deutschland GmbH

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A5.3.1(02) IIA, V 5.3	Exner, O.	1997	Preventol O Extra: Determination of bactericidal effectiveness in a qualitative suspension disinfection test in accordance with German Society of Hygiene and Microbiology (DGHM) guidelines. Date: 1997-11-28	Bayer AG, Material Protection Business Unit, Krefeld, Germany	--	No	No	Yes	LANXESS Deutschland GmbH
A6.1.1(01) IIA, VI 6.1.1	[redacted]	1994	Dowicide™ 1 Antimicrobial: Acute Oral Toxicity Study in Fischer 344 Rats. Date: 1994-07-29	Dow Chemical Company	K-001024-057A	Yes	No	Yes	Dow Chemical Company
A6.1.2(01) IIA, VI 6.1.2	[redacted]	1991	Preventol O Extra (Schuppen) – Acute Dermal Toxicity Study in Male and Female Wistar Rats. Date: 1991-01-09	Bayer AG	19831	Yes	No	Yes	LANXESS Deutschland GmbH

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A6.1.3(01) IIA, VI 6.1.3	[redacted] and [redacted]	1992	*ortho*-Phenylphenol: Acute Aerosol Inhalation Toxicity Study in Fischer 344 Rats. Date: 1992-02-24	Dow Chemical Company	K-001024-049	Yes	No	Yes	Dow Chemical Company
A6.1.3(01)	Marple et al.	1978	A Dust Generator for Laboratory Use.	--	*Am. Ind. Hyg. Assoc. J.***39**: 26-32	--	--	--	--
A6.1.4(01) IIA, VI 6.1.4	[redacted]	1994a	Dowicide™ 1 Antimicrobial: Primary Dermal Irritation Study in New Zealand White Rabbits. Date: 1994-07-29	Dow Chemical Company	K-001024-057B	Yes	No	Yes	Dow Chemical Company
A6.1.4(02) IIA, VI 6.1.4	[redacted]	1981b	Report on the test of Preventol O Extra for irritation of the mucous membrane. Date: 1981-11-04	Fraunhofer-Institut für Toxikologie und Aerosol-forschung, Schmallenberg, Germany	T2004666	No	No	Yes	LANXESS Deutschland GmbH

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A6.1.5(01) IIA; VI 6.1.5	[redacted]	1994b	Dowicide™ 1 Antimicrobial: Dermal Sensitization Potential in the Hartley Albino Guinea Pig. Date: 1994-07-29	Dow Chemical Company	K-001024-057E	Yes	No	Yes	Dow Chemical Company
A6.1.5(02) IIA; VI 6.1.5	[redacted] and [redacted]	1984	The Sensitizing Potential of Metalworking Fluid Biocides (Phenolic and Thiazole Compounds) in the Guinea-Pig Maximization Test in Relation to Patch-Test Reactivity in Eczema Patients.	Department of Dermatology, GentofteHospital, Hellerup, Denmark	*Fd. Chem Toxic.* **22**(8), pp. 655-660	No	Yes	No	--
A6.2(01) IIA, VI 6.2	Bartels, M.J., Brzak, K.A., McNett, D. and Shabrang, S.N.	1997	*ortho*-Phenylphenol (OPP): Limited Metabolism Study in Human. Date: 1997-02-03	Dow Chemical Company	HET K-001024-059	Yes	No	Yes	Dow Chemical Company

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A6.2(02) IIA, VI 6.2	[redacted] and [redacted]	1997	*ortho*-Phenylphenol (OPP): Metabolism of ^{14}C-Labelled OPP in $B_6B_3F_1$ Mice and Fischer 344 Rats. Date: 1997-02-06	Dow Chemical Company	HET K-001024-060	Yes	No	Yes	Dow Chemical Company
A6.2(03) IIA, VI 6.2	Selim, S.	1996	A Single Open Dose Label Study to Investigate the Absorption and Excretion of ^{14}C/^{13}C-Labeled *ortho*-Phenylphenol Formulation after Dermal Application to Healthy Volunteers. Date: 1996-09-19	Bayer AG	P0995002	Yes (GCP)	No	Yes	LANXESS Deutschland GmbH
A6.3.1(01) IIA, VI 6.3.1 also filed: A6.5(02)	[redacted] and [redacted]	1990	*ortho*-Phenylphenol: Palatability/Probe, Four-Week and One-Year Oral Toxicity Studies in Beagle Dogs. Date: 1990-09-24	Dow Chemical Company	K-001024-039	Yes	No	Yes	Dow Chemical Company

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A6.3.2(01) IIA, VI 6.3.2	[redacted]	1993	*ortho*-Phenylphenol: 21-Day Repeated Dermal Dose Study of Systemic Toxicity in Fischer 344 Rats. Date: 1993-03-03	Dow Chemical Company	K-001024-056	Yes	No	Yes	Dow Chemical Company
A6.4.1(01) IIA, VI 6.4	[redacted] and [redacted]	1996a	Technical Grade *ortho*-Phenylphenol: A Special Subchronic Dietary Study to Examine the Mechanism of Urinary Bladder Carcinogenesis in the Male Rat. Date: 1996-11-11	Bayer AG	92-972-MS	No	No	Yes	LANXESS Deutschland GmbH

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A6.5(01) IIA, VI 6.5 also filed: A6.7(01)	[redacted] and [redacted]	1996	Technical Grade *ortho*-Phenylphenol: A Combined Chronic Toxicity / Oncogenicity Testing Study in the Rat. Date: 1996-02-23, Amended: 1999	Bayer AG	92-272-SC	Yes	No	Yes	LANXESS Deutschland GmbH
A6.6.1(01) IIA, VI 6.6.1	San, R.H.C. and Springfield, K.A.	1989	Salmonella/Mammalian-Microsome Plate Incorporation Mutagenicity Assay (Ames Test). Date: 1989-12-22	Bayer AG	C141.501017	Yes	No	Yes	LANXESS Deutschland GmbH
A6.6.1(01)	Ames et al.	1975	Methods for detecting carcinogens and mutagens with salmonella-mammalian-microsome mutagenicity test	--	**Mutation Res. 31**, 347-363	--	--	--	--
A6.6.1(01)	Maron & Ames	1983	Revised methods for the salmonella mutagenicity test	--	**Mutation Res.113**, 173-215	--	--	--	--

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A6.6.2(01) IIA, VI 6.6.2	Tayama, S., Kamiya, N. and Nakagawa, Y.	1989	Genotoxic effects of *o*-Phenylphenol metabolites in CHO-K1 cells.	Dept. of Toxicology, Tokyo Metropolitan Research Laboratory of Public Health, Tokyo, Japan	*Mutat. Res.* **223**, pp. 23–33	No	Yes	No	--
A6.6.3(01) IIA, VI 6.6.3	Brendler, S.	1992	Preventol O Extra – Mutagenicity Study for the Detection of Induced Forward Mutations in the CHO-HGPRT Assay In Vitro. Date: 1992-04-09	Bayer AG	21278	Yes	No	Yes	LANXESS Deutschland GmbH
A6.6.5(01) IIA, VI 6.6.5	[redacted]	2000	Preventol O Extra – Comet Assay In Vivo in Mouse Liver and Kidney. Date: 2000-08-08	Bayer AG	PH 30130	Yes	No	Yes	LANXESS Deutschland GmbH
A6.8.1(02) IIA, VI 6.8.1	[redacted] and [redacted]	1991	*ortho*-Phenylphenol (OPP): Gavage Teratology Study in New Zealand White Rabbits. Date: 1991-04-23	Dow Chemical Company	K-001024-045	Yes	No	Yes	Dow Chemical Company

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A6.8.1(01) IIA, VI 6.8.1	Kaneda, M., Teramoto, S., Shingu, A. and Yasuhiko, S.	1978	Teratogenicity and Dominant-Lethal Studies with *o*-Phenylphenol.	Toxicology Division, Institute of Environmental Toxicology, Kodaira, Tokyo, Japan	*J. Pesticide Sci.* **3,** pp. 365-370	No	Yes	No	--
A6.8.2(01) IIA, VI 6.8.2	[redacted] and [redacted]	1995	A Two-Generation Dietary Reproduction Study in Sprague-Dawley Rats Using Technical Grade *ortho*-Phenylphenol. Date: 1995-09-28	Bayer AG	93-672-VX	Yes	No	Yes	LANXESS Deutschland GmbH
A6.8.2(02) IIA, VI 6.8.2	[redacted]	1990	Two-Generation Dietary Reproduction Study in Rats Using *ortho*-Phenylphenol. Date: 1990-09-17 (revised report, original report date: 1989-01-13)		85-671-02	Yes	No	Yes	LANXESS Deutschland GmbH

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A6.10(01)	Fukushima, S., Kurata, Y., Shibata, M., Ikawa, E. and Ito, N.	1983	Promoting Effect of Sodium *o*-Phenylphenate and *o*-Phenylphenol on Two-Stage Urinary Bladder Carcinogenesis.	First Department of Pathology, NagoyaCityUniversityMedical School, Nagoya, Japan	*Gann*.,**74**, pp. 625-632	No	Yes	No	--
A6.10(02)	Fujii, T., Nakamura, K. and Hiraga, K.	1987	Effects of pH on the Carcinogenicity of *o*-Phenylphenol and Sodium *o*-Phenylphenate in the Rat Urinary Bladder.,	Dept. of Toxicology, Tokyo Metropolitan Research Laboratory of Public Health, Tokyo, Japan	*Fd. Chem. Toxic.***25**(5), pp. 359-362	No	Yes	No	--

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A6.10(03)	[redacted]	1994	*o*-Phenylphenol – Interactions of *o*-Phenylphenol (OPP) and its metabolites with microsomal prostaglandin-H-synthase: possible implications for OPP-induced tumour formation in the rat urinary bladder. Date: 1994-01-12	Bayer AG	22788	No	No	Yes	LANXESS Deutschland GmbH
A6.12.1(01) IIA, VI 6.12.1	Heyne, R. and Attig, G.	2004	Occupational Medical Experiences with *o*-Phenylphenol. Date: 2004-12-06	Bayer Industry Services, Leverkusen, Germany	--	No	No	Yes	LANXESS Deutschland GmbH
A6.12.6(01) IIA, VI 6.9.6	Adams, R.M.	1981	Allergic contact dermatitis due to *o*-Phenylphenol.	Palo Alto Medical Clinic, Palo Alto, CA, USA	*Contact Dermatitis***7**, p. 332	No	Yes	No	--
A6.12.6(02) IIA, VI 6.9.6	van Hecke, E.	1986	Contact sensitivity to *o*-Phenylphenol in a coolant.	Dept. of Dermatology, UniversityHospital, Gent, Belgium	*Contact Dermatitis* **15**(1)**,** p. 46	No	Yes	No	--

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A6.12.6(03) IIA, VI 6.9.6	Schnuch, A., Geier, J., Uter, W. and Frosch, P.J.	1998	Patch testing with preservatives, antimicrobials and industrial biocides. Results from a multicentre study.	Information Network of Dermatological Clinics in Germany (IVDK)	*Br. J. Dermatology* **138,** pp. 467-476	No	Yes	No	--
A6.12.6(04) IIA, VI 6.9.6	Geier, J., Kleinhans, D. and Peters, K.-P.	1996	Kontaktallergien durch industriell verwendete Biozide – Ergebnisse des Informationsverbunds Dermatologischer Kliniken (IVDK) und der Deutschen Kontaktallergiegruppe. (Contact Allergy Due to Industrial Biocides–Results of the IVDK and the German Dermatitis Research Group.)	Information Network of Departments of Dermatology in Germany (IVDK)	*Dermatosen / Occup. Environ.* **44,** pp. 154-159	No	Yes	No	--

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A6.12.6(05) IIA, VI 6.12.6	Brasch, J., Henseler, T. and Frosch, P.	1993	Patch Test Reactions to a Preliminary Preservative Series – A retrospective study based on data collected by the "Information Network of Dermatological Clinics" (IVDK) in Germany.	Information Network of Departments of Dermatology in Germany (IVDK)	*Dermatosen* **41**(2)**,** pp. 71-76	No	Yes	No	--
A6.15(01) IIIA, VI 4	Stroech, K.D.	2013	Residue determination of 4-chloro-3-methylphenol and 2-phenylphenol in edible tissues of 15 broiler chicken that were reared on an area disinfected with the LCB trial product "CMK/OPP 32". date: 2013-01-22	LANXESS Deutschland GmbH,	--	No	No	Yes	LANXESS Deutschland GmbH,

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A7.1.1.1.1(01) IIA, VII.7.6.2.1	Reusche, W.	1991	Hydrolysis study of 2-phenylphenol according to OECD guideline 111. Date: 1991-01-02, amended: 2004-12-02	Bayer AG, Leverkusen, Germany	G 89/0056/02 LEV	Yes	No	Yes	Bayer Crop Science AG
A7.1.1.1.2(01) IIA, VII.7.6.2.2	Heinemann, O.	2005	[Phenyl-UL-^{14}C]-2-phenylphenol: Phototransformation in Water. Date: 2005-03-15.	Bayer CropScience AG, Monheim, Germany	MEF-05/018	Yes	No	Yes	Bayer Crop Science AG
A7.1.1.1.2(02) IIA, VII.7.6.2.2	Wick, L.Y. and Gschwend, P.M.	1998	Source and chemodynamic behaviour of diphenyl sulfone and *ortho*- and *para*-hydroxybiphenyl in a small lake receiving discharges from an adjacent superfund site.	Ralph M. Parsons laboratory, Massachusetts Institute of Technology, Cambridge, Massachusetts02139, USA	*Environ. Sci. Technol*. **32**, pp. 1319-1328.	No	Yes	No	--

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A7.1.1.1.2(02)	Haag, W. and Hoigné J.	1986	Singlet oxygen in surface waters .3. Photochemical formation and steady-state concentrations in various types of waters	--	*Environ. Sci. Technol.*, **20**, pp. 341-348	--	Yes	No	--
A7.1.1.1.2(02)	Leifer, A.	1988	The Kinetics of Environmental Aquatic Photochemistry.	--	American Chemical Society, Washington, DC, USA	--	Yes	No	--
A7.1.1.2.1(01) IIA, VII.7.6.1.1	Gonsior, S.J. and Tryska, T.J.	1997	Evaluation of the Ready Biodegradability of *o*-Phenylphenol. Date: 1997-08-01	Environmental Chemistry Research Laboratory, The Dow Chemical Company, Midland, Michigan	971080	Yes	No	Yes	The DOW Chemical Company
A7.1.1.2.1(02) IIA, VII.7.6.1.1	Kanne, R.	1989a	Preventol O Extra. Biodegradation. Date: 1989-07-24	Bayer AG, Institut für Umweltanalyse und Bewertungen, Leverkusen, Germany	51A/88/I	Yes	No	Yes	Bayer AG

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A7.1.1.2.1(03)	Painter H.A. and King E.F.	1985	Ring test programme 1983-84. Assessment of biodegradability of chemicals in water by manometric respirometry	Ring test, monitored by the Water Research Centre, Elder Way, UK -Stevenage Herts	EUR 9962 EN	No	No	No	Commission of the EC: Environment and Quality of life
A7.1.1.2.1(04)	Kanne, R.	1989 b	Preventol O Extra. Biodegradation in Rhine River Water. Date: 1989-07-24	Bayer AG, Institut für Umweltanalyse und Bewertungen, Leverkusen, Germany	Report-No. 51A/88/II	Yes	No	Yes	Bayer AG
A7.1.1.2.2(01) IIA, VII.7.6.1.2	Wellens, H.	1990	Zur biologischen Abbaubarkeit mono- und disubstituierter Benzolderivate.	Abwasser-biologische Laboratorien der HOECHST AG, Frankfurt, Gedrmany	Z. Wasser-Abwasser-Forsch. 23, 85-98	No	Yes	No	--
A7.1.2.1.1(01) IIIA, XII.2.1	Körner W., Bolz U., Süßmuth W., Hiller G., Schuller W., Hanf V. & Hagenmaier H.	2000	Input/Output Balance of Estrogenic Active compounds in a Major Municipal Sewage Plant in Germany.	Institute of Organic Chemistry, University of Tübingen, Germany	*Chemosphere* **40**, 1131-1142.	No	Yes	No	--

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A7.1.2.1.1(01) IIIA, XII.2.1	Bolz, U., Körner, W., Hagenmeier, H.	2000	Development and validation of a GC/MS method for determination of phenolic xenoestrogens in aquatic samples.	Institute of Organic Chemistry, University of Tübingen, Germany	Chemosphere **40**, 929-935.	No	Yes	No	--
A7.1.2.1.1(02) IIIA, XII.2.1	Ternes, T., Stumpf, M., Schuppert, B., Haberer, K.	1998	Simultaneous Determination of Antiseptics and Acidic Drugs in Sewage and River Water.	ESWE-Institute for Water Research and Water Technology, Wiesbaden, Germany	Vom Wasser, 90, 295-309.	No	Yes	No	--
A7.1.2.1.1(03) IIIA, XII.2.1	Lee, H.-B., Peart, T.E., Svoboda, M.L.	2005	Determination of endocrine-disrupting phenols, acidic pharmaceuticals,and personal-care products in sewage by solid-phase extraction andgas chromatography–mass spectrometry.	Aquatic Ecosystem Protection Research Branch, National Water Research Institute, Environment Canada. Ontario, Canada.	Journal of Chromatography A, 1094, 122–129.	No	Yes	No	--

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A7.1.2.2.2(01) IIIA, XII 2.1	Bruns, E.	2005	Preventol O Extra (*ortho*-Phenylphenol). Summary of screening experiments concerning the behaviour of *ortho*-Phenylphenol (OPP) in a "water-sediment system". Date: 2005-03-29	Bayer Industry Services GmbH & Co. OHG, Leverkusen, Germany	--	Yes	No	Yes	Bayer Crop Science AG
A7.1.3(01) IIA, VII 7.7	Erstling, K.	2001c	Preventol O Extra in Schuppen – Adsorption/Desorption, during the period June to September 2001. Date: 2001-09-17	Bayer AG, Zentrale Analytik, Leverkusen, Germany	A 0/0068/04 LEV	Yes	No	Yes	LANXESS Deutschland GmbH
A7.2.1(01) IIIA, VII 4, XII 1.1	Fliege, R.	2005	[phenyl-UL-^{14}C]-*ortho*-Phenylphenol: Aerobic soil metabolism in one European soil. Date: 2005-03-23	Bayer CropScience AG, Development, Metabolism / Environmental fate, Germany	MEF-05/072	Yes	No	Yes	Bayer Crop Science AG

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A7.2.2.1(02)	Nitsche, M.	2011	Biodegradation of Preventol® O Extra (2-phenylphenol) in soil under aerobic conditions	Lanxess Deutschland GmbH, Leverkusen, Germany	-	No	No	Yes	Lanxess Deutschland GmbH
A7.2.2.1 (02)	Loehr, Raymond C. and Matthews, John E.	1992	Loss of organic chemicals in soil: Pure compound treatability studies	*Journal of Soil Contamination* **1***(4) 339-360*	--	--	--	--	--
A7.2.3.1(01) IIIA, XII.1.2	Oddy, A. and Jacob, O.	2005	[^{14}C]-2-Phenylphenol: Adsorption to and Desorption from four soils. Date: 2005-03-16	Battelle AgriFood Ltd., Essex, UK	CX/04/019	Yes	No	Yes	LANXESS Deutschland GmbH
A7.3.2 IIIA 12.3	Wasser, C.	2014	Residues of the Combustion of OPP20, Residues in fumes and gases.	Anadiag Laboratories, France 67500 Haguenau	R B4256	No	No	Yes	LANXESS Deutschland GmbH
A7.4.1.1(01) IIA, VII.7.1	[redacted]	1990	Acute Fish Toxicity of Preventol O Extra. Date: 1990-04-10	Bayer AG, Institut für Umweltanalysen und Bewertungen, Leverkusen, Germany	51 A/88 F	Yes	No	Yes	LANXESS Deutschland GmbH

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A7.4.1.1(02)	[redacted]	1991	*o*-Phenylphenol Toxicity to Fish *Chinook salmon* (Oncorhynchus tschawytscha). Date: 1991-10-22	British Columbia Research Corp., Vancouver, Canada	2-11-200-222-91001	No	No	Yes	LANXESS Deutschland GmbH
A7.4.1.2(01) IIA, VII.7.2	[redacted] and [redacted]	1985	Evaluation of the toxicity of Dowicide 1 Antimicrobial, Technical *o*-Phenylphenol to representative aquatic organisms. Date: 1985-12-12	Mammalian and Environmental Toxicology, Health & Environmental Sciences, Midland, Michigan, USA	ES-811	No	No	Yes	Dow Chemical Company
A7.4.1.2(02)	Kühn, R., Pattard, M., Pernak, K.-D. Winter,	1988	Harmful effects of chemicals in the *Daphnia* reproduction test as a basis for assessing their environmental hazard in aquatic systems. March 1988	Institute for Water, Land and Air Hygiene of the Federal German Health Office	10603052	No	Yes	No	--

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A7.4.1.3(01) IIA, VII.7.3	Hicks, S.	2002	*ortho*-Phenylphenol: Growth Inhibition Test with the Green Alga, Selenastrum capricornutum. Date: 2002-03-12	ABC Laboratories, Inc., Missouri, USA	ABC Study No. 46980, Dow Study No. 010167	Yes	No	Yes	Dow Chemical Company
A7.4.1.3(02)	Caspers, N.	1989	Cellular proliferation inhibitory test: *Scenedesmus subspicatus* CHODAT (green alga). Date: 1989-07-04	Bayer AG	No. 51 A/88	No	No	Yes	LANXESS Deutschland GmbH
A7.4.1.4(01) IIA, VII.7.4	Mueller, G.	1990	Preventol O Extra, 2-phenylphenol, Toxicity to Bacteria. Date: 1990-08-08	Bayer AG, Institute of Environmental Analysis, Leverkusen, Germany	51 A/88B	Yes	No	Yes	LANXESS Deutschland GmbH

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A7.4.1.4(01) IIA, VII.7.4	Weyers, A.	2006	Preventol O Extra, Toxicity to Bacteria. Re-Evaluation based on Study Report No. 51 A/88 B, corresponding raw data and additional information provided by the sponsor. Date: 2006-09-05	Bayer Industry Services, Leverkusen, Germany	--	Yes	No	Yes	LANXESS Deutschland GmbH
A7.4.1.4(02)	Klecka, G.M., Landi, L.P. and Rodner, K.M.	1985	Evaluation of the OECD Activated Sludge, Respiration Inhibition Test	--	*Chemosphere* **14**, pp. 1239-1251	No	Yes	No	--
A7.4.2(01) IIA, VII.7.5	Fàbregas, E.	2007	*o*-Phenylphenol - Calculation of the Bioconcentration Factor (BCF). Date: 2007-06-05	Dr. Knoell Consult GmbH, Leverkusen, Germany	Report-No. KC-BCF-08/07	No	No	Yes	LANXESS Deutschland GmbH

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A7.4.3.2(01) IIIA, XIII 2.2	[redacted] and [redacted]	2002	Preventol O Extra: Determination of Effects on the Reproduction of Fathead minnow (Pimephales promelas). Date: 2002-03-25	Brixham Environmental Laboratory, AstraZeneca UK Limited, Brixham, UK	BL7213/B	Yes	No	Yes	LANXESS Deutschland GmbH
A7.4.3.3.1(01) IIIA, XIII.2.3	Caspers, N.	1999	Investigation of the Ecological Properties of Preventol O Extra, Test on Bioaccumulation. Date: 1999-05-27	Bayer AG, Leverkusen, Germany	793 A/98	Yes	No	Yes	LANXESS Deutschland GmbH
A7.4.3.4(01) IIIA, XIII 2.4	Bruns, E.	2001	Preventol O Extra, *Daphnia magna* Reproduction Test. Date: 2001-12-13	Bayer AG, WD-UWS, Institute of Environmental Analysis and Evaluation, Leverkusen	1092 A/01 DL	Yes	No	Yes	LANXESS Deutschland GmbH
7.4.3.4/02	Caspers, N.	1989	Life cycle test with water fleas - *Daphnia magna* - EC_{50} immobilisation and EC_{50} reproduction. Date: 1989-10-13	Bayer AG	No. 51 A/88	No	No	Yes	LANXESS Deutschland GmbH

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A7.4.3.5.1(01) IIIA, XIII 2.4	Egeler, P. and Gilberg, D.	2005	Preventol O Extra: A study on the toxicity to the sediment dweller Chironomus riparius. Date: 2005-02-28	ETC Oekotoxikologie GmbH, Germany	Al1ME	Yes	No	Yes	LANXESS Deutschland GmbH
A7.5.1.1/01	Reis, K-H.	2007	Effects of 2-Phenylphenol (Preventol O Extra) on the Activity of the Soil Microflora in the Laboratory. Date: 2007-06-21	Institut für Biologische Analytik und Consulting IBACON GmbH, Rossdorf, Germany	35591080	Yes	No	Yes	LANXESS Deutschland GmbH
A7.5.1.1(02)	Schulz, L.	2012	Effects on the activity of soil microflora (Nitrogen transformation test) Date: 2012-02-10	BioChem agrar, Labor für biologische und chemische Analytik GmbH 04827 Gerichshain, Germany	Project-No. 12 10 48 003 N	No	No	Yes	LANXESS Deutschland GmbH

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
A7.5.1.2(01) IIIA, XIII 3.2	Moser, Th. and Scheffczyk, A.	2004	Preventol O Extra: Acute toxicity to the earthworm *Eisenia fetida* in an artificial soil test. Date: 2004-12-08	ETC Oekotoxikologie GmbH, Flörsheim, Germany	AI1RA	Yes	No	Yes	LANXESS Deutschland GmbH
A7.5.1.3	Bützler, R., Meinerling, M.	2008	Effects of 2-Phenylphenol (Preventol O Extra) on Terrestrial (Non-Target) Plants: Seedling Emergence and Seedling Growth Test. Date: 2008-10-17	IBACON GmbH, Rossdorf, Germany,	Report No. 35594084	Yes	No	Yes	LANXESS Deutschland GmbH
A7.5.3.1.1(01) IIIA, XIII 1.1	[redacted]	1986a	*ortho*-Phenylphenol Technical: An Acute Oral Toxicity Study with the Mallard. Date: 1986-06-06	Wildlife International Ltd., St. Michaels, Maryland, USA	ES-874 (103-248)	Yes	No	Yes	Dow Chemical Company
A7.5.3.1.2(01) IIIA, XIII 1.2	[redacted]	1986b	*ortho*-Phenylphenol Technical: A Dietary LC_{50} Study with the Bobwhite. Date: 1986-06-06	Wildlife International Ltd., St. Michaels, Maryland, USA	ES-873 (103-246)	Yes	No	Yes	Dow Chemical Company

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A7.5.3.1.2(02) IIIA, XIII 1.2	[redacted]	1986c	*ortho*-Phenylphenol Technical: A Dietary LC_{50} Study with the Mallard. Date: 1986-06-06	Wildlife International Ltd., St. Michaels, Maryland, USA	ES-875 (103-247)	Yes	No	Yes	Dow Chemical Company
A7.5.5.1(01) IIIA, 13.3	Fàbregas, E.	2007	*o*-Phenylphenol - Calculation of the Bioconcentration Factor in Earthworms (BCFearthworm). Date: 2007-06-05	Dr. Knoell Consult GmbH, Leverkusen, Germany	Report-No. KC-BCF-09/07	No	No	Yes	LANXESS Deutschland GmbH
A8.1(01) IIA, VIII 8.1 also filed: A8.2(01) also filed: A8.3(01) also filed: A8.4(01) also filed: A8.5(01)	Anonymous	2004	Safety Data Sheet Preventol O Extra. Date: 2004-03-10	LANXESS Deutschland GmbH, Leverkusen, Germany	011472/23	No	No	--	LANXESS Deutschland GmbH

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B2.2(01) IIB, I 2.2 also filed B3.4(02)	Anonymous	2004a	International Chemical Safety Card 1-Propanol.	International Program of Chemical Safety.	0553	No	Yes	No	--
B2.2(02) IIB, I 2.2 also filed B3.4(03)	Anonymous	2005a	International Chemical Safety Card 2-Propanol.	International Program of Chemical Safety.	0554	No	Yes	No	--
B2.2(03) IIB, I 2.2	Anonymous	2003a	Safety Data Sheet 1-Propanaminium, 3-amino-*N*-(carboxymethyl)-*N*,*N*-dimethyl-, *N*-coco acyl derivs., inner salts. Date: 2003-08-15	--	Version 1.3	No	No	No	--
B2.2(04) IIB, I 2.2	Anonymous	2005b	Safety Data Sheet Sodium chloride 99,99 Suprapur®. Date: 2005-04-01	Merck KGaA, Darmstadt, Germany	--	No	No	No	Merck KGaA
B2.2(05) IIB, I 2.2	Anonymous	2000	International Chemical Safety Card Potassium hydroxide.	International Program of Chemical Safety.	0357	No	Yes	No	--
B2.2(06) IIB, I 2.2	Anonymous	2003b	Safety Data Sheet Tefacid Coconut 8-18.	Karlshamns Tefac AB, Karlshamn, Sweden	--	No	No	No	Karlshamns Tefac AB

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B2.2(07) IIB, I 2.2	Anonymous	2004b	International Chemical Safety Card Hydroxyethylcellulose.	International Program of Chemical Safety.	1559	No	Yes	No	--
B2.2(08) IIB, I 2.2	Anonymous	2004c	Material Safety Data Sheet Ethylenediamine-tetraacetic acid, disodium salt.	Acros Organics BVBA, Geel, Belgium	--	No	No	No	Acros Organics BVBA
B2.2(09) IIB, I 2.2	Anonymous	1996	Material Safety Data Sheet Quinoline yellow, water soluble.	Acros Organics BVBA, Geel, Belgium	--	No	No	No	Acros Organics BVBA
B2.2(10) IIB, I 2.2	Anonymous	2007	Safety Data Sheet Biancaflor PH #799979MF Date: 2007-01-11 **CONFIDENTIAL**	Symrise GmbH & Co. KG, Holzminden, Germany	Version 2	No	No	No	Symrise GmbH
B3.1(01) IIB, III 3.1	Hendrich, S.	2006a	Appearance of Qualysept Industrial. Date: 2006-12-12	Schülke & Mayr GmbH, Norderstedt, Germany	--	No	No	Yes	Schülke & Mayr GmbH
B3.4(01) IIB, III 3.4	Hendrich, S.	2006b	Physical and chemical data of Qualysept Industrial. Date: 2006-12-11	Schülke & Mayr GmbH, Norderstedt, Germany	--	No	No	Yes	Schülke & Mayr GmbH

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B3.4(02) IIB, III 3.4 also filed B2.2(01)	Anonymous	2004a	International Chemical Safety Card 1-Propanol	International Program of Chemical Safety.	0553	No	Yes	No	--
B3.4(03) IIB, III 3.4 also filed B2.2(02)	Anonymous	2005a	International Chemical Safety Card 2-Propanol.	International Program of Chemical Safety.	0554	No	Yes	No	--
B3.5(01) IIB, III 3.5 also filed: B3.6(01) also filed: B3.7(01) also filed: B3.10(02)	Hendrich, S.	2006c	Qualysept Industrial–Stability. Date: 2006-12-15	Schülke & Mayr GmbH, Norderstedt, Germany	--	No	No	Yes	Schülke & Mayr GmbH
B3.6(01) IIB, III 3.6 also filed: B3.5(01) also filed: B3.7(01) also filed: B3.10(02)	Hendrich, S.	2006c	Qualysept Industrial–Stability. Date: 2006-12-15	Schülke & Mayr GmbH, Norderstedt, Germany	--	No	No	Yes	Schülke & Mayr GmbH

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B3.7(01) IIB, III 3.7 also filed: B3.5(01) also filed: B3.6(01) also filed: B3.10(02)	Hendrich, S.	2006c	Qualysept Industrial–Stability. Date: 2006-12-15	Schülke & Mayr GmbH, Norderstedt, Germany	--	No	No	Yes	Schülke & Mayr GmbH
B3.7(02) IIB, III 3.7	Hendrich, S.	2006d	Stability of Qualysept Industrial at low temperatures. Date: 2006-12-15	Schülke & Mayr GmbH, Norderstedt, Germany	--	No	No	Yes	Schülke & Mayr GmbH
B3.10(01) –	Hendrich, S.	2007a	Surface tension of Qualysept Industrial. Date: 2007-02-07	Schülke & Mayr GmbH, Norderstedt, Germany	--	No	No	Yes	Schülke & Mayr GmbH
B3.10(02) – also filed: B3.5(01) also filed: B3.6(01) also filed: B3.7(01)	Hendrich, S.	2006c	Qualysept Industrial–Stability. Date: 2006-12-15	Schülke & Mayr GmbH, Norderstedt, Germany	--	No	No	Yes	Schülke & Mayr GmbH
B4.1(01) IIB, IV 4.1	Hendrich, S.	2007b	Determination of active substances in Qualysept Industrial. Date: 2007-01-11	Schülke & Mayr GmbH, Norderstedt, Germany	--	No	No	Yes	Schülke & Mayr GmbH

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B5 IIB 5.8	Russell, A.D., Hugo, W.B. and Ayliffe, G.A.J.	1990	Principles and practice of disinfection, preservation and sterilisation.	--	--	--	Yes	No	Second Edition, Blackwell Scientific Public
B5.10(01) IIB, V 5.10	Goroncy-Bermes, P.	2002	Qualysept – Test of Fungicidal Efficacy according to DIN EN 1275 (1997) Date: 2002-03-12	Schülke & Mayr GmbH, Biological Laboratory, Norderstedt, Germany	--	No	No	Yes	Schülke & Mayr GmbH
B5.10(02) IIB, V 5.10	Brill, H.	2003	Efficacy of Qualysept when used for Hand Disinfection. Test according to Guidelines of the German Society of Hygiene and Microbiology. Date: 2003-11-17	Schülke & Mayr GmbH, Biological Laboratory, Norderstedt, Germany	--	No	No	Yes	Schülke & Mayr GmbH
B5.10(03)	Brill, H	2010	Qualysept – Test of Fungicidal Efficacy according to DIN EN 1275 (1997) Date: 2002-03-12	Lanxess Deutschland	-	-	No	Yes	Lanxess Deutschland

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B5.10(04)	Heeg, P.	2003	Expert´s report on Qualysept for use as a disinfectant hand wash in accordance with EN1499	Institute for Medical Microbiology and Hygiene, University Hospital Tübingen, Germany	-	-	No	Yes	Schülke & Mayr GmbH
B6.4(01) IIB, VI 6.4	Cnubben, N.H.P., Elliott, G.R., Hakkert,B.C., Meuling, W.J.A.,and van de Sandt J.J.M.	2002	Comparative *in vitro–in vivo* Percutaneous Penetration of the Fungicide *ortho*-Phenylphenol. *Regulatory Toxicology and Pharmacology* 35, pp. 198–208	TNO Nutrition and Food Research, Zeist, The Netherlands	--	No	Yes	No	TNO Nutrition and Food Research
B8.1(01) IIB, VIII 8.1 also filed B8.2(01) also filed B8.4(01) also filed B8.5(01) also filed B8.6(01)	Anonymous	2006	Safety Data Sheet Qualysept Industrial. Date: 2006-01-31	Schülke & Mayr GmbH, Norderstedt, Germany	Version 01.01	No	No	No	Schülke & Mayr GmbH

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B8.2(01) IIB, VIII 8.2 also filed B8.1(01) also filed B8.4(01) also filed B8.5(01) also filed B8.6(01)	Anonymous	2006	Safety Data Sheet Qualysept Industrial. Date: 2006-01-31	Schülke & Mayr GmbH, Norderstedt, Germany	Version 01.01	No	No	No	Schülke & Mayr GmbH
B8.4(01) IIB, VIII 8.4 also filed B8.1(01) also filed B8.2(01) also filed B8.5(01) also filed B8.6(01)	Anonymous	2006	Safety Data Sheet Qualysept Industrial. Date: 2006-01-31	Schülke & Mayr GmbH, Norderstedt, Germany	Version 01.01	No	No	No	Schülke & Mayr GmbH
B8.5(01) IIB, VIII 8.5 also filed B8.1(01) also filed B8.2(01) also filed B8.4(01) also filed B8.6(01)	Anonymous	2006	Safety Data Sheet Qualysept Industrial. Date: 2006-01-31	Schülke & Mayr GmbH, Norderstedt, Germany	Version 01.01	No	No	No	Schülke & Mayr GmbH

(Sub)Section / Annex point	Authors (s)	Year	Title	Testing Company	Report No.	GLP Study (Yes/No)	Published (Yes/No)	Data Protection Claimed (Yes/No)	Data Owner
B8.6(01) IIB, VIII 8.6 also filed B8.1(01) also filed B8.2(01) also filed B8.4(01) also filed B8.5(01)	Anonymous	2006	Safety Data Sheet Qualysept Industrial. Date: 2006-01-31	Schülke & Mayr GmbH, Norderstedt, Germany	Version 01.01	No	No	No	Schülke & Mayr GmbH