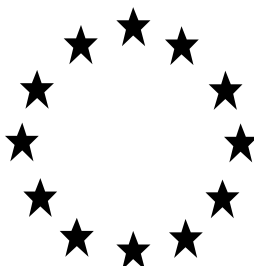


Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



Biphenyl-2-ol
Product-type PT 3
(Preventol O Extra)

November 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 [3] (Veterinary hygiene biocidal product), 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 3.

Commission Regulation (EC) No 1451/2007 of 4 December 2007¹ 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 3 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 3, 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 3, 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 loses 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 Biphenyl-2-ol as manufactured and for the analysis of impurities. Validated analytical methods are also available for the determination of Biphenyl-2-ol soil, water, air and food/feeding stuffs matrices. Other analytical methods are not deemed 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.

The active substance Biphenyl-2-ol 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.

Biphenyl-2-ol has a broad efficacy against potentially harmful germs (bacteria, fungi and yeasts), e.g. , *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Enterococcus hirae*, *Staphylococcus aureus*, , *Aspergillus niger* and *Candida albicans*.

The biocidal product has passed the EN1656 (bactericidal activity) under simulated low level soiling conditions (3 g/L BSA) at concentration of 0.4% Biphenyl-2-ol a.i.) at contact time of 30 minutes.

The biocidal product has passed the EN1657 (fungicidal activity) under simulated low level soiling conditions (3 g/L BSA) at concentration of 0.4% Biphenyl-2-ol a.i.) at contact time of 30 minutes.

The test methods according to EN1656 and EN1657 demonstrate the efficacy against bacteria, fungi and yeasts of the products to for use in veterinary area.

Due to the unspecific mode of action (multi-site activity) a development of resistance against biocidal use of Biphenyl-2-ol is not expected.

Biphenyl-2-ol is used in industrial poultry barn, other intensive livestock farming installations and similar facilities. It is intended for disinfection of surfaces in pig and poultry units by professional users exclusively which comprises farmers and cleaning contractors. Biphenyl-2-ol is applied to surfaces using a rod and nozzle that sprays an even layer across the surface to be disinfected. A solution containing 5,000 ppm (0.5%) Biphenyl-2-ol is recommended for the application.

Disinfection of livestock husbandries is performed when no animals are present. The bedding has been removed and discarded. The treatment solution is left to dry on the treated walls and floors. Re-entry is then allowed after a specific period of time when most of the residues have been removed through ventilation.

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 | H319 |
| | Skin Irrit. 2 | H315 |
| | STOT SE 3 | H335 |
| | Aquatic Acute 1 | 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 | H319 |
| | Skin Irrit. 2 | H315 |
| | STOT SE 3 | H335 |
| | Carc 2 | H351 |
| | Aquatic Acute 1 | H400 |
| | Aquatic Chronic 1 | 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 | M = 1 (Aquatic Acute 1 (H400)) M = 1 (Aquatic Chronic 1 (H410)) |

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1. 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 Biphenyl-2-ol 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% \cong 0.006 mg Biphenyl-2-ol/kg bw). This indicates that the ^{14}C -Biphenyl-2-ol 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 Biphenyl-2-ol (Bartels 6.2-01). Metabolites of Biphenyl-2-ol 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 Biphenyl-2-ol, accounting for 68.33% of the absorbed dose. Conjugation of Biphenyl-2-ol 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). Biphenyl-2-ol, 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 -Biphenyl-2-ol in the B6C3F1 mouse (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). This suggests a low potential for bioaccumulation. The excretion of ^{14}C -Biphenyl-2-ol 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 -Biphenyl-2-ol in the B6C3F1 mouse and Fischer rats (6.2-02). In mice Biphenyl-2-ol was completely metabolized and rapidly eliminated via the urine predominantly as a sulphate and glucuronide conjugate of Biphenyl-2-ol. Qualitatively the extent of metabolism was comparable between mice and rats, although quantitative differences in the extent of Biphenyl-2-ol 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 Biphenyl-2-ol 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 Biphenyl-2-ol 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 Biphenyl-2-ol 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 Biphenyl-2-ol. The risk of exposure for Biphenyl-2-ol 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 Biphenyl-2-ol 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 Biphenyl-2-ol 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 ¹⁴C-Biphenyl-2-ol in the B6C3F1 mouse (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 Biphenyl-2-ol will be applied.

No specific study to determine the inhalation absorption of Biphenyl-2-ol is available. For inhalation application of Biphenyl-2-ol 100% absorption is assumed for risk characterization.

Acute toxicity

The oral acute toxicity was evaluated in the available document (6.1.1-01). Under the conditions of this study, the acute oral LD₅₀ of Dowicide 1 Antimicrobial (99.9% Biphenyl-2-ol) for male and female Fischer 344 rats was 2733 mg/kg (2730.3 mg Biphenyl-2-ol/kg), by nonlinear interpolation.

The dermal acute toxicity was evaluated in the available document (6.1.2-01). The LD₅₀ 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 (6.1.3-01a). The LD₅₀ values for male and female Fischer rats were greater than 36 mg/m³ (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 (6.1.3-01b).

Irritation and Corrosivity

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

Biphenyl-2-ol is currently classified as Eye Irrit. 2 (H319: Causes serious eye irritation). To investigate eye irritation properties of Biphenyl-2-ol a test in the eye of albino rabbit was performed (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 Biphenyl-2-ol 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

Biphenyl-2-ol was tested for its skin sensitisation potential in Buehler test on Guinea pigs (██████████ 6.1.5-01/1994b) with Dowicide 1 Antimicrobial (99.9% Biphenyl-2-ol). 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% Biphenyl-2-ol) did not cause delayed contact hypersensitivity in guinea pigs.

A paper is submitted where Biphenyl-2-ol was tested for its skin sensitisation potential in Magnusson-Kligman test on Guinea pigs (██████████ 6.1.5-02) with Preventol O Extra (Biphenyl-2-ol concentration \geq 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.

Repeated dose toxicity

Biphenyl-2-ol was examined in a 21-day dermal study (██████████ 6.3.2-01a) in Fischer 344 rats, in a 28-day oral study with Dog Beagle (██████████ 6.3.1-01, 6.5-02), in a 91-day oral study (██████████ 6.4.1-01a) in male Fischer rats, in a 1-year oral study in dog (██████████ 6.3.1-01, 6.5-02) and a 2-years oral study in Fischer rats (██████████ 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 (██████████ 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 % Biphenyl-2-ol) is considered to be non mutagenic in the CHO-HGPRT Forward Mutation Assay, (██████████ 6.6.3-01) both with and without metabolic activation.

Biphenyl-2-ol was clastogenic in Chinese hamster ovary cells at cytotoxic concentrations. In the presence of S9 mix, phenylhydroquinone (metabolite produced from Biphenyl-2-ol) is formed which has a higher cytotoxic and clastogenic potential than Biphenyl-2-ol (██████████ 6.6.2-01).

In-vivo

Preventol O Extra (99.9 % Biphenyl-2-ol) was evaluated as non-genotoxic in the in vivo comet assay in hepatocytes and kidney cells of male mice (██████████ 6.6.5-01).

Carcinogenicity

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

- In the rat Fischer 344 (██████████ 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 (██████████ 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 Biphenyl-2-ol.

For Biphenyl-2-ol 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 it was discussed the relevance of tumours for humans. The no relevance of the liver tumours in mice was agreed. The bladder tumour observed in male rats has been discussed in depth 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 alkalinisation 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 Biphenyl-2-ol is examined in two studies:

- (1) in Wistar rats (██████████ 6.8.1- 01)
- (2) in New Zealand White rabbits (██████████ 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 Biphenyl-2-ol in fertility in Sprague-Dawley rats (██████████ 6.8.2-02a and ██████████ 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

Biphenyl-2-ol 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 Biphenyl-2-ol" is submitted (Heyne 6.12.1-01; no GLP). Occupational medical surveillance of workers exposed to Biphenyl-2-ol, performed every 3 years on a routine basis. The workers have been in the production of Biphenyl-2-ol in average for 13,9 years. During this period accidents with Biphenyl-2-ol or unwanted contamination with Biphenyl-2-ol haven't been recorded and consultations of the Medical Department due to work or contact with Biphenyl-2-ol 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). Biphenyl-2-ol did not reveal any unwanted effects in the workers. Especially no sensitization of airways or skin to Biphenyl-2-ol 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 Biphenyl-2-ol 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 Biphenyl-2-ol 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% Biphenyl-2-ol 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 Biphenyl-2-ol 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 Biphenyl-2-ol 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 Dermatologischer 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 Biphenyl-2-ol was included. This series was tested in patients clinically suspected to suffer from contact allergy to preservatives. Of 2043 subjects tested with Biphenyl-2-ol (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". Biphenyl-2-ol was one of the test compounds. Biphenyl-2-ol was applied as a 1% solution in petrolatum. Of 1131 patients tested with Biphenyl-2-ol, 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 Biphenyl-2-ol 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 Biphenyl-2-ol 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 Biphenyl-2-ol 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 Biphenyl-2-ol containing products (1) germicidal agent (2) coolant | allergic contact dermatitis in both cases due to Biphenyl-2-ol | Adams 6.12.6 (01) |
| 6.12.6 Key study | Clinical case | One case of sensitivity to Biphenyl-2-ol due to occupational contact to a coolant containing Biphenyl-2-ol | Contact sensitivity to Biphenyl-2-ol 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 % Biphenyl-2-ol 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". Biphenyl-2-ol was one of the test compounds. | Of 1131 patients tested with Biphenyl-2-ol, 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% Biphenyl-2-ol. 40 workers were tested. 39 of them presented with dermatitis of hands and/or forearms. 5 had incidences of dermatitis in the past. | Biphenyl-2-ol was not a contact allergen in any of the cases. | De Boer 6.12.6 (08) |

Table 2.2.1.1-1: Effects of Biphenyl-2-ol 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% Biphenyl-2-ol 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 (██████████ 6.10-01/AIII 6.10-1) where the effects of sodium biphenyl-2-olate (OPP-Na) and Biphenyl-2-ol 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. Biphenyl-2-ol had no significant tumour-promoting or initiating effects. The increase in urinary pH caused by OPP-Na but not by Biphenyl-2-ol might cause the difference in the carcinogenic potential of the two compounds.

A paper is submitted (██████████ 6.10-03/ AIII 6.10-2) where the effects of an alkalizer or an acidifier on bladder carcinogenesis induced by Biphenyl-2-ol or OPP-Na were examined. The results indicate that the administration of an alkalizer enhanced the carcinogenicity of Biphenyl-2-ol 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 Biphenyl-2-ol resulted from the higher alkalinity of OPP-Na.

A study is submitted (██████████ 6.10-15/ AIII 6.10-3; no guideline; no GLP) where the possible role of prostaglandin-*H*-synthase (PGHS) in Biphenyl-2-ol-induced bladder tumour formation is investigated. Biphenyl-2-ol and phenylhydroquinone (PHQ) stimulate cyclooxygenase activity and are oxidised by PGHS. Biphenyl-2-ol, 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 Biphenyl-2-ol 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 Biphenyl-2-ol

| Type of study | Dosage | Results | Reference |
|-------------------------------------|---|--|------------------------------------|
| 32-week, dietary, rats Key study | 20000 ppm, with and without tumour initiator <i>ad libitum</i> | Biphenyl-2-ol had no significant tumour-promoting or -initiating effects in the urinary bladder. | ██████████ 6.10 (01)/AIII 6.10 (1) |

Table 2.2.1.1-2: Other/special studies with Biphenyl-2-ol

| Type of study | Dosage | Results | Reference |
|--|--|---|--------------------------|
| 26-week, dietary, rats Key study | 12500 ppm, with/without NaHCO ₃ <i>ad libitum</i> | Urinary bladder tumourigenesis of Biphenyl-2-ol is enhanced by NaHCO ₃ . | 5.10 (03)/ AIII 6.10 (2) |
| <i>In-vitro</i> interaction with PGHS Key study | Biphenyl-2-ol, PHQ, PBQ: 100 µM | Biphenyl-2-ol and PHQ stimulate cyclooxygenase activity and are oxidised by PGHS. Biphenyl-2-ol, PHQ and PBQ inhibit PGHS at higher concentrations. | 6.10 (15)/ AIII 6.10 (3) |
| 32-week, dietary, rats | 12,500 ppm, with varying amounts of NaHCO ₃ <i>ad libitum</i> | Morphological changes of the bladder epithelium, correlating with increased urinary pH. | 6.10 (01) |
| 32-week, dietary, rats | 20,000 ppm, <i>ad libitum</i> | Reduced urinary osmolality. Increased pH and Na ⁺ correlate with tumourigenesis. | 6.10 (04) |
| 12-week, dietary, rats | 0, 2500, 5000, 10,000, 20,000 ppm, <i>ad libitum</i> | At 20,000 ppm: morphological changes of the bladder luminal surface evident by SEM | 6.10 (02) |
| 90-day, dietary + acute DNA-binding study in rats | 90-day study: Biphenyl-2-ol, Na Biphenyl-2-olate: 2% in diet Acute assay: Biphenyl-2-ol, Na Biphenyl-2-olate: 500 mg/kg | Na Biphenyl-2-olate, but not Biphenyl-2-ol, caused regenerative hyperplasia of the urinary bladder. Biphenyl-2-ol-treated rats revealed renal damage. No interactions with DNA could be demonstrated for either compound. | 6.10 (06) |
| 8-week, dietary, rats | Biphenyl-2-ol: 1.25% with or without NaHCO ₃ Na Biphenyl-2-olate: 2% with or without NH ₄ Cl | Males are more sensitive to Biphenyl-2-ol than females under alkaline conditions with respect to bladder hyperplasia. | 6.10 (07) |
| 1-week, dietary, rats | Biphenyl-2-ol, Na Biphenyl-2-olate: 0.1-2.0% | Biphenyl-2-ol and Na Biphenyl-2-olate caused a dose-dependent increase in agglutinability of bladder epithelial cells by Con A which is an indication for carcinogenic potential. | 6.10 (08) |
| Acute oral, | Biphenyl-2-ol, PHQ, PBQ: | Biphenyl-2-ol treatment led to GSH depletion and eosinophilic | 6.10 (09) |

Table 2.2.1.1-2: Other/special studies with Biphenyl-2-ol

| Type of study | Dosage | Results | Reference |
|--|---|--|-----------|
| <i>rat</i> | 700, 1400 mg/kg bw, single oral gavage, with or without inhibition of GSH synthesis | degeneration of centrilobular hepatocytes. Inhibition of GSH synthesis aggravated hepatotoxicity of Biphenyl-2-ol. | |
| <i>Cytotoxicity test in primary rat hepatocytes</i> | Biphenyl-2-ol, PHQ: 0–1 mM | Biphenyl-2-ol cytotoxicity is enhanced by monooxygenase inhibition and GSH depletion. PHQ-induced cell death can be inhibited by sulfhydryl compounds. | 6.10 (10) |
| <i>In-vitro and in-vivo macromolecular binding assay</i> | ¹⁴ C-Biphenyl-2-ol: 1 µCi <i>In vivo</i> : Biphenyl-2-ol, Na Biphenyl-2-olate: 50-500 mg/kg, oral gavage, 16-18 h | A non-linear increase in macromolecular binding of Biphenyl-2-ol and Na Biphenyl-2-olate was observed in vivo and in vitro. This may be caused by the saturation of detoxification pathways. | 6.10 (11) |
| <i>In-vitro metabolism of Biphenyl-2-ol</i> | Biphenyl-2-ol: 1-100 µM | Biphenyl-2-ol 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). | 6.10 (12) |
| <i>In-vivo assay of DNA synthesis in bladder</i> | Biphenyl-2-ol, Na Biphenyl-2-olate: 2% in diet; 4–24 weeks | Biphenyl-2-ol and Biphenyl-2-olate cause a proliferative response in renal pelvis and papilla when given at a dietary level of 2%. | 6.10 (13) |
| <i>In-vitro and in-vivo GSH conjugation</i> | <i>In-vitro</i> study: 79 µg/mL <i>In-vivo</i> study: 1000 mg/kg, single oral dose | PHQ-GSH is excreted via the bile after Biphenyl-2-ol administration to rats. In vitro, PHQ-GSH can be formed non-enzymatically from PBQ and GSH or enzymatically from Biphenyl-2-ol and GSH. | 6.10 (14) |
| <i>In-vivo assay of DNA and protein adducts in rats</i> | 0, 15, 50, 125, 250, 500, 1000 mg/kg Biphenyl-2-ol, single oral gavage | Biphenyl-2-ol or its metabolites form protein, but not DNA, adducts in urinary bladder tissue. | 6.10 (16) |
| <i>Ten-week feeding study in</i> | Biphenyl-2-ol: 1.25% in diet Na Biphenyl-2-olate: 2.0% | Biphenyl-2-ol and SOPP caused urothelial hyperplasia in rats as evident by histology and increased | 6.10 (17) |

Table 2.2.1.1-2: Other/special studies with Biphenyl-2-ol

| Type of study | Dosage | Results | Reference |
|--|--|--|--|
| <i>rats</i> | in diet 10 weeks | cell proliferation. | |
| <i>7 and 14 days feeding study in male B6C3F1 mice</i> | 0, 500, and 1000 mg/kg/day Biphenyl-2-ol in the diet for 7 and 14 days | The results indicate that Biphenyl-2-ol may be an agonist ligand for PPAR α . | OPP_TOX_chronMaus_PPAR tumors_REPORT_2009-10 |

2.2.1.2. 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 establishing critical endpoints

The acute AEL for risk characterization was deduced from a teratogenicity oral study in New Zealand White rabbits (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 AEL_{acute} 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 (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 established after a follow up discussion (See comment below). Therefore, considering an assessment factor of 100, an AEL_{medium} and AEL_{long} of 0.39 mg/kg bw/day was calculated.

Conclusion of the follow up discussion for establishing AF

In the combined chronic toxicity and carcinogenicity study of (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 (██████████ 1985). The NOAEL of 39 mg/kg bw/d from ██████████ 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 (██████████ 6.1.5-01/1994b). An additional Assessment Factor (AF) is applied for deriving AEC for short exposure from a LOAEC. A AF of 10 (10 for intraspecies variability) is applied.

No NOAEC/LOAEC/AEC 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

2.2.1.3. Exposure assessment

The human exposure assessment towards the active substance, Biphenyl-2-ol or Preventol O Extra as biocidal group Product-type 3 (Veterinary hygiene biocidal product) was performed according to the TNsG on Human Exposure to Biocidal Products (2002, 2007, taking into account User Guidance to report 2002), and computer program ConsExpo 4.1.

Professional exposure is considered for specialised disinfectors which provide cleaning services for animal facilities which might be exposed on a long-term basis.

Non professional use is not envisaged.

Farmers and their employees might be exposed when re-entering the premises after treatment via the inhalatory and dermal routes. Also there is a potential risk of residues entering the food chain for human consumption due to the exposure of livestock to residues of biocidal product as a result of its use to disinfect animal houses.

Human exposure assessment for professional users:

The application of biocidal products containing Biphenyl-2-ol as disinfectant in livestock 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.

Professional exposure is addressed using Spray model 2 (TNSG on human exposure). During spray application of the biocidal product is assumed that coveralls will be worn by professional cleaners (10% penetration) and also RPE (FF P2, EN 149) with a protection factor of 10. The use of respiratory protective equipment is considered relevant for this scenario due to the hazard properties of the biocidal product and its volatility.

Exposure associated to maintenance activities as well as cleaning of the equipment after use is also considered.

Indirect human exposure as results of use:

In order to assess the inhalation exposure of workers at re-entry the Biphenyl-2-ol concentration in air was simulated using the constant rate evaporation model from computer program ConsExpo 4.1 (RIVM) and the default parameters from EC Document 'Technical Notes for Guidance, Guidance on Estimating Livestock Exposure to Active Substances used in Biocidal Products' (CA-Dec10-Doc.6.2.b). Dermal contact to treated surfaces is also considered based on the application rate (0.75 g/m² Biphenyl-2-ol) and the assumption that the palms of both hands are exposed.

A preliminary estimation of potential dietary exposure of consumers is performed based on the initial external exposure of fattening pigs to Biphenyl-2-ol residues is addressed according to EC Document 'Technical Notes for Guidance, Guidance on Estimating Livestock Exposure to Active Substances used in Biocidal Products' (CA-Dec10-Doc.6.2.b) and affords a worst case value of 3.39 mg/kg bw. Also, a metabolism study in lactating goats is available.

Metabolic patterns in rats and lactating goats are similar according to the studies provided by the Applicant. Hence it is safely assumed that Biphenyl-2-ol metabolism in pigs follows a similar pattern².

The metabolism study on lactating goats indicates that Biphenyl-2-ol does not accumulate in tissues. Hence considering also that Biphenyl-2-ol does not accumulate in rats, exposure of consumers to Biphenyl-2-ol residues via meat or edible offal from mammals (ruminants and pigs) can be excluded. However, no conclusion can be drawn regarding exposure of consumers to Biphenyl-2-ol via meat or edible offal from birds (broilers/turkeys) in absence of metabolism study.

Hence Dietary exposure of consumers to Biphenyl-2-ol residues in food as a consequence of its use for the disinfection of livestock units is inconclusive.

2.2.1.4. Risk characterisation

The results shown below indicate an acceptable risk for the professional use of biocidal product when using Preventol O Extra as disinfectant in livestock units provided that PPE is worn (coverall, gloves and RPE) during the application step.

The results shown below indicate also an acceptable risk for the professional (acute) indirect exposure to disinfectant in livestock units containing Biphenyl-2-ol.

² guideline for plant protection products APPENDIX F METABOLISM AND DISTRIBUTION IN DOMESTIC ANIMALS http://ec.europa.eu/food/plant/resources/publications_en.htm

| Chronic Exposure Scenario | Exposure Adults (mg/kg bw/[d]) | AEL (mg/kg bw/[d]) | Exposure % AEL |
|--|--------------------------------|--------------------|----------------|
| Specialized disinfectors providing cleaning services, medium pressure spraying, 0.5% Biphenyl-2-ol, 126 min, plus cleaning of spray equipment, daily, Tier 1 | | | |
| Inhalation | 1.66E-02 | 0.4 | 4 |
| Dermal | 2.274342 | 0.4 | 569 |
| Total | 2.290964 | 0.4 | 573 |
| | | | |
| Chronic Exposure Scenario | Exposure Adults (mg/kg bw/[d]) | AEL (mg/kg bw/[d]) | Exposure % AEL |
| Specialized disinfectors providing cleaning services, medium pressure spraying, 0.5% Biphenyl-2-ol, 126 min, plus cleaning of spray equipment, daily, Tier 2 | | | |
| Inhalation* | 1.66E-03 | 0.4 | 0.4 |
| Dermal* | 0.139392 | 0.4 | 35 |
| Total | 0.141054 | 0.4 | 35 |
| *RPE PF 10 during spraying, overall, gloves | | | |
| Acute Exposure Scenario | Exposure Adults (mg/kg bw) | AEL (mg/kg bw) | Exposure % AEL |
| Specialized disinfectors providing cleaning services, maintenance of equipment, Tier 1 | | | |
| Inhalation | - | 1 | - |
| Dermal | 3.58E-02 | 1 | 3.6 |
| Total | 3.58E-02 | 1 | 3.6 |
| | | | |
| Acute Exposure Scenario | Exposure Adults (mg/kg bw) | AEL (mg/kg bw) | Exposure % AEL |
| Professionals re-entering livestock units 8 after disinfection (fattening pig housing; application at 0.75 g Biphenyl-2-ol/m ²), Tier 1 | | | |
| Inhalation* | 8.7E-05 | 1 | - |
| Dermal** | 4.01E-02 | 1 | 4 |
| Total | 4.02E-02 | 1 | 4 |
| * At 0.00207 mg Biphenyl-2-ol/m ³ in air (estimated); | | | |
| ** palms of hands | | | |

Dietary exposure:

Exposure of consumers to Biphenyl-2-ol residues via meat or edible offal from mammals (ruminants and pigs) can be excluded. No conclusion can be drawn regarding exposure of consumers to Biphenyl-2-ol via meat or edible offal from birds (broilers/turkeys), in absence of a metabolism study on poultry,

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 Biphenyl-2-ol in the aquatic systems (estimated $DT_{50} > 1$ year).

Biphenyl-2-ol 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 Biphenyl-2-ol was estimated using the AOPWIN program (v. 1.91, 2000). Using a mean daily OH concentration in air of 0.5×10^6 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, Biphenyl-2-ol has a low vapour pressure.

Biphenyl-2-ol 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 Körner, 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 Biphenyl-2-ol 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 classification K_{oc} value of 347 $L \cdot kg^{-1}$, Biphenyl-2-ol can be classified as a moderately mobile substance.

Although a $\log P_{ow}$ of 3.18 was determined, no indication for a possible bioaccumulative potential of Biphenyl-2-ol 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 OECD 209 with activated sludge, $EC_{50} = 56$ mg Biphenyl-2-ol $\cdot L^{-1}$), an assessment factor of 100 can be applied. Thus, a $PNEC_{microorganisms}$ of 0.56 mg a.i./L is derived.

Surface water compartment

The toxicity of Biphenyl-2-ol 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}).

$$\begin{aligned} \text{PNEC}_{\text{sed}} &= (\text{K}_{\text{susp-water}}/\text{RHO}_{\text{susp}}) * \text{PNEC}_{\text{water}} * 1000 && \text{(page 113 of TGD)} \\ \text{K}_{\text{susp-water}} &= \text{F}_{\text{water}_{\text{susp}}} + (\text{F}_{\text{solid}_{\text{susp}}} * (\text{Kp}_{\text{susp}}/1000) * \text{RHO}_{\text{solid}}) && \text{(page 47 of TGD)} \\ &= 0.9 + (0.1 * (34.7/1000) * 2500) = 9.575 \text{ m}^3/\text{m}^3 \\ \text{PNEC}_{\text{sed}} &= (9.575/1150) * 0.0006 * 1000 = 0.0049 \text{ mg/kg} \\ \text{PNEC}_{\text{sed}} &= 0.0049 \text{ mg/kg Biphenyl-2-ol/kg wet sediment} \end{aligned}$$

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):

$$\text{EC}_{50} \text{ (28 days)} = 633.5 \text{ mg a.s.} \cdot \text{kg}_{\text{dw}}^{-1} \text{ soil}$$

- Earthworms (*Eisenia fetida*):

$$\text{LC}_{50} \text{ (14 days)} = 198.2 \text{ mg a.i.} \cdot \text{kg}^{-1} \text{ soil}$$

$$\text{NOEC} \text{ (14 days)} = 125 \text{ mg a.i.} \cdot \text{kg}_{\text{dw}}^{-1} \text{ soil}$$

- Terrestrial plants (*Avena sativa*):

$$\text{LC}_{50} \text{ (14 days)} = 53.9 \text{ mg a.i.} \cdot \text{kg}^{-1} \text{ soil}$$

$$\text{NOEC} \text{ (14 days)} = 12.5 \text{ mg a.i.} \cdot \text{kg}_{\text{dw}}^{-1} \text{ soil}$$

The lowest result was obtained in the study with plants. A PNEC_{soil} was calculated on basis of the lowest LC₅₀ of three trophic levels using an assessment factor of 1000 (TGD, Table 20).

$$\begin{aligned}
 \text{PNEC}_{\text{soil}} &= 53.9 \text{ mg Biphenyl-2-ol}\cdot\text{kg}^{-1} \text{ dry weight soil}\cdot 10^{-3} \\
 &= 0.054 \text{ mg Biphenyl-2-ol}\cdot\text{kg}^{-1} \text{ dry weight soil} \\
 &= 0.054 / 1.13 \\
 \text{PNEC}_{\text{soil}} &= 0.048 \text{ mg Biphenyl-2-ol}\cdot\text{kg}^{-1} \text{ wet weight soil}
 \end{aligned}$$

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

A flow-through study was conducted to evaluate the bioconcentration of Biphenyl-2-ol 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 Biphenyl-2-ol can be ruled out, since these data show that Biphenyl-2-ol 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] |
|----------------------------|--|---------------------|
| <i>Oncorhynchus mykiss</i> | Fish acute 96 h - LC ₅₀ Mortality | 4 |

| | | |
|--|--|------------------|
| <i>Daphnia magna</i> | Aquatic invertebrates acute 48 h - LC ₅₀ Mortality | 2.7 |
| <i>Pseudo-kirchneriella subcapitata</i> | Algae growth inhibition 72 h - NOEC Growth inhibition | 0.468 |
| Activated sludge | Microorganisms 3 h - respiration inhibition | 56 |
| <i>Pimephales promelas</i> (Fathead minnow) | Fish chronic 21 d - NOEC Reproduction (Egg hatch F1) 21 d - LOEC Reproduction (Egg hatch F1) | 36 293 |
| <i>Daphnia magna</i> | Aquatic invertebrates chronic 21 d - NOEC Reproduction | 0.006 |
| <i>Avena sativa</i> | 14 d - EC ₅₀ Germination rate, mortality and phytotoxicity | 53.9 |
| <i>Eisenia fetida</i> | 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 + 2 weeks 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

Biphenyl-2-ol can be considered readily biodegradable. Monitoring and laboratory studies have also shown that Biphenyl-2-ol is easily removed in STP systems. Based on literature studies, Biphenyl-2-ol is also not persistent water-sediment systems, and a soil biodegradation study also has shown that Biphenyl-2-ol 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 Biphenyl-2-ol in the aquatic systems (estimated DT₅₀ > 1 year), however, from the photolysis study in water, it has been shown that Biphenyl-2-ol is photolytically unstable in the aqueous medium. Therefore, it is unlikely that Biphenyl-2-ol 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 (K_{ow}) 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 Biphenyl-2-ol to bioaccumulate. Therefore, Biphenyl-2-ol 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 Biphenyl-2-ol 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 Biphenyl-2-ol 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 and half-life in air > 2 days) is not fulfilled. In soil, biodegradation and sorption study was performed to understand the persistence of Biphenyl-2-ol in this compartment, indicating that Biphenyl-2-ol 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 Biphenyl-2-ol.

In conclusion, considering the above rationale, it can be concluded that Biphenyl-2-ol does not fulfil the POPs criteria.

Conclusion:

Biphenyl-2-ol must not be regarded as a Persistent or Bioaccumulative, Toxic, POP or ED substance because it does not fulfil the criteria. Therefore, Biphenyl-2-ol is not PBT/vPvB.

2.2.2.4. Exposure assessment

The releases of b.p. Biphenyl-2-ol to the environment are assessed by applying emission models to soil after manure applications on grassland and arable land followed by emission models to groundwater and surface water.

2.2.2.5. Risk characterisation

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 2.2.2.5-1).

Table 2.2.2.5-1: PEC_{soil} and PEC/PNEC for Biphenyl-2-ol as veterinary hygiene biocidal product after one manure application on arable land or four manure applications on grassland (without and with degradation: DT₅₀ = 30 days and DT₅₀ = 15.08 days)

| Subcategory | Nitrogen emission standard | | | | Phosphate emission standard | | | |
|---|--|--|-----------------------------|-----------------------------|---|---|-----------------------------|-----------------------------|
| | PIEC _{grs-N} [mg/kg _{wwt}] | PIEC _{ars-N} [mg/kg _{wwt}] | PEC/ PNEC _{grs} | PEC/ PNEC _{ars} | PIEC _{grs-P2O5} [mg/kg _{wwt}] | PIEC _{ars-P2O5} [mg/kg _{wwt}] | PEC/ PNEC _{grs} | PEC/ PNEC _{ars} |
| Without degradation | | | | | | | | |
| Sows in individual pens | 0.2912 | 0.0546 | 6.066 | 1.137 | 0.2405 | 0.0348 | 5.011 | 0.726 |
| Sows in groups | 0.3319 | 0.0622 | 6.915 | 1.296 | 0.2742 | 0.0397 | 5.712 | 0.828 |
| Fattening pigs | 0.2348 | 0.0294 | 4.893 | 0.612 | 0.2274 | 0.0220 | 4.739 | 0.458 |
| Broilers, free range with litter floor | 0.0743 | 0.0186 | 1.548 | 0.387 | 0.1136 | 0.0220 | 2.367 | 0.457 |
| Turkeys, free range with litter floor | 0.1416 | 0.0089 | 2.951 | 0.184 | 0.1920 | 0.0093 | 4.001 | 0.193 |
| With degradation Soil DT₅₀ = 30 days | | | | | | | | |
| Sows in individual pens | 0.10233 | 0.0546 | 2.132 | 1.137 | 0.0845 | 0.0348 | 1.761 | 0.726 |
| Sows in groups | 0.11665 | 0.0622 | 2.430 | 1.296 | 0.0964 | 0.0397 | 2.007 | 0.828 |
| Fattening pigs | 0.08253 | 0.0294 | 1.719 | 0.612 | 0.0799 | 0.0220 | 1.665 | 0.458 |
| Broilers, free range with litter floor | 0.02611 | 0.0186 | 0.544 | 0.387 | 0.0399 | 0.0220 | 0.832 | 0.457 |
| Turkeys, free range with litter floor | 0.04977 | 0.0089 | 1.037 | 0.184 | 0.0675 | 0.0093 | 1.406 | 0.193 |
| With degradation Soil DT₅₀ = 15.08 days | | | | | | | | |
| Sows in individual pens | 0.07975 | 0.0546 | 1.662 | 1.137 | 0.0659 | 0.0348 | 1.373 | 0.726 |
| Sows in groups | 0.09091 | 0.0622 | 1.894 | 1.296 | 0.0751 | 0.0397 | 1.565 | 0.828 |
| Fattening pigs | 0.06432 | 0.0294 | 1.340 | 0.612 | 0.0623 | 0.0220 | 1.298 | 0.458 |
| Broilers, free range with litter floor | 0.02035 | 0.0186 | 0.424 | 0.387 | 0.0311 | 0.0220 | 0.648 | 0.457 |
| Turkeys, free range with litter floor | 0.03879 | 0.0089 | 0.808 | 0.184 | 0.0526 | 0.0093 | 1.096 | 0.193 |

Regarding the direct exposure of soil via manure, there is an acceptable risk in the arable land scenario, even in the worst case in which no degradation is taken into account, for the animal (sub) category 'broiler in free range with litter floor (cat.12)'. But, there is an unacceptable risk in the grassland scenario when no biodegradation of Biphenyl-2-ol in soil is considered. However, when a soil $DT_{50} = 30$ days is taken into account, an acceptable risk for soil was demonstrated for broilers in the cases of the nitrogen and phosphate immissions standard for grassland scenario.

Groundwater compartment

Biphenyl-2-ol concentrations in soil pore water as an indicator for a possible groundwater contamination have been assessed and the results are shown in the following table.

Table 2.2.2.5-2: PEC_{groundwater} for Biphenyl-2-ol as veterinary hygiene biocidal product after one manure application on arable land or four manure applications on grassland (with degradation: DT₅₀ = 30 days and DT₅₀ = 15.08 days)

| Subcategory | PEC values [µg/L] | | | |
|---|----------------------|-------------------------|-------------------------|-------------------------|
| | PEC _{grs-N} | PEC _{grs-P205} | PEC _{ara-N} | PEC _{ara-P205} |
| Without degradation | | | | |
| Sows in individual pens | 46.70 | 38.58 | 8.76 | 5.59 |
| Sows in groups | 53.23 | 43.97 | 9.98 | 6.37 |
| Fattening pigs | 37.66 | 36.48 | 4.71 | 3.52 |
| Broilers, free range with litter floor | 11.91 | 18.22 | 2.98 | 3.52 |
| Turkeys, free range with litter floor | 22.71 | 30.80 | 1.42 | 1.49 |
| With degradation Soil DT₅₀ = 30 days | PEC _{grs-N} | | PEC _{grs-P205} | |
| Sows in individual pens | 16.41 | | 13.56 | |
| Sows in groups | 18.71 | | 15.45 | |
| Fattening pigs | 13.24 | | 12.82 | |
| Broilers, free range with litter floor | 4.19 | | 6.40 | |
| Turkeys, free range with litter floor | 7.98 | | 10.82 | |
| With degradation Soil DT₅₀ = 15.08 days | PEC _{grs-N} | | PEC _{grs-P205} | |
| Sows in individual pens | 12.79 | | 10.57 | |
| Sows in groups | 14.58 | | 12.04 | |
| Fattening pigs | 10.32 | | 9.99 | |
| Broilers, free range with litter floor | 3.26 | | 4.99 | |
| Turkeys, free range with litter floor | 6.22 | | 8.44 | |

A refinement step, which leads to a more realistic estimation, is the use of EU FOCUS models. The results of the groundwater modelling investigation conducted using FOCUS PEARL are shown in Table 2.2.2.5-3 for all 9 representative FOCUS scenarios.

Table 2.2.2.5-3: Predicted 80th percentile concentrations for Biphenyl-2-ol in groundwater

| FOCUS Scenarios | | |
|-----------------|--|------------------------------|
| | Concentration closest to the 80 th percentile [$\mu\text{g}\cdot\text{L}^{-1}$] | |
| | Alfalfa (grassland) | Winter cereals (arable land) |
| Châteaudun | <0.0001 | <0.0001 |
| Hamburg | <0.0001 | <0.0001 |
| Jokioinen | <0.0001 | <0.0001 |
| Kremsmünster | <0.0001 | <0.0001 |
| Okehampton | <0.0001 | <0.0001 |
| Piacenza | <0.0001 | <0.0001 |
| Porto | <0.0001 | <0.0001 |
| Sevilla | <0.0001 | <0.0001 |
| Thiva | <0.0001 | <0.0001 |

For groundwater the trigger value according to Directive 2006/118/EC was exceeded (0.1 $\mu\text{g}/\text{L}$) indicating an unacceptable risk to this compartment. However, when FOCUS groundwater scenarios were applied (for more details see Doc. II-B Section 10.4.1), all PEC values were found to be below of this trigger value for all scenarios and for both grassland and arable land situations. Therefore, no unacceptable risk to groundwater after application of b.p containing Biphenyl-2-ol is indicated.

Aquatic compartment (surface water and sediment)

It is assumed that the potential for transport of biocides to surface waters could be via runoff or fields drainage systems.

All PEC values in surface water arose from the direct application of manure to agricultural soils and the subsequent translocation of a.s. to groundwater and surface water.

The concentration in porewater of agricultural soil, adjusted to account for dilution in the receiving water body, may be used to indicate potential for runoff and drainage. The PECs in surface water are derived from the PEC in groundwater assuming a dilution factor of 10 for the entry of run-off water into the receiving water.

Table 2.2.2.5-3: PEC/PNEC surface water for Biphenyl-2-ol as veterinary hygiene biocidal product after one manure application on arable land or four manure applications on grassland (with degradation: $DT_{50} = 30$ days and $DT_{50} = 15.08$ days)

| Subcategory | Nitrogen emission standard | | Nitrogen emission standard | |
|--|----------------------------|---------------|----------------------------|--------------------|
| | PEC_{grs-N} | PEC_{ars-N} | $PEC/PNEC_{grs-N}$ | $PEC/PNEC_{ars-N}$ |
| With degradation Soil $DT_{50} = 30$ days | | | | |
| Sows in individual pens | 1.641E-03 | 1.356E-03 | 2.735 | 2.260 |
| Sows in groups | 1.871E-03 | 1.545E-03 | 3.118 | 2.576 |
| Fattening pigs | 1.324E-03 | 1.282E-03 | 2.206 | 2.137 |
| Broilers - free range with litter floor | 4.187E-04 | 6.404E-04 | 0.698 | 1.067 |
| Turkeys - free range with litter floor | 7.983E-04 | 1.082E-03 | 1.330 | 1.804 |
| With degradation Soil $DT_{50} = 15.08$ days | | | | |
| Sows in individual pens | 1.279E-03 | 1.057E-03 | 2.132 | 1.761 |
| Sows in groups | 1.458E-03 | 1.204E-03 | 2.430 | 2.007 |
| Fattening pigs | 1.032E-03 | 9.991E-04 | 1.719 | 1.665 |
| Broilers - free range with litter floor | 3.264E-04 | 4.991E-04 | 0.544 | 0.832 |
| Turkeys - free range with litter floor | 6.221E-04 | 8.436E-04 | 1.037 | 1.406 |

Table 2.2.2.5-4: PEC/PNEC sediment for Biphenyl-2-ol as veterinary hygiene biocidal product after one manure application on arable land or four manure applications on grassland (with degradation: $DT_{50} = 30$ days and $DT_{50} = 15.08$ days)

| Subcategory | Nitrogen emission standard [mg/kg _{wwt}] | | Nitrogen emission standard | |
|--|---|-----------------------|----------------------------|---------------------------|
| | PIEC _{grs-N} | PIEC _{ars-N} | PEC/PNEC _{grs-N} | PEC/PNEC _{ars-N} |
| With degradation Soil $DT_{50} = 30$ days | | | | |
| Sows in individual pens | 1.367E-02 | 1.129E-02 | 2.790 | 2.305 |
| Sows in groups | 1.558E-02 | 1.287E-02 | 3.180 | 2.627 |
| Fattening pigs | 1.103E-02 | 1.068E-02 | 2.250 | 2.179 |
| Broilers - free range with litter floor | 3.488E-03 | 5.335E-03 | 0.712 | 1.089 |
| Turkeys - free range with litter floor | 6.650E-03 | 9.017E-03 | 1.357 | 1.840 |
| With degradation Soil $DT_{50} = 15.08$ days | | | | |
| Sows in individual pens | 1.066E-02 | 8.802E-03 | 2.175 | 1.796 |
| Sows in groups | 1.215E-02 | 1.003E-02 | 2.479 | 2.048 |
| Fattening pigs | 8.594E-03 | 8.323E-03 | 1.754 | 1.699 |
| Broilers - free range with litter floor | 2.719E-03 | 4.158E-03 | 0.555 | 0.849 |
| Turkeys - free range with litter floor | 5.183E-03 | 7.028E-03 | 1.058 | 1.434 |

Regarding the direct application of manure to agricultural soils and the subsequent translocation to groundwater and surface water, there is an unacceptable risk to surface water and sediment in most of animals scenarios assessed. Only for broilers, and when a soil DT_{50} of 15.08 days is considered, there is an acceptable risk for surface water and sediment.

For Broilers and Turkeys, it is also assumed there are emissions to the STP and the PECs values in this compartment are derived from emission of liquid manure via STP in the poultry farms.

Table 2.2.2.5-5: PEC/PNEC for Poultry farms with release to STP.

| | | PEC _{STP} [mg/L] | PEC _{water} [mg/L] | PEC _{sed} [mg/kg _{wwt}] | PEC/PNEC STP | PEC/PNEC WATER | PEC/PNEC SEDIMENT |
|----------|---------------------|------------------------------|--------------------------------|---|-----------------|-------------------|----------------------|
| Broilers | Tier 1 ¹ | 2.52E-02 | 2.52E-03 | 2.10E-02 | 0.045 | 4.20 | 4.28 |
| | Tier 2 ² | 2.05E-03 | 2.05E-04 | 1.70E-03 | 0.005 | 0.341 | 0.348 |
| Turkeys | Tier 1 ¹ | 7.42E-02 | 7.42E-03 | 6.17E-02 | 0.132 | 12.36 | 12.60 |
| | Tier 2 ² | 6.03E-03 | 6.03E-04 | 5.02E-03 | 0.011 | 1.00 | 1.02 |

¹ Tier 1: 12.3% of the influent residues being present in the STP effluent water phase

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

Regarding the emissions from Broilers and Turkeys to the STP, there was no unacceptable risk for the microorganisms in the STP, but there was an unacceptable risk for the surface water and sediment compartments when a worst case of 12.3% of the influent residues being present in the STP effluent water phase is taken into account. However, when refinement was carried out (1% of the influent residues being present in the STP effluent water phase) there is an acceptable risk for broilers in the surface water and sediment compartments.

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

A flow-through study was conducted to evaluate the bioconcentration of Biphenyl-2-ol 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 Biphenyl-2-ol can be ruled out, since these data show that Biphenyl-2-ol does not accumulate in the environment. There is no need to assess this exposure route further.

A secondary exposure of Biphenyl-2-ol 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 Biphenyl-2-ol can be ruled out, since these data show that Biphenyl-2-ol 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 Biphenyl-2-ol to interfere with the hormone system, Biphenyl-2-ol is present in one of the documents-lists of the Commission staff working document on implementation of the Community Strategy for Endocrine Disruptors - 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 Biphenyl-2-ol to fathead minnow (*Pimephales promelas*) was tested in a reproductive performance test by [REDACTED] (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 Biphenyl-2-ol 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 Biphenyl-2-ol 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·kg_{bw}⁻¹·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 Biphenyl-2-ol above which reproduction of the invertebrate *Daphnia magna* and fish (fathead minnow) are reduced (NOECs = 0.036 mg·L⁻¹ and 0.009 mg·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 CSTE (2003)

Thus, it can be stated that, to date, no evidence of endocrine disruption activity can be attributed to Biphenyl-2-ol.

2.3. Overall conclusions

The outcome of the assessment for Biphenyl-2-ol in Product-type 3 is specified in the BPC opinion following discussions at the [number of BPC meeting] meeting of the Biocidal Products Committee (BPC). The BPC opinion is available from the ECHA website.

2.4. List of endpoints

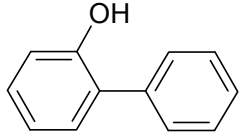
The most important endpoints, as identified during the evaluation process, are listed in [Appendix I](#).

Appendix I: List of endpoints

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

| | |
|-----------------------------|---|
| Active substance (ISO Name) | <i>o</i> -Phenylphenol (ISO) Synonymous: Biphenyl-2-ol (EINECS name), OPP |
| Product-type | Veterinary hygiene |

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 °C (purity: 99.9%) |
| Boiling point (state purity) | 287 °C (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) | 58.72 mN/m at 20.1 °C (0.558 g/L) |
| Vapour pressure (in Pa, state temperature) | 0.474 Pa at 20 °C, 0.906 Pa at 25 °C |

| | |
|---|---|
| Henry's law constant ($\text{Pa m}^3\text{mol}^{-1}$) | Ratio between vapour pressure and water solubility: 0.15 $\text{Pa}\times\text{m}^3\times\text{mol}^{-1}$ at 20 °C and pH 5 0.14 $\text{Pa}\times\text{m}^3\times\text{mol}^{-1}$ at 20 °C and pH 7 0.13 $\text{Pa}\times\text{m}^3\times\text{mol}^{-1}$ 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: <i>n</i> -heptane: 50.3 g/L acetone, 1,2-dichloroethane, ethyl acetate, methanol, <i>p</i> -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 ($\log P_{\text{ow}}$) (state temperature) | $\log P_{\text{ow}}$: 3.18 at 22.51 °C. (more accurate value which is to be used exclusively) "the $\log P_{\text{ow}}$ of Biphenyl-2-ol is nearly independent from pH value when investigated at pH 5, pH 7 and pH 9." |
| Dissociation constant | $\text{pK} = 9.5$ 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-ol is 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/m³.

Water (principle of method and LOQ)

Surface and drinking water: HPLC-MS/MS; LOQ = 0.1 µg/L

Body fluids and tissues (principle of method and LOQ)

Not applicable since Biphenyl-2-ol 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

Subchronic

Species/ target / critical effect

Rats /urinary bladder/ 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 = 200 mg/kg bw/day (2-years oral study)

Relevant dermal NOAEL / LOAEL

No Data

Relevant inhalation NOAEL / LOAEL

No Data

Long term

Species/ target / critical effect

Rats /urinary bladder/ 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 = 200 mg/kg bw/day (2-years oral study)

Relevant dermal NOAEL / LOAEL

No Data

Relevant inhalation NOAEL / LOAEL

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 toxicityDevelopmental 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-term} | 0.4 mg/kg bw/day | 2-years oral study | 100 |
| AEL _{medium-term} | 0.4 mg/kg bw/day | 2-years oral study | 100 |
| AEL _{short-term} | 1 mg/kg bw/day | teratogenicity oral study in New Zealand White rabbits | 100 |
| ADI ³ | 0.4 mg/kg bw/day | 2-years oral study | 100 |
| ARfD | No relevant | | |

MRLs

| | |
|----------------------|--|
| Relevant commodities | |
|----------------------|--|

Reference value for groundwater

| | |
|-------------------------------------|--|
| According to BPR Annex VI, point 68 | |
|-------------------------------------|--|

Dermal absorption

| | |
|---|--|
| Study (<i>in vitro/vivo</i>), species tested | Dermal absorption, excretion <i>in vivo</i> , humans. |
| Formulation (formulation type and including concentration(s) tested, vehicle) | 0.4% (w/v) Biphenyl-2-ol 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 | Not assessed |
| Intended uses | Surface disinfection in pig and poultry units (farmers and professional cleaners in intensive livestock farming installations) by means of hand-held medium pressure spraying at 4-7 bar., 0.5% Biphenyl-2-ol. |
| Industrial users | Not applicable |

³If residues in food or feed.

| | |
|------------------------------|--|
| Professional users | Chronic exposure: Spray model 2 (TNSG on human exposure). PPE required: coverall, gloves and RPE. No risk. Worker re-entry: inhalation exposure estimated using constant rate evaporation model from ConsExpo 4.1 (RIVM) & default parameters from EC Document 'Technical Notes for Guidance, Guidance on Estimating Livestock Exposure to Active Substances used in Biocidal Products' (CA-Dec10-Doc.6.2.b). Dermal exposure considering Biphenyl-2-ol application rate and contact with palms of both hands. No risk. |
| Non professional users | Not applicable. |
| General public | Not applicable. |
| Exposure via residue in food | Dietary exposure of consumers to Biphenyl-2-ol residues from meat/ edible offal from ruminants/ pigs is excluded as metabolism in lactating goats shows that no residues accumulate in tissues. No conclusion can be drawn regarding birds (chicken, turkey) in absence of metabolism study. |

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 15.08 days (recalculated considering a biphasic approach) DT _{90 lab} (20 °C, aerobic): 8.81 hours* (n = 1), r ² = 0.994 0.34 days (recalculated considering a biphasic approach) |
| 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

| | |
|---|--|
| <p>Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)</p> | <p>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)</p> <p>Adsorption, OECD Guideline 121: estimated mean K_{oc} value: 346.7 K_d was not reported pH dependence was not apparent</p> |
| 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), activated sludge treatment, biological nitrate removal (nitrification/denitrification), 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

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

Ground water (indicate location and type of study)

No data presented

Air (indicate location and type of study)

No data presented

Chapter 5: Effects on Non-target Species

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

| Species | Time-scale | Endpoint | Toxicity |
|----------------------------|------------|-------------------------|--|
| Fish | | | |
| <i>Oncorhynchus mykiss</i> | 96 hours | Mortality | LC ₅₀ = 4.0 mg/L Dill <i>et al.</i> (1985) |
| <i>Pimephales promelas</i> | 21 days | Reproduction | NOEC = 0.036 mg/L [REDACTED] (2002) |
| Invertebrates | | | |
| <i>Daphnia magna</i> | 48 hours | Mortality | LC ₅₀ = 2.7 mg/L Dill <i>et al.</i> (1985) |
| <i>Daphnia magna</i> | 21 days | Survival & reproduction | NOEC = 0.006 mg/L Bruns (2001) |
| Algae | | | |

| | | | |
|--|----------|--------------------------------|---|
| <i>Pseudokirchneriella subcapitata</i> | 72 hours | Growth inhibition | $E_rC_{50} = 3.57 \text{ mg/L}$ $E_bC_{50} = 1.35 \text{ mg/L}$ $NOEC = 0.468 \text{ mg/L}$ Hicks (2001) |
| Microorganisms | | | |
| Activated sludge | 3 hours | Inhibition of respiratory rate | $EC_{50} = 56 \text{ mg/L}$ 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} (28 days) = 633.5 mg a.s./kg d.wt. soil
 Schulz.L (2012)

Carbon mineralization

Effects on terrestrial vertebrates

Acute toxicity to mammals

$LD_{50} = 2733 \text{ mg/kg bw}$ (♂+♀)
 ██████████ (1994)

Chronic toxicity to mammals
 (Annex IIA, point VI.6.5)

NOAEL = 300 mg/kg diet (1 year)
 Cosse *et al.* (1990)

Acute toxicity to birds

$LC_{50} > 2250 \text{ mg/kg bw}$
 ██████████ (1986)

Dietary toxicity to birds

$LD_{50} > 5620 \text{ mg/kg diet}$
 ██████████ (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)

[REDACTED] (1999)

Depuration time(DT₅₀)

< 1 h (5 µg/L) / < 19 h (50 µg/L)

Depuration time(DT₉₀)

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 | | | Re marks: |
|----------------------------|-------------------|--|--------------|------------------|-------------------------------|----------------|-------------------------------------|------------------------------|--------------------------------|-------------------------------|-----------|
| | | | 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 | |
| Veterinary hygiene PT 3 | Preventol O Extra | Bacteria, fungi and yeasts 30 min of contact time to support the efficacy | XX Flakes | 995 g/kg | hand-held spraying 4-7 bar | ~ 3 per year | ? | 5 g/L | ~ 0.15 L/m ² | ~0.75 g/m ² | -- |

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 | Stroeck, K. | 2014 | Quality Control Data from the production plant covering approximately 68 months (Jan. 2009 to Sept. 2014) to derive a specification limit for Biphenyl-2-ol. 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 (<i>o</i> -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 | <i>o</i> -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 (<i>n</i> -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 |
| A3.9(03) IIA, III 3.6 | Feldhues, E. | 2006 b | Statement Partition coefficient <i>n</i> -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 |

| (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 |
|---|-------------|-----------|--|--|------------|--------------------|--------------------|----------------------------------|--------------------------|
| A3.11(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 | <i>o</i> -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 | <i>o</i> -Phenylphenol / Oxidising properties. Date: 2004-07-29 | Bayer Chemicals AG, Leverkusen, Germany | -- | No | No | Yes | LANXESS Deutschland GmbH |
| A3.17(01) IIA, III 3.13 also filed A8.1(02) | Kraus, H. | 2006 | <i>o</i> -Phenylphenol (OPP) / Reactivity towards container material. Date: 2006-05-30 | LANXESS Deutschland GmbH, 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 |
|----------------------------|--------------|-----------|---|--|--|--------------------|--------------------|----------------------------------|--------------------------|
| 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 |
| 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 |

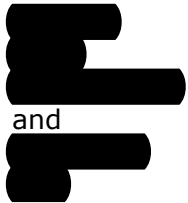

| (Sub)Section / Annex point | Authors (s) | Year | Title | Testing Company | Report No. | GLP Study (Yes/No) | Published (Yes/No) | Data Protection Claimed (Yes/No) | Data Owner |
|----------------------------|--------------|-----------|--|--|---|--------------------|--------------------|----------------------------------|--------------------------|
| A4.2(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 |
| A4.2(03) IIA, IV 4.2 | Königer, 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 |

| (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(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 |
| A4.3(02) IIA, IV 4.3 | Semrau, J | 2011 | Determination of residues of Biphenyl-2-ol (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 |

| (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 |
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| 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 |
| 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 | ██████████ and ██████████ | 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 |

| (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 |
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| 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 |
| A6.1.3(01) IIA, VI 6.1.3 | [REDACTED] and [REDACTED] | 1992 | <i>ortho</i> -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. | -- | <i>Am. Ind. Hyg. Assoc. J.</i> 39 : 26-32 | -- | -- | -- | -- |
| A6.1.4(01) IIA, VI 6.1.4 | [REDACTED] | 1994 a | 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 |

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| A6.1.4(02) IIA, VI 6.1.4 | [REDACTED] | 1981 b | Report on the test of Preventol O Extra for irritation of the mucous membrane. Date: 1981-11-04 | Fraunhofer-Institut für Toxikologie und Aerosolforschung, Schmallenberg, Germany | T2004666 | No | No | Yes | LANXESS Deutschland GmbH |
| A6.1.5(01) IIA; VI 6.1.5 | [REDACTED] | 1994 b | 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 | Andersen, K.E. and Hamann, K. | 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, Gentofte Hospital, Hellerup, Denmark | <i>Fd. Chem Toxic.</i> 22(8) , pp. 655-660 | No | Yes | No | -- |


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| A6.2(01) IIA, VI 6.2 | Bartels, M.J., Brzak, K.A., McNett, D. and Shabrang, S.N. | 1997 | <i>Biphenyl-2-ol</i> (OPP): Limited Metabolism Study in Human. Date: 1997-02-03 | Dow Chemical Company | HET K-001024- 059 | Yes | No | Yes | Dow Chemical Company |
| A6.2(02) IIA, VI 6.2 |  and  | 1997 | <i>Biphenyl-2-ol</i> (OPP): Metabolism of ¹⁴ C- Labelled OPP in B ₆ B ₃ F 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 <i>ortho</i> - Phenylphenol Formulation after Dermal Application to Healthy Volunteers. Date: 1996-09-19 | Bayer AG | P0995002 | Yes (GCP) | No | Yes | LANXESS Deutschlan d GmbH |

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| A6.3.1(01) IIA, VI 6.3.1 also filed: A6.5(02) | [REDACTED] and [REDACTED] | 1990 | <i>ortho</i> -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 |
| A6.3.2(01) IIA, VI 6.3.2 | [REDACTED] and [REDACTED] | 1993 | <i>ortho</i> -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] | 1996 a | Technical Grade <i>ortho</i> -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 |

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| A6.5(01) IIA, VI 6.5 also filed: A6.7(01) | ██████████ and ██████████ | 1996 | Technical Grade <i>ortho</i> -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 | -- | -- | -- | -- |

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| A6.6.2(01) IIA, VI 6.6.2 | Tayama, S., Kamiya, N. and Nakagawa, Y. | 1989 | Genotoxic effects of <i>o</i> -Phenylphenol metabolites in CHO- K1 cells. | Dept. of Toxicology, Tokyo Metropolitan Research Laboratory of Public Health, Tokyo, Japan | <i>Mutat. Res.</i> 223 , pp. 23- 33 | No | Yes | No | -- |
| A6.6.3(01) IIA, VI 6.6.3 | ██████████ | 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 Deutschlan d GmbH |
| A6.6.5(01) IIA, VI 6.6.5 | ██████████ | 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 Deutschlan d GmbH |
| A6.8.1(02) IIA, VI 6.8.1 | ██████████ ██████████ and ██████████ | 1991 | <i>Biphenyl-2-ol</i> (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 <i>o</i> -Phenylphenol. | Toxicology Division, Institute of Environmental Toxicology, Kodaira, Tokyo, Japan | <i>J. Pesticide Sci.</i> 3 , pp. 365-370 | No | Yes | No | -- |
| A6.8.2(01) IIA, VI 6.8.2 | ██████████ and ██████████ | 1995 | A Two-Generation Dietary Reproduction Study in Sprague-Dawley Rats Using Technical Grade <i>ortho</i> -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 | ██████████ | 1990 | Two-Generation Dietary Reproduction Study in Rats Using <i>ortho</i> -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 <i>o</i> -Phenylphenate and <i>o</i> -Phenylphenol on Two-Stage Urinary Bladder Carcinogenesis. | First Department of Pathology, Nagoya City University Medical School, Nagoya, Japan | <i>Gann.</i> , 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 <i>o</i> -Phenylphenol and Sodium <i>o</i> -Phenylphenate in the Rat Urinary Bladder., | Dept. of Toxicology, Tokyo Metropolitan Research Laboratory of Public Health, Tokyo, Japan | <i>Fd. Chem. Toxic.</i> 25 (5), pp. 359-362 | No | Yes | No | -- |
| A6.10(03) |  | 1994 | <i>o</i> -Phenylphenol – Interactions of <i>Biphenyl-2-ol</i> (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 |

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| A6.12.1(01) IIA, VI 6.12.1 | Heyne, R. and Attig, G. | 2004 | Occupational Medical Experiences with <i>o</i> -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 <i>o</i> -Phenylphenol. | Palo Alto Medical Clinic, Palo Alto, CA, USA | <i>Contact Dermatitis</i> 7 , p. 332 | No | Yes | No | -- |
| A6.12.6(02) IIA, VI 6.9.6 | van Hecke, E. | 1986 | Contact sensitivity to <i>o</i> -Phenylphenol in a coolant. | Dept. of Dermatology, University Hospital, Gent, Belgium | <i>Contact Dermatitis</i> 15 (1), p. 46 | No | Yes | No | -- |
| 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) | <i>Br. J. Dermatology</i> 138 , pp. 467-476 | No | Yes | No | -- |

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| 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) | <i>Dermatosen / Occup. Environ.</i> 44 , pp. 154-159 | No | Yes | No | -- |
| 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) | <i>Dermatosen</i> 41(2) , pp. 71-76 | No | Yes | No | -- |

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| 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/ Biphenyl-2-ol 32". date: 2013-01-22 | LANXESS Deutschland GmbH, | -- | No | No | Yes | LANXESS Deutschland GmbH, |
| 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 |

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| 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 <i>ortho</i> - and <i>para</i> -hydroxybiphenyl in a small lake receiving discharges from an adjacent superfund site. | Ralph M. Parsons laboratory, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA | <i>Environ. Sci. Technol.</i> 32 , pp. 1319-1328. | No | Yes | No | -- |
| 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 | -- | <i>Environ. Sci. Technol.</i> , 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 | -- |

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| 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 <i>o</i> -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. | 1989 | 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 |
| 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 |

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| A7.1.1.2.1(04) | Kanne, R. | 1989b | 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. | Abwasserbiologische Laboratorien der HOECHST AG, Frankfurt, Germany | 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 | <i>Chemosphere</i> 40 , 1131-1142. | No | Yes | No | -- |
| 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 | <i>Chemosphere</i> 40 , 929-935. | No | Yes | No | -- |

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| 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 and gas 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 (<i>ortho</i> -Phenylphenol). Summary of screening experiments concerning the behaviour of <i>Biphenyl-2-ol</i> (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. | 2001 | 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]- <i>ortho</i> -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 |

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| 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 | <i>Journal of Soil Contamination</i> 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 Biphenyl-2-ol 20, Residues in fumes and gases. | Anadiag Laboratories, France 67500 Haguenau | R B4256 | No | No | Yes | LANXESS Deutschland GmbH |

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| 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 |
| A7.4.1.1(02) | [REDACTED] | 1991 | <i>o</i> -Phenylphenol Toxicity to Fish <i>Chinook salmon</i> (<i>Oncorhynchus tshawytscha</i>). 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 <i>o</i> -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 |

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| A7.4.1.2(02) | Kühn, R., Pattard, M., Pernak, K.- D. Winter, | 1988 | Harmful effects of chemicals in the <i>Daphnia</i> 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 | -- |
| A7.4.1.3(01) IIA, VII.7.3 | Hicks, S. | 2002 | <i>ortho</i> -Phenylphenol: Growth Inhibition Test with the Green Alga, <i>Selenastrum capricornutum</i> . 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: <i>Scenedesmus subspicatus</i> 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 | -- | <i>Chemosphere</i> 14 , pp. 1239-1251 | No | Yes | No | -- |
| A7.4.2(01) IIA, VII.7.5 | Fàbregas, E. | 2007 | <i>o</i> -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 |
| A7.4.3.2(01) IIIA, XIII 2.2 | ██████████ and ██████████ | 2002 | Preventol O Extra: Determination of Effects on the Reproduction of Fathead minnow (<i>Pimephales promelas</i>). Date: 2002-03-25 | Brixham Environmental Laboratory, AstraZeneca UK Limited, Brixham, UK | BL7213/B | Yes | No | Yes | LANXESS Deutschland GmbH |

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| A7.4.3.3.1(01) IIIA, XIII.2.3 | ██████████ | 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, <i>Daphnia magna</i> 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 - <i>Daphnia magna</i> - EC ₅₀ immobilisation and EC ₅₀ reproduction. Date: 1989-10-13 | Bayer AG | No. 51 A/88 | No | No | Yes | LANXESS Deutschland GmbH |
| 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 <i>Chironomus riparius</i> . Date: 2005-02-28 | ETC Oekotoxikologie GmbH, Germany | AI1ME | Yes | No | Yes | LANXESS Deutschland GmbH |

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| 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 |
| A7.5.1.2(01) IIIA, XIII 3.2 | Moser, Th. and Scheffczyk, A. | 2004 | Preventol O Extra: Acute toxicity to the earthworm <i>Eisenia fetida</i> in an artificial soil test. Date: 2004-12-08 | ETC Oekotoxikologie GmbH, Flörsheim, Germany | AI1RA | Yes | No | Yes | LANXESS Deutschland GmbH |

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| 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 | ██████████ | 1986 a | <i>ortho</i> -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 | ██████████ | 1986 b | <i>ortho</i> -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 |
| A7.5.3.1.2(02) IIIA, XIII 1.2 | ██████████ | 1986 c | <i>ortho</i> -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 |

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| A7.5.5.1(01) IIIA, 13.3 | Fàbregas, E. | 2007 | <i>o</i> -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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| B2.3(01) IIB, I 2.3 also filed B3.1(01) | Stroech, K. | 2006 | <i>o</i> -Phenylphenol / Appearance. Date: 2006-04-11 | LANXESS Deutschland GmbH, Leverkusen, Germany | -- | No | No | Yes | LANXESS Deutschland GmbH |
| B3.1(01) IIB, III 3.1 also filed B2.3(01) | Stroech, K. | 2006 | <i>o</i> -Phenylphenol / Appearance. Date: 2006-04-11 | LANXESS Deutschland GmbH, Leverkusen, Germany | -- | No | No | Yes | LANXESS Deutschland GmbH |
| B3.2(01) IIB, III 3.2 | Stroech, K. | 2004a | <i>o</i> -Phenylphenol / Explosive properties. Date: 2004-07-29 | Bayer Chemicals AG, Leverkusen, Germany | -- | No | No | Yes | LANXESS Deutschland GmbH |
| B3.3(01) IIB, III 3.3 | Stroech, K. | 2004b | <i>o</i> -Phenylphenol / Oxidising properties. Date: 2004-07-29 | Bayer Chemicals AG, Leverkusen, Germany | -- | No | No | Yes | LANXESS Deutschland GmbH |

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| B3.4(01) IIB, III 3.4 | 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 |
| B3.5(01) IIB, III 3.4 | Erstling, K. | 2007 | Determination of acidity/alkalinity | Bayer Industry Services, Leverkusen, Germany | 2007/0045/02 | Yes | No | Yes | LANXESS Deutschland GmbH |
| B3.6(01) IIB, III 3.6 | Erstling, K. | 2001 | Physicochemical properties. Date: 2001-09-13 Amended: 2004-12-02, 2006-03-02 and 2006-04-24 | Bayer AG, Leverkusen, Germany | A 00/0068/01 LEV | Yes | No | Yes | LANXESS Deutschland GmbH |

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| B3.7(01) IIB, III 3.7 | European Commission (Ed.) | 2006 | Content of the product dossier accompanying the active substance for Annex I inclusion. Date: 2006-09-14 | European Commission, Directorate-General-JRC, Institute for Health and Consumer Protection, Unit: Toxicology and Chemical Substances, European Chemicals Bureau | -- | No | Yes | No | European Commission, European Chemicals Bureau |
| B3.8(01) IIB, III 3.8 also filed B3.6(02) | Erstling, K. | 2007 | Physicochemical properties of Preventol O Extra | Bayer Industry Services, Leverkusen, Germany | 2007/0045/02 | Yes | No | Yes | LANXESS Deutschland GmbH |
| B3.10(01) - | 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 |

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| B4.1(01) IIA, IV 4.1 | Feldhues, E. | 2005a | Validation of analytical methods for the determination of main and minor components in Preventol O Extra. Date: 2005-02-04 Amended: 2006-04-24 | Bayer Industry Services GmbH & Co. OHG, BIS-SUA-Analytics, Leverkusen, Germany | A 02/0162/08 LEV | Yes | No | Yes | LANXESS Deutschland GmbH |
| 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 IIB, V 5.10 | Groetsch, W. and Nothhelfer, B. | 2000 | SF Preventol Biphenyl-2-ol. Determination of the bacteriostatic and fungistatic efficacy according to the DGHM-guideline (I/2.1). Date: 2000-06-27 | Labor L + S, Bad-Bocklet-Großenbrach, Germany | Report No. 01020970 | No | No | Yes | LANXESS Deutschland GmbH |

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| B5.10(02) | Gerharz, T | 2014 | Determination of disinfectant properties of Preventol OExtra in accordance to EN1656 and EN1657 | LANXESS Deutschland GmbH | D 2012-27, 2014-09-08 | - | No | Yes | LANXESS Deutschland GmbH |
| B6.7.1.1 IIIA, XI.1.5 | Thalacker, F.W. | 1997 | Nature of the Residue of ¹⁴ C- <i>ortho</i> -Phenylphenol in Lactating Goats. | Corning Hazleton Inc., Madison, WI, USA, | Report No. CHW 6578-105 | Yes | No | Yes | Dow Chemical Company LANXESS Deutschland GmbH |
| 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 | 2004 | Safety Data Sheet Preventol O Extra. Date: 2004-03-10 | LANXESS Deutschland GmbH, Leverkusen, Germany | SDS No.: 011472/23 | No | No | -- | LANXESS Deutschland GmbH |
| B8.1(02) IIB, VIII 8.1 | Kraus, H. | 2006 | <i>Biphenyl-2-ol</i> (OPP)/ Reactivity towards container material. Date: 2006-05-30 | LANXESS Deutschland GmbH, Leverkusen, Germany | -- | No | No | Yes | LANXESS Deutschland 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 | 2004 | Safety Data Sheet Preventol O Extra. Date: 2004-03-10 | LANXESS Deutschland GmbH, Leverkusen, Germany | SDS No.: 011472/23 | No | No | -- | LANXESS Deutschland 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 | 2004 | Safety Data Sheet Preventol O Extra. Date: 2004-03-10 | LANXESS Deutschland GmbH, Leverkusen, Germany | SDS No.: 011472/23 | No | No | -- | LANXESS Deutschland 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 | 2004 | Safety Data Sheet Preventol O Extra. Date: 2004-03-10 | LANXESS Deutschland GmbH, Leverkusen, Germany | SDS No.: 011472/23 | No | No | -- | LANXESS Deutschland GmbH |

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| 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 | 2004 | Safety Data Sheet Preventol O Extra. Date: 2004-03-10 | LANXESS Deutschland GmbH, Leverkusen, Germany | SDS No.: 011472/23 | No | No | -- | LANXESS Deutschland GmbH |