European Food Safety Authority

EFSA Scientific Report (2008) 217, 1-67

CONCLUSION ON PESTICIDE PEER REVIEW

Peer review of the pesticide risk assessment of the active substance 2-phenylphenol[1]

(Question No EFSA-Q-2008-392)

Issued on 19 December 2008

SUMMARY

2-Phenylphenol is one of the 295 substances of the fourth stage of the review programme covered by Commission Regulation (EC) No 2229/2004,[2] as amended by Regulation (EC) No 1095/2007.[3] This Regulation requires the European Food Safety Authority (EFSA) to organise upon request of the EU-Commission a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within six months a conclusion on the risk assessment to the EU-Commission.

Spain being the designated rapporteur Member State submitted the DAR on 2-phenylphenol in accordance with the provisions of Article 21(1) of the Regulation (EC) No 2229/2004, which was received by the EFSA on 11 February 2008. The peer review was initiated on 17 March 2008 by dispatching the DAR for consultation of the Member States and the notifiers LANXESS Deutschland GmbH and Dow Benelux BV. Subsequently, the comments received on the DAR were examined and responded by the rapporteur Member State in the reporting table. This table was evaluated by the EFSA to identify the remaining issues. The identified issues as well as further information made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in October 2008.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in November – December 2008 leading to the conclusions as laid down in this report.

This conclusion was reached on the basis of the evaluation of the representative use as a post harvest fungicide on citrus and pears (indoor use, closed drench chamber). Full details of the GAP can be found in the endpoints.

The representative formulated product for the evaluation was 'AGF/1-04', an emulsifiable concentrate (EC).

[1] For citation purposes: Conclusion on pesticide peer review regarding the risk assessment of the active substance 2-phenylphenol. *EFSA Scientific Report* (2008) 217, 1-67.
[2] OJ L379, 24.12.2004, p.13.
[3] OJ L246, 21.9.2007, p.19.

A partially validated method is available for citrus but there is currently no validated method for pears. Acceptable methods are available for soil and water but a method for air has been identified as a data gap. Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

Tested in mammals, 2-phenylphenol showed low acute oral, dermal and inhalation toxicity (oral LD_{50} 2733 mg/kg bw; dermal LD_{50} >2000 mg/kg, inhalation LC_{50} >0.036 mg/L). 2-Phenylphenol is irritating to skin (R38, "Irritating to skin" proposed) and to eyes (R36, "Irritating to the eyes" and R41 "Risk of serious damage to eyes" proposed) and to respiratory system (R37 "Irritating to respiratory system"). 2-Phenylphenol is not a sensitising agent. The relevant short-term oral NOAEL is 391 mg/kg bw/day from a study in rats, based on hyperplasia in the bladder urothelium and kidney damage in males. 2-Phenylphenol is not genotoxic. Systemic long-term toxicity and carcinogenicity NOAEL is 39 mg/kg bw/day, based on increased incidences of urinary bladder papillomas, transitional cell carcinomas, and/or combined papillomas and/or transitional cell carcinomas. The mechanism of tumorigenesis in rats was assumed to be non-genotoxic, probably based on chronic irritation of the epithelium by a combination of high pH, high sodium-ion concentration and/or high concentration of free metabolites at high doses. In mice, 2-phenylphenol caused an increased incidence of liver adenoma, carcinoma and hepatoblastoma at 500 mg/kg bw/day and 1000 mg/kg bw/day. The NOAEL for systemic toxicity in mice was <250 mg/kg bw/day, whereas the NOAEL for tumours was 250 mg/kg bw/day. Considering the occurrence of liver tumours in mice and urinary bladder tumours in rats, where the mechanism is not known, R40 Carc. Cat 3 "Limited evidence of a carcinogenic effect" was proposed. Reproductive parameters were not affected at any dose level. The overall parental and offspring NOAEL was established at 100 mg/kg bw/day, and the reproductive NOAEL was 500 mg/kg bw/day. The relevant maternal and developmental NOAELs in rats were established at 150 mg/kg bw/day, whereas in rabbits the relevant maternal and developmental NOAEL were proposed to be 100 mg/kg bw/day and 250 mg/kg bw/day, respectively. 2-Phenylphenol did not show any evidence of neurotoxicity. The **Acceptable Daily Intake (ADI) and the Acceptable Operator Exposure Level (AOEL) are 0.4 mg/kg bw/day** (NOAEL 39 mg/kg bw/day applying an SF of 100). An **Acute Reference Dose (ARfD) was not allocated**, based on the toxicological profile. The default dermal absorption value 100% was regarded as appropriate. Operator and worker exposure was estimated to be below the AOEL even without the use of Personal Protective Equipment (PPE). As the representative formulation 'AGF/1-04' is used in closed facilities, bystander exposure is not expected.

Metabolism of 2-phenylphenol was investigated in oranges and pears having received a post-harvest treatment. In oranges, substantial amounts of residues only penetrated into the peel and, in addition to 2-phenylphenol and its conjugates, 2-phenylhydroquinone and its conjugates were also found. In pears, residues penetrated into the pulp and 2-phenylhydroquinone or its conjugates were not found.

Concern was raised with regard to the toxicological potential of the metabolite 2-phenylhydroquinone. Therefore, the experts meeting proposed a provisional residue definition for plant matrices including 2-phenylphenol, 2-phenylhydroquinone and their conjugates, expressed as 2-phenylphenol. It is pending information on the toxicological potential of 2-phenylhydroquinone which was requested from the notifier.

The notifier made a case that treated fruits are destined only for direct human consumption and will not be part of livestock diet. Therefore an assessment with regard to livestock exposure and residues in food of animal origin would not be necessary. However,

consideration of the issue by risk managers is required. Therefore, as a precautionary measure, an assessment was carried out assuming livestock exposure to 2-phenylphenol residues from treated crops.

Intake of fruit pomace is only relevant for ruminants. A metabolism study on ruminants was submitted and showed only very low transfer of residues into milk and tissues. 2-Phenylphenol and metabolites could not be identified in the matrices analysed. Therefore, no residue definition for animal matrices could be proposed. Based on the intake calculation for pomace of citrus fruit treated with 2-phenylphenol according to the notified GAP, no significant residues are expected in milk or tissues of ruminants. However, this estimation might have to be re-addressed for pears when relevant data are available.

A provisional MRL for citrus fruit was proposed on the basis of six residue trials on mandarins and oranges respectively. To confirm this MRL the notifier was asked to demonstrate that the analytical methods used in the residue trials and processing studies correctly quantify the residues of 2-phenylphenol, 2-phenylhydroquinone and their conjugates and to provide two further residue trials and valid storage stability data. No MRL could be proposed for pears as no valid residue trials were available.

A provisional chronic dietary intake estimate for citrus fruit was carried out by the rapporteur Member State. The TMDI was below the ADI for all considered consumer groups. However, the risk assessment is provisional pending further information on the toxicological potential of the metabolite 2-phenylhydroquinone and on additional residue data for citrus fruit and a full set of residue data for pears.

With regard to the applied for representative uses and considering that the waste water, including the cleaning water of the drenching system, must be collected and handled as hazardous chemical waste, the contamination of the environment was deemed to be negligible. However reliable data indicated that 2-phenylphenol is not persistent and exhibits medium mobility in soil (based on short duration batch experiments in which equilibrium was not reached). The formation of unextractable residues in soil was a significant sink, accounting for 77.4% AR, while the mineralisation to carbon dioxide accounted for 9.6% AR after 127 days. No major soil metabolites were found.

No reliable natural water sediment study was available, however a range of DT_{50} values of 5.5 – 19 days was estimated for the dissipation of 2-phenylphenol from the water column. 2-Phenylphenol exhibited a relatively fast photolytic degradation in water to innumerable minor photoproducts and to a diketohydroxy-compound (2-hydroxy-1,2-dihydrodibenzo[b,d]furan-3,4-dione) as major transformation product (maximum observed 13.6% AR), which also exhibited photolytic degradation. 2-Phenylphenol is readily biodegradable.

No Predicted Environmental Concentrations (PEC) were calculated (or regarded as necessary for this applied for representative use at EU level), since it was considered that the contamination of the environment is excluded during the normal work flow, where the waste water must be handled as hazardous chemical waste. 2-Phenylphenol was found in the majority of the samples taken from rivers and streams in Germany in a monitoring study (2-phenylphenol is not used exclusively as a pesticide).

2-phenylphenol was toxic to aquatic organisms (the proposal classification was R50 “Very toxic to aquatic organisms”). Since the exposure of surface water was excluded by the environmental fate and behaviour expert meeting, the risk to aquatic organisms was not assessed. Due to the representative use (indoor), the risk was considered low for terrestrial

vertebrates, bees, non-target arthropods, earthworms, soil macro and micro-organisms, other non-target organisms and biological methods for sewage treatment.

Key words: 2-phenylphenol, peer review, risk assessment, pesticide, fungicide

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BACKGROUND

Commission Regulation (EC) No 2229/2004 laying down the detailed rules for the implementation of the fourth stage of the work program referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 1112/2002, as amended by Commission Regulation (EC) No 1095/2007, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. 2-Phenylphenol is one of the 295 substances of the fourth stage, covered by the amended Regulation (EC) No 2229/2004 designating Spain as rapporteur Member State.

In accordance with the provisions of Article 21(1) of the Regulation (EC) No 2229/2004, Spain submitted the report of its initial evaluation of the dossier on 2-phenylphenol, hereafter referred to as the draft assessment report, received by the EFSA on 11 February 2008. Following an administrative evaluation, the draft assessment report was distributed for consultation in accordance with Article 24(2) of the Regulation (EC) 1095/2007 on 17 March 2008 to the Member States and to the notifiers LANXESS Deutschland GmbH and Dow Benelux BV, as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, the EFSA identified and agreed on lacking information to be addressed by the notifier as well as issues for further detailed discussion at expert level.

Taking into account the requested information received from the notifier, a scientific discussion took place in expert meetings in October 2008. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in November – December 2008 leading to the conclusions as laid down in this report.

During the peer review of the draft assessment report and the consultation of technical experts no critical issues were identified for consultation of the Scientific Panel on Plant Protection Products and their Residues (PPR).

In accordance with Article 24c(1) of the amended Regulation (EC) No 2229/2004, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period provided for by the same Article. A list of the relevant endpoints for the active substance as well as the formulation is provided in appendix A.

The documentation developed during the peer review was compiled as a peer review report comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's draft assessment report:

- the comments received,
- the resulting reporting table (revision 1-1, 18 June 2008),

as well as the documents summarising the follow-up of the issues identified as finalised at the end of the commenting period:

- the reports of the scientific expert consultation,
- the evaluation table (revision 2-1, 16 December 2008).

Given the importance of the draft assessment report including its addendum (compiled version of November 2008 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

2-phenylphenol is the used name for biphenyl-2-ol (IUPAC). There is no ISO common name for this compound.

2-phenylphenol acts as a general disinfectant disrupting cell walls and cell membranes.

The representative formulated product for the evaluation was 'AGF/1-04', an emulsifiable concentrate (EC).

The evaluated representative uses are as a post harvest fungicide on citrus and pear (indoor use, closed drench chamber). Full details of the GAP can be found in the endpoints.

SPECIFIC CONCLUSIONS OF THE EVALUATION

1. Identity, physical/chemical/technical properties and methods of analysis

The minimum purity of 2-phenylphenol as manufactured should not be less than 998 g/kg. At the moment no FAO specification exists. The technical material does not contain any significant or relevant impurities. The content of 2-phenylphenol in the representative formulation is 100 g/L (pure).

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of 2-phenylphenol or the respective formulation. The main data regarding the identity of 2-phenylphenol and its physical and chemical properties are given in appendix A.

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of 2-phenylphenol in the technical material and in the representative formulation. A method for impurities is not required as there are no significant or relevant impurities

Therefore, enough data are available to ensure that quality control measurements of the plant protection product are possible.

A GC-MS method for citrus with a proposed LOQ of 0.1 mg/kg for free and conjugated 2-phenylphenol and a LOQ of 0.2 mg/kg for free and conjugated phenylhydroquinone is available. However, this method has not been validated for the hydrolysis step and there are no validation data available for pears. Data gaps have therefore been identified for validation data to demonstrate the efficiency of the hydrolysis step and to demonstrate that the citrus method (Pollmann 2005a) is also applicable for pears.

Soil is analysed for 2-phenylphenol by LC-MS/MS with a LOQ of 0.005 mg/kg. Water is analysed for 2-phenylphenol by LC-MS/MS with a LOQ of 0.1 µg/L. An acceptable method of analysis for air is not available and a data gap has been identified.

Methods are not required for products of animal origin as no MRLs are proposed. A method for body fluids and tissues is not required as 2-phenylphenol is not classified as toxic or highly toxic.

2. Mammalian toxicity

2-phenylphenol was discussed at the meeting of experts PRAPeR 59 held in Parma in October 2008. The notifier was asked to address the toxicological comparison of different batches tested to the proposed specification. The notifier stated that the minimum purity is 99.7%, and the toxicological studies were performed with similar purity material. The toxicological batches were therefore considered equivalent to the declared specification.

During the commenting phase, a Member State raised a comment on possible consumer exposure via the dermal route: concern was brought forward for possible exposure to the metabolite 2-phenylhydroquinone (PHQ), based on its ability to cause depigmentation when applied to skin. It was noted that there was no information concerning degradation of 2-phenylphenol on the surface of the fruit, so it was not possible to address the point further. It was agreed this does not impact on the risk assessment, in terms of setting reference values. However, it was agreed that the notifier should be asked to clarify the potential for skin depigmentation for workers and consumers due to possible exposure to metabolite PHQ on citrus peel. Thus, a new data gap was then identified. Furthermore, the mammalian toxicological profile of PHQ should be provided with regard to setting specific reference values.

2.1. Absorption, Distribution, Excretion and Metabolism (Toxicokinetics)

Absorption of 2-phenylphenol is relatively rapid and almost complete, based on urinary and faecal excretion. Most of 2-phenylphenol is eliminated within the first 24 h (87.8% in urine and 2.9% in faeces). 2-Phenylphenol is widely distributed, with no accumulation in organs and tissues. It is extensively metabolised: in rodents sulphation is the predominant metabolic pathway at the low dose levels, while glucuronidation gained significance at high dose levels. Excretion is rapid and complete (mainly via urine) after single and repeat doses.

During the PRAPeR meeting, member states were asked to confirm the proposed metabolic pathway of 2-phenylphenol *in vivo*, and to check the relevance of metabolites to which consumers might be exposed (e.g. PHQ and phenylbenzoquinone - PBQ). If PBQ were present in animal metabolism, mutagenic effects would have been observed in the toxicity studies, but this was not the case. It was noted PBQ could be a transient form of PHQ, and for this reason may not have been detected in the metabolism studies. Genotoxic potential of PBQ was not established adequately, though showed positive *in vitro* results and also *in vivo* in a study of DNA damage. PHQ showed genotoxic potential in vitro and was negative in a *in vivo* study of DNA damage. No further information was available. However, taking into account the genotoxic potential *in vitro* and the toxicological properties of 2-phenylphenol (R40 was proposed), the metabolites should be considered relevant to consumers. No specific reference values were set due to the lack of information.

2.2. Acute toxicity

The oral LD_{50} in rats is 2733 mg/kg bw; the dermal LD_{50} was higher than 2000 mg/kg bw, and the LC_{50} was >0.036 mg/L (the maximum attainable concentration, 4-hours exposure). 2-Phenylphenol is irritating when applied topically to rabbits at dose level of 0.5 g (R38, “Irritating to skin” proposed). 2-Phenylphenol is irritating when applied to the rabbit eye (R36, “Irritating to the eyes” proposed) and to respiratory system (R37 “Irritating to respiratory system”). 2-Phenylphenol did not show sensitising properties in a Buehler test. As a reliable maximisation test was missing, the meeting of experts discussed the sensitising potential of 2-phenylphenol. Normally a Magnusson & Kligman test would be required.

Extensive human case reports indicated a low percentage of sensitisation (0.3%). The lymph node assay performed with the formulation (although not accepted) was also negative. The US Environmental Protection Agency (US EPA; 2006) and European Chemical Bureau (ECB; 26th ATP) did not propose classification for sensitisation, but the database for this decision was not known. The majority of experts agreed 2-phenylphenol should not be classified. As it was agreed it was not sensitiser, a data gap for a further study was not identified. Also the classification based on ocular effects was discussed. Some findings were not reversible after 8 days. It was agreed the findings were sufficiently severe to propose R41 "Risk of serious damage to eyes". It was noted the ECB did not classify 2-phenylphenol as R41.

2.3. Short-term toxicity

Oral studies in rat, dog and rabbit and dermal studies in rat and mice were summarised in the DAR.

Critical effects in repeat dose studies in rats were hyperplasia in the bladder urothelium and kidney damage in males. A NOAEL of 3130 ppm, corresponding to 391 mg/kg bw/day, was established.

In rabbits receiving 100, 500 and 1000 ppm by gavage, only signs of general toxicity were observed. The NOAEL was established at 100 mg/kg bw/day based on decreased bodyweight and bodyweight gains at 500 mg/kg bw/day.

In two subchronic studies in dog (4-weeks gavage and 1-year gavage) the NOAEL was set at 100 mg/kg bw/day, based on increased emesis with respect to the controls at highest doses. However, all the short-term studies in dog were considered of limited validity with regard to the setting of the NOAELs.

Two dermal studies (21 days in rat and 4 weeks in mice) were submitted. The relevant dermal NOAEL was 100 mg/kg bw/day.

2.4. Genotoxicity

2-Phenylphenol showed positive results in gene mutation, chromosome aberration, DNA damage and DNA binding tests. This positive response was clear in the presence of metabolic activation. *In vivo*, 2-phenylphenol gave mostly negative responses including for chromosome aberration, DNA damage and DNA binding. During the PRAPeR meeting the experts discussed 2-phenylphenol genotoxicity taking into account the outcomes of *in vivo* and *in vitro* tests. The meeting concluded that *in vitro* studies gave some indication of positive results but at cytoxic concentrations, but the *in vivo* studies were generally negative; however one published study (Sasaki 1997) showed positive results not reproducible in a second Comet assay. The positive results were considered not relevant to humans and did not affect the overall risk assessment. Overall the meeting agreed 2-phenylphenol is not genotoxic.

2-phenylphenol caused protein-binding (non-linear increase) and cell proliferation in bladder epithelial cells from treated male F344 rats, supporting a non-genotoxic mechanism for tumour formation in the bladder of treated male rats (a threshold mechanism was proposed - see section 2.5).

2.5. Long-term toxicity

In a combined chronic toxicity/carcinogenicity study Fischer rats received 2-phenylphenol in the diet. Systemic toxicity was noted as decreased body weight at mid and high doses for both sexes during all treatment periods. There was an increase in the urinary bladder hyperplasia at 12 and 24 month in high dose males (and high dose females at 24 months) along with an increase in congestion, haemorrhage, mineralisation and necrosis. Non-neoplastic findings consisted of increased incidence of calculi in the kidneys in high dose males and in the urinary bladder at 12 and 24 months, respectively. High dose males and females also had an increase in cysts of the kidneys at 24 months. High dose females had an increase in hyperplasia of the kidney along with increase infarct, acute inflammation and mineralisation of the kidney. In male rats there was an increased incidence of urinary bladder papillomas, transitional cell carcinomas, and/or combined papillomas and/or transitional cell carcinomas at 8000 ppm. The NOAEL for systemic long-term toxicity and for carcinogenicity was 800 ppm (39 mg/kg bw/day). The mechanism of tumorigenesis in rats was assumed to be non-genotoxic, probably based on chronic irritation of the epithelium by a combination of high pH, high sodium-ion concentration and/or high concentration of free metabolites at high doses.

In a carcinogenicity study in mice administered with 2-phenylphenol in the diet for 24 months, systemic toxicity was noted as decreased body weight gain throughout the study, an increase in absolute and relative liver weights at 12 and 24 months in all treated males and females, dose-related decrease of microvacuolation in the tubular epithelial cells of the kidney cortex and a decrease in the incidence and severity of degeneration/regeneration of their tubules at 12 and 24 months in males. Mice did not develop any treatment-related effects in the urinary bladder. An increased incidence of liver adenoma, carcinoma and hepatoblastoma was observed in male mice at 500 mg/kg bw/day and 1000 mg/kg bw/day, and a data gap for historical control values was set by the experts. The NOAEL for systemic toxicity in mice was <250 mg/kg bw/day, whereas the NOAEL for tumours was 250 mg/kg bw/day. There was no evidence to support a mode of action for the development of liver tumors in mice.

In a 2-year dermal study in rats, 2-phenylphenol caused non-neoplastic lesions, which included ulceration, inflammation and hyperkeratosis at the site of application.

During the PRAPeR 59 meeting, the carcinogenic potential of 2-phenylphenol was discussed. The exact mechanism for liver tumours in mice was not known but it was likely a non-genotoxic mechanism. The strain used has high background level of these tumours. For the bladder tumours in rats a mechanism was postulated (non-genotoxic), involving chronic irritation of the epithelium. This proposal was in accord with the US Environmental Protection Agency. The relevance of the mechanism for humans was discussed: although it could not be excluded that the mechanism was relevant, the high doses where tumours occurred were not relevant for humans. Considering the occurrence of liver tumours in mice and urinary bladder tumours in rats, where the mechanism is not known, Carc. Cat 3 R40 “Limited evidence of a carcinogenic effect” was proposed.

The use of an increased safety factor (SF) of 200 for the derivation of reference values, to take into account the occurrence of tumours in chronic studies, was discussed in the meeting. It was noted that the tumours were seen at high doses only, and the margin of safety was still high when applying 100 SF. The majority of experts supported an SF 100.

2.6. Reproductive toxicity

The reproductive toxicity of 2-phenylphenol was assessed in two multigeneration studies in rats.

Reproductive parameters were not affected at any dose level. Kidneys and urinary bladder (hyperplasia of the transitional epithelium cells, chronic inflammation) were the target organs. The overall parental and offspring NOAEL was established at 100 mg/kg bw/day, and the reproductive NOAEL was 500 mg/kg bw/day. The low fertility index in F0 females for F1b in one of the studies was considered in the meeting. The finding was considered occasional and not reproducible.

In developmental toxicity studies, when administered to pregnant rats at doses of 0, 150, 300, 600 and 1200 mg/kg bw/day, 2-phenylphenol caused ataxia in dams and excessive mortality (9 of 11) at the highest dose. In addition, females showed a noticeable bodyweight gain depression at the dosage level of >300 mg/kg bw/day. Toxicity to the foetus consisted of an increased incidence of foetal death, and a statistically significant reduction of the bodyweight at birth. The study did not reveal increased incidence of malformations up to the dose of 600 mg/kg bw/day. The relevant maternal and developmental NOAELs in rats were established at 150 mg/kg bw/day.

In rabbits, body weight and body weight gain were reduced at the high dose. Rabbits showed reduced activity and faeces, perineal soiling and faeces stained with blood. At necropsy, the main microscopic lesions were tubule degeneration and chronic inflammation in kidneys. A slight foetal weight reduction was observed at 250 mg/kg bw/day. There were no malformations recorded or any increased incidence of foetal variations or anomalies. The relevant maternal and developmental NOAEL were proposed to be 100 mg/kg bw/day and 250 mg/kg bw/day, respectively. In the meeting, an expert considered that the developmental NOAEL should be lowered from 250 mg/kg bw/day to 100 mg/kg bw/day based on some foetus resorptions in rabbits. However, there was not a clear teratogenic response. The resorptions were noted, but other parameters were without findings. The meeting concluded that the NOAELs in developmental studies proposed by the rapporteur Member State were appropriate.

2.7. Neurotoxicity

No specific studies were available; however, in the data package there was no evidence of neurotoxicity.

2.8. Further studies

In vitro genotoxicity studies performed with the main 2-phenylphenol metabolites, PHQ and PBQ, showed positive results for oxidative damage and cytotoxicity.

A series of *in vivo* studies in F344 rats were summarised in the DAR to clarify the mechanism of bladder carcinogenesis of 2-phenylphenol and its sodium salt. In a 13-week study, kidney damage and mitogenesis of the urinary bladder epithelium, leading to a hyperplasia, were seen in male rats. No neoplasic lesions were yet observed at this time; in a second subchronic study papillomas in urothelium were described. Some of these other studies investigated the influence of urinary pH and sodium concentration on the incidence of urinary bladder lesions. In summary, there was a positive correlation between urinary pH and the incidence of hyperplasic lesions of the bladder epithelial surface. The tumorigenic potential of 2-phenylphenol was enhanced by co-administration of sodium bicarbonate as an alkalinising

agent while the tumorigenesis by S2-phenylphenol was attenuated by co-administration of ammonium chloride as an acidifier. S2-phenylphenol, was found to be a promoter of the urinary bladder epithelium tumours with prior initiation and also weakly tumorigenic without initiation. 2-Phenylphenol or its metabolites were found able to form protein adducts in the bladder whereas DNA adducts could not be found. The bladder carcinogenesis was most likely mediated by a cytotoxic rather than a genotoxic effect.

2.9. Medical data

Periodical investigations performed in workers involved in the 2-phenylphenol production during more than 20 years showed that no accidents or contamination with 2-phenylphenol have been reported and medical consultations were not required due to work or contact with 2-phenylphenol. The urinary phenol levels have always been far below the German biological tolerance level of 200 mg/L and no airway or skin sensitisation towards 2-phenylphenol has occurred. Few cases of delayed hypersensitivity towards 2-phenylphenol have been described in occupationally exposed individuals. In five epidemiological studies, patch test reactions of patients that were occupationally exposed to 2-phenylphenol-containing products were evaluated. In two of these studies the analysed data corresponded to about 500 metalworkers. No positive reactions were recorded in the first study and 0.72% of the subjects showed a positive reaction in the second case. In other three studies, the sensitising potential of 2-phenylphenol was very low with weak to medium positive reactions in 0.29%, 0.40% or 0.30% of the study subjects.

2.10. Acceptable daily intake (ADI), acceptable operator exposure level (AOEL) and acute reference dose (ARfD)

Acceptable Daily Intake (ADI):

In the DAR the rapporteur Member State proposed an ADI of 0.2 mg/kg bw/day, based on the relevant NOAEL of 39 mg/kg bw/day, corrected by a SF of 200, considering the unknown mechanism of tumour formation in two species. At the PRAPeR meeting, the ADI was discussed: it was agreed to start from the same NOAEL, but applying a SF of 100, leading to an **ADI of 0.4 mg/kg bw/day**.

Acute Reference Dose (ARfD):

In the DAR the rapporteur Member State proposed an ARfD of 1.00 mg/kg bw based on decreased bodyweight gain and clinical signs of toxicity in rabbits during the first three days of dosing of a developmental toxicity study. During the PRAPeR 59 meeting it was discussed whether an ARfD is needed for 2-phenylphenol based on the toxicological profile. It was noted that the Joint Meeting on Pesticide Residues (JMPR) and US EPA had not set an ARfD. After discussion, it was concluded that an **ARfD was not required,** based on the toxicological profile.

Acceptable Operator Exposure Level (AOEL):

The AOEL proposed in the DAR was derived as the ADI. For the same reasons, the PRAPeR meeting established the **AOEL at 0.4 mg/kg bw/day** (NOAEL from the 2-year study in rats, SF 100).

2.11. Dermal absorption

Two reports were presented by the notifier to determine the extent of dermal absorption of 2-phenylphenol formulation 'AGF/1-04', containing 10% (w/v) 2-phenylphenol in a water-based formulation. Neither report was considered acceptable to address properly the issue. Based on the physical chemical characteristics of 2-phenylphenol (molecular weight 170.2 and log P_{ow} 3.18 at 22.5ºC) the proposal of the rapporteur Member State to consider the default 100% dermal absorption was regarded as appropriate.

2.12. Exposure to operators, workers and bystanders

'AGF/1-04' is a formulated product intended for incorporation into an automated drenching system for application directly to the fruit.

Operator

Exposure to 2-phenylphenol is estimated to occur during mixing/loading of 'AGF/1-04' into the automated drenching system: to assess this exposure there is no specific method to evaluate exposure, thus the operator exposure calculation was performed using the UK-POEM. Based on this consideration, operators would be exposed to 0.008 mg/kg bw/day (2% AOEL) using gloves during mixing/loading, and 0.16 mg/kg bw/day (40% AOEL) when no protective gloves are used.

Worker

Worker exposure was not calculated according to the known exposure models. The notifier presented a worker exposure study in which dermal and inhalation exposure was measured in workers at three citrus facilities. During the meeting the experts agreed to consider worker exposure in every task performed, which were pre-sorting, sorting and packing activities. Since there were few individuals (n= 6 – 15) involved in the different tasks within the study, it was agreed during the meeting to provide the most conservative assessment, taking into account maximum exposure figures.

Worker exposure assessment

Without gloves	**75th percentile**		**Maximum values**	
	Systemic exposure (mg/kg bw/day)	% AOEL	Systemic exposure (mg/kg bw/day)	% AOEL
PRE-SORTERS	0.14	35	0.24	60
SORTERS	0.047	12	0.091	23
PACKERS	0.022	6	0.054	14
With gloves	**75th percentile**		**Maximum values**	
	Systemic exposure (mg/kg bw/day)	% AOEL	Systemic exposure (mg/kg bw/day)	% AOEL
PRE-SORTERS	0.11	28	0.186	47
SORTERS	0.027	7	0.036	9
PACKERS	0.0133	3	0.016	4

The total estimated worker exposure is below the AOEL, even without the use of PPE.

Bystander

As 'AGF/1-04' is used in closed facilities, bystander exposure is not expected.

3. Residues

3.1. Nature and magnitude of residues in plant

The active substance 2-phenylphenol was discussed at the PRAPeR experts meeting for residues (PRAPeR 60, round 12) in October 2008.

3.1.1. Primary crops

The metabolism was studied with [^{14}C] phenol ring labelled sodium salt of 2-phenlylphenol in oranges and pears treated post harvest.

After dipping in 0.1% and 0.5% solutions respectively for 3 minutes (representing approximately 2 and 10 times the dose rate of the notified cGAP) the oranges were kept in cold storage at 11 – 13 °C for the first 4 weeks and at 5 °C for the following weeks. Samples of fruit were taken for analysis 2 hours, 2 days and 1, 2, 4, 6, 8 and 12 weeks after the application.

The amount of total radioactive residues found in the whole fruits after the low dose application remained relatively constant throughout the study at approximately 10 mg/kg. The residues penetrated from the surface of the fruits into the peel. TRR in the peel increased to 95% within 12 weeks. Further penetration into the fruit pulp was low with only approximately 0.2% of TRR found in juice and pulp throughout the storage period. Metabolites were identified in samples stored for 12 weeks. 2-phenlylphenol showed moderate metabolism. After 12 weeks, 86% of TRR were identified as 2-phenylphenol and its conjugates, 7% as 2-phenylhydroquinone and its conjugates and 0.3% as 2-methoxybiphenyl.

The PRAPeR 60 meeting discussed whether the study was representative of the commercial practice. The study was carried out for a period of 12 weeks only whereas according to information of the rapporteur Member State oranges are stored for up to six months after post harvest treatment. It was concluded that due to the fact that the fruits were stored at a higher temperature during the first 4 weeks the metabolism was increased during this time and the metabolism observed at the end of the study might represent a longer commercial storage period. Furthermore, it was discussed whether unidentified radioactive residues in rinse and peel of the treated fruits were of concern. On the basis of additional information submitted by the notifier on the characterisation of the radioactive residues it was decided that identification/characterisation of metabolites was sufficient. This information was summarised by the rapporteur Member State after the PRAPeR 60 meeting in addendum II B.7 (November 2008).

After dipping in a 4% solution for 3 minutes (representing approximately 60 times the dose rate of the notified cGAP) treated pears were kept in cold storage at approximately -1 to 4 °C for 28 weeks. Samples of fruit were taken for analysis 2 hours, 2 days and 1, 2, 4, 6, 8, 12, 16, 20 and 28 weeks after the application.

The amount of total radioactive residues found in the whole fruits was 22 mg/kg two hours after the treatment, increased to 57 mg/kg by day two and afterwards remained relatively constant throughout the study at approximately 40 mg/kg. Penetration of residues from the surface of the fruits into the peel and the pulp was observed. TRR in the peel and the pulp increased to approximately 70% and 30% respectively within 28 weeks of storage.

Metabolites were analysed in samples stored for 28 weeks. The main residues found in extracts of the different fractions of the fruits were 2-phenylphenol (6% of TRR) and its conjugates (74% of TRR). Rinse and peel contained also the unidentified metabolite C and further polar and non-polar unidentified compounds. Post extraction solids of peel and pulp were further characterised by hydrolysis steps which released conjugates of 2-phenylphenol.

The PRAPeR 60 meeting discussed the validity of the study. The notifier could not provide a conclusive explanation for the low TRR found in samples 2 hours after treatment. The PRAPeR 60 meeting suggested that it could be explained by loss during handling of the samples. The results from days 2 to 28 weeks were regarded as conclusive. The PRAPeR 60 meeting concluded that the unidentified metabolite C was expected at very low concentrations after application of 2-phenylphenol at the notified dose rate and therefore further efforts to identify the residues were not required.

The rapporteur Member State proposed in the DAR to include the parent 2-phenylphenol, the metabolite 2-phenylhydroquinone and their conjugates in the residue definition for plant products. During the peer review concern was raised regarding the toxicological potential of the metabolite 2-phenylhydroquinone (see also sections 2. and 2.8). The notifier was asked to address the toxicological potential of 2-phenylhydroquinone.

Based on the discussions of the PRAPeR 60 meeting, 2-phenylhydroquinone was included in the residue definition as a conservative measure since its toxicological significance could not be determined. The PRAPeR 60 meeting concluded that it was justified to propose residue definitions for the whole group of fruit crops as the metabolism in citrus and pears was considered as sufficiently investigated. The following provisional residue definition for monitoring and risk assessment in plant products has been proposed for fruit crops: sum of 2-phenylphenol and 2-phenylhydroquinone and their conjugates, expressed as 2-phenylphenol. EFSA states that the residue definition is based on the assumption that the ADI of 2-

phenylphenol can be applied also for the metabolite and should be re-addressed when information on the toxicological potential of 2-phenylhydroquinone is available.

A total of 14 residue trials carried out in Spain (2002, 2004 and 2006) and the USA (1995) were submitted to support the notified representative use on citrus fruit. Only two and four residue decline trials for oranges and mandarins, respectively, were acceptable as they were carried out following the notified cGAP and the analytical method used included a hydrolysis step and therefore covered the analysis of 2-phenylphenol and 2-phenylhydroquinone and their conjugates. However, the hydrolysis step of the analytical method (see section 1) was not validated. The PRAPeR 60 meeting concluded that the notifier should demonstrate that the analytical method correctly quantifies the residues of 2-phenylphenol and 2-phenylhydroquinone and their conjugates to confirm the validity of the residue trials.

According to the notified uses, a withholding period of 0 days should apply for post harvest treatment of citrus fruit. However, the residue level found immediately after treatment was usually lower than residues found in samples taken several days later. Therefore, the meeting decided that the highest residue level of the decline studies, which were carried out during a period of 28 days after treatment, should be used for the establishment of a provisional MRL. The PRAPeR 60 meeting set a data gap concerning two further valid trials on oranges to confirm the proposed MRL.

A total of 8 residue trials carried out in Spain (2003) were submitted to support the notified representative use on pears. The PRAPeR 60 meeting decided that they were not acceptable as the method of analysis used in the trials did not include a hydrolysis step and therefore was not in accordance with the residue definition. Therefore, a data gap concerning a complete data set of valid residue trials on pears was identified.

Submitted data on freezer storage stability of 2-phenylphenol and 2-phenylhydroquinone in citrus fruit and pears were not regarded as valid because the results were not conclusive. Therefore, data gaps concerning valid freezer storage stability studies were confirmed by the PRAPeR 60 meeting.

Effects of processing on the nature of the residue of 2-phenylphenol were investigated in hydrolysis studies simulating pasteurisation, boiling and sterilisation respectively. Whereas 2-phenylphenol was shown to be stable under conditions simulating pasteurisation and boiling, a loss of approximately 15% was found in the experiment simulating sterilisation, however no metabolites were detected. The notifier could not provide a conclusive explanation for this loss of radioactivity. Nevertheless, the PRAPeR 60 meeting concluded that no breakdown of 2-phenylphenol was observed and that the compound could be regarded as stable under the conditions studied.

Studies on the level of residues in processed orange commodities were submitted providing information on residues in juice, dry pomace and oil and home-made marmalade respectively. Concentration of 2-phenylphenol was observed only in dry pomace and oil. In these studies analytical methods were used which included a hydrolysis step. In line with the data gap formulated for the residue trials the notifier was asked to demonstrate that the analytical methods used in the processing studies correctly quantify the residues of 2-phenylphenol and 2-phenylhydroquinone and their conjugates. Further details of the processing studies were not discussed by the PRAPeR 60 meeting as the maximum estimated daily intake (TMDI) for citrus was not expected to exceed 10% of the ADI. This was confirmed by the calculation provided by the rapporteur Member State after the PRAPeR 60 meeting (see section 3.3). EFSA notes that full evaluation of the processing studies might be required if for additional crops the TMDI exceeds 10% of the ADI.

A processing study on pears was carried out to provide information on residue levels in juice, wet pomace and jelly. However, the study was performed with an analytical method not including a hydrolysis step and therefore not in compliance with the residue definition. Depending on the results of the requested residue trials on pears it has to be decided if valid processing studies on pears are required.

EFSA notes that the residue trials on oranges and mandarins accepted by the PRAPeR 60 meeting provide information on the distribution of residues in the fruits. Measurable residues were only found in the peel. In the pulp residues were below the LOQ (<0.1 mg/kg for 2-phenylphenol and <0.2 mg/kg for 2-phenylhydroquinone).

3.1.2. Succeeding and rotational crops

Since the representative use is a post harvest treatment, studies on residues in rotational and succeeding crops are not a requirement to support the notified uses.

3.2. Nature and magnitude of residues in livestock

The notifier argued that it is intended to label treated crops as “treated fruit cannot be used as raw material for feeding” and therefore it is not necessary to take into account intake of residues of 2-phenylphenol by livestock. However, it is noted that any restriction with respect to the use of treated fruit or commodities derived from treated fruit in animal feeding is not in the remit of the risk assessor. Therefore, as a precautionary measure, an assessment was carried out assuming livestock exposure to 2-phenylphenol residues from treated crops to forecast whether residues in animal matrices could be expected and MRLs would have to be proposed.

The intake of fruit pomace is relevant for ruminants, but not for poultry or pigs. Therefore, for the notified uses only an assessment for ruminants is required. Metabolism studies were carried out with lactating goats to determine the manner in which 2-phenylphenol is metabolised in ruminants. For lactating goats dosed at 11 mg/kg feed (representing approximately 6 and 2 times the residue intake calculated for dairy and beef cattle respectively) and 32 mg/kg feed for 5 consecutive days the majority of the applied radioactivity was found in excreta, mainly in urine. Transfer of radioactivity into milk and tissues was low. The duration of the study was not long enough to reach a residue plateau in milk. For the low dose group TRR in milk was max. 0.008 mg/kg. In tissues the highest residue levels were found in kidney and liver (approximately 0.005 mg/kg). Radioactive residues in milk, kidney and liver were further analysed by extraction and HPLC analysis. Radioactive compounds could not be identified and therefore no metabolic pathway could be established. As no metabolites could be identified it was not possible to establish a residue definition for animal matrices.

The PRAPeR 60 meeting carried out a dietary burden calculation for livestock. On the basis of the transfer factor calculated for citrus dry pulp (4.5) in one processing study on oranges, a transfer factor of 1.5 was estimated for citrus wet pomace. EFSA notes that the acceptability of this result is pending confirmation that the analytical method applied in the residue trials correctly quantifies the residues of 2-phenylphenol, 2-phenylhydroquinone and their conjugates.

The residue intake for dairy and beef cattle fed with citrus pomace was calculated as 2 and 6 mg/kg diet (DM) which is below the residue intake of the goats of the low dose group in the livestock metabolism study. Therefore, the PRAPeR 60 meeting concluded that no significant

residues are expected in milk or tissues of cattle fed with pomace from citrus fruit treated according to the notified use. No livestock feeding studies are required. EFSA states that the assessment might have to be readdressed for pears or further intended uses depending on the results of residue trials and processing studies for these crops.

3.3. Consumer risk assessment

The rapporteur Member State provided a provisional dietary intake estimate in addendum II B.7, November 2008 (not peer reviewed) taking into account the ADI of 0.4 mg/kg bw/day established by PRAPeR meeting 59. The rapporteur Member State used consumption data in the EFSA PRAPeR model (PRIMO, rev. 1). The maximum estimated daily intake (TMDI) using the proposed MRL of 5 mg/kg for citrus fruit is about 6% of the ADI for a German child and 5% for a Dutch child. The TMDI for the WHO Clusters B, D and F is 1 – 2% of the ADI.

In the corrigendum B-7 (June 2008), the rapporteur Member State proposed a provisional risk assessment also including the intake of pears. However, the experts in the PRAPeR 60 meeting regarded this estimate as not acceptable since a conversion factor used in the calculation was regarded as non conclusive. The PRAPeR 60 meeting concluded that they did not expect a risk for the consumer for the notified use of 2-phenylphenol on citrus fruit.

EFSA notes that this risk assessment is only provisional and that it might underestimate the actual risk. The residue definition applied is based on the assumption that the ADI of 2-phenylphenol can also be applied for the metabolite 2-phenylhydroquinone which has not been confirmed yet. Furthermore, the risk assessment for citrus can only be finalised when outstanding data on residue levels (additional residue trials, confirmation that the analytical method applied in the residue trials correctly quantify the residues of 2-phenylphenol, 2-phenylhydroquinone and their conjugates and valid storage stability studies). The intake of pears could not be taken into account because no valid residue trials are available.

No ARfD was allocated and therefore no acute risk assessment was carried out.

EFSA notes that 2-phenylphenol is more widely used than in the area of plant protection (e.g. biocides) and that therefore there may be other routes of exposure that have not been considered in the assessment performed in the review under Council Directive 91/414/EEC.

3.4. Proposed MRLs

For the notified use on citrus fruit treated with 2-phenlyphenol by drench application a provisional MRL of 5 mg/kg is proposed. This is pending confirmation that the analytical method applied in the residue trials correctly quantifies the residues of 2-phenylphenol, 2-phenylhydroquinone and their conjugates, the submission of two additional residue trials and valid storage stability studies.

For the notified use on pears no MRL can be proposed as the PRAPeR 60 meeting regarded the submitted residue data as not acceptable (see section 3.1).

MRLs for products of animal origin are not necessary for the notified use on citrus as no significant residues are expected in milk or tissues of cattle fed by pomace from citrus fruit treated according to the notified use. EFSA states that the assessment might have to be readdressed for pears or further intended uses depending on the results of the residue trials and processing studies.

4. Environmental fate and behaviour

2-Phenylphenol was discussed at the PRAPeR 57 experts' meeting for environmental fate and behaviour in October 2008 on basis of the DAR (May 2007_V3 (01/08)) and the corrigendum to B-8 (June 2008).

4.1. Fate and behaviour in soil

4.1.1. Route of degradation in soil

A soil experiment on a sandy loam soil (pH 6.0, OC 2.5%, clay 10%) was carried out under aerobic conditions in the laboratory (20°C, 50% maximum water holding capacity (MWHC)) in the dark. The formation of residues not extracted by several extraction steps were a significant sink for the applied phenyl-UL-^{14}C-radiolabelled 2-phenylphenol (80.0% or 77.4% of the applied radiolabel (AR) after 91 or 127 days, respectively). Mineralisation to carbon dioxide of this radiolabel accounted for 8.4% AR after 91 days and 9.6% AR after 127 days. No extracted metabolite accounted for >2% AR at any sampling time.

Data on anaerobic degradation or photolysis in soil were not available for 2-phenylphenol. However these data are not necessary to complete an assessment for the applied for representative use, which is only an indoor application.

4.1.2. Persistence of the active substance and their metabolites, degradation or reaction products

The rate of degradation of 2-phenylphenol was estimated from the results of the study described in section 4.1.1 above. The calculated DT_{50} was 0.11 day (single first-order non linear regression, 20°C, 50% MWHC, n=1). After normalisation to FOCUS reference conditions[4] (20°C and -10kPa soil moisture content) this value of single first-order DT_{50} remained unchanged.

Since contamination of soil is not expected from the applied for representative uses of 2-phenylphenol, the predicted environmental concentration in soil was not calculated.

4.1.3. Mobility in soil of the active substance and their metabolites, degradation or reaction products

The adsorption/desorption of 2-phenylphenol was investigated in four soils (pH 5.2 – 7.3, OC 1.9 – 3.0%, clay 12.4 – 30.1%) in batch adsorption experiments. In the preliminary tests of the study a strong adsorption of 2-phenylphenol to soil was observed, which continued over 168 hours thus the equilibrium could not be reached within a reasonable time interval. The adsorption and desorption times in the definitive test was therefore shortened to 1 or 4 hours. In these circumstances the calculated adsorption K_{foc} values varied from 252 to 393 mL/g, (mean 347 mL/g) (1/n 0.784 – 0.870, mean 0.82). The K_{foc} values reflect the reversibly adsorbed portion of 2-phenylphenol only with no equilibrium being reached after a short incubation period, therefore they would represent a worst case if they were used for modelling the leaching behaviour. There was no evidence of a correlation of adsorption with pH.

[4] Using section 2.4.2 of the generic guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002.

4.2. Fate and behaviour in water

4.2.1. Surface water and sediment

No information was available on the hydrolytic degradation of 2-phenylphenol at ambient temperature, however a study conducted at 50°C (considered as additional information) showed that 2-phenylphenol is stable at pH 4, pH 7 and pH 9.

In a laboratory study where the aqueous photolysis of 2-phenylphenol was investigated under sterile pH 7 conditions, a rate of degradation (single first-order DT_{50}) of 1.7 day equated to summer sunlight at 33.3°N (Phoenix, USA) or 2.6 days at 38.0°N (Athens) was determined. 2-Phenylphenol degraded to innumerable unidentified minor photoproducts. One of the minor photoproducts was identified as benzoic acid, which accounted for 7.9% AR on days 1 and 2 of the experiment. The only major transformation product was a diketohydroxy-compound (2-hydroxy-1,2-dihydrodibenzo[b,d]furan-3,4-dione) reaching the maximum of 13.6% AR at day 1 of the experiment. The rate of degradation (single first-order DT_{50}) of this diketohydroxy-compound equated to summer sunlight at 33.3°N (Phoenix, USA) was 7.2 days or if equated to 38.0°N (Athens), it was 11.1 days. In another laboratory study the direct and the direct-plus-indirect aqueous photolysis of 2-phenylphenol was investigated in pure water and in contaminated natural lake water (taken from 10 cm depth) using natural sunlight in July and August (Woburn, MA, USA; solar irradiance data were obtained from tables). The direct photodegradation rate of 2-phenylphenol observed in pure water under summer sunlight was 0.13 d^{-1} (DT_{50} = 5.3 days) and had a quantum yield of 0.044 (s = ±0.001, n = 3). In lake water, the direct-plus-indirect photolysis rate constant was of 0.15 d^{-1}. This study was considered as additional information.

Altogether five ready biodegradability tests were available. The valid and relied on studies indicated that 2-phenylphenol is ‘readily biodegradable’ using the criteria defined by the tests.

Information on the degradation of 2-phenylphenol under aerobic aquatic conditions was available only from two range finding tests using spiked sediment or spiked water and a respective water spiked definitive test (the used guidelines were OECD TG 218 and OECD TG 219 for investigation of possible toxic effects on chironamids). Only dissipation from the water columns could be estimated from the limited number of analytical measurements (3 – 4 sampling points) of these experiments. The range of the calculated DT_{50} values was 5.5 to 19 days. These data are included in the Appendix A of this conclusion, but since the methodology of these experiments significantly deviated from the appropriate methodology of a water-sediment study, they were regarded as only supplementary information.

In a study, the fate of 2-phenylphenol in a municipal waste water treatment plant (STP) was investigated in Germany (Steinhäule). Representative samples of sewage influent and effluent were taken for analysis over a period of 24 hours in March and June (1998). The results showed that more than 99% of 2-phenylphenol was removed from the waste water by this German waste water treatment plant in these periods. In the frame of a monitoring study (see below of this point), the influent and effluent of another STP in Germany (Frankfurt/Main) was monitored, where 98% elimination of 2-phenylphenol was observed.

The need for calculations of the PEC_{sw} and PEC_{sed} was discussed in the meeting. It was agreed that during the normal work flow, there is no emission into the environment as the application (based on the applied for representative uses) is made in a closed drenching system and the waste water, including the cleaning water, must be collected and handled as hazardous chemical waste by an authorised waste management company. Unintended

exposure via sewage systems, as considered in the original DAR, was considered to be outside of the risk assessment necessary under the Directive 91/414/EEC.

Forty-nine municipal sewage treatment plant effluents and several surface water bodies (rivers and streams) in Germany were monitored for different chemicals, including 2-phenylphenol. 2-Phenylphenol was found in the majority of the samples (LOD = 0.01 μg/L) up to 2.6 μg/L in the effluents of the STPs and 0.25 μg/L in the natural surface waters.

4.2.2. Potential for ground water contamination of the active substance their metabolites, degradation or reaction products

Since environmental contamination is not expected from the applied for representative uses (including appropriate waste disposal management) of 2-phenylphenol, the predicted environmental concentration for groundwater was not calculated.

4.3. Fate and behaviour in air

The vapour pressure of 2-phenylphenol (0.474 Pa at 20°C) means that 2-phenylphenol would be classified under the national scheme of The Netherlands as moderately volatile, indicating that losses due to volatilisation would not be excluded. Calculations using the method of Atkinson (using the software APOWIN, v.1.91) for indirect photo oxidation in the atmosphere through reaction with hydroxyl radicals resulted in an atmospheric half-life estimated at 0.59 day (assuming an atmospheric hydroxyl radical concentration of $0.5x10^6$ OH-radicals cm^3 as an average for 24 hours a day). This half-life indicates that the proportion of 2-phenylphenol which is volatilised is unlikely to be subject to long-range atmospheric transport.

5. Ecotoxicology

2-phenylphenol was discussed at the experts' meeting for ecotoxicology (PRAPeR 58) in October 2008. The representative use evaluated was against fruit rotting fungi on post-harvest citrus and pears (indoor use, closed drenching chamber). The formulation product was 'AGF/1-04' containing 100 g/l 2-phenylphenol. The application rate was 600 mg a.s./l treatment solution.

5.1. Risk to terrestrial vertebrates

Acute and short-term studies were submitted on mallard duck (*Anas platyrhynchos*) and bobwhite quail (*Colinus virginianus*). No effects were observed at the highest tested doses (LD_{50} >2250 mg a.s./kg bw for mallard duck and LC_{50} >2810 and >1905 mg a.s./kg bw for bobwhite and mallard duck, respectively). No chronic study was conducted because it was considered not necessary due the proposed indoor use.

On the basis of toxicity data on mammals the LD_{50} was 2733 mg a.s./kg bw (2-phenylphenol) and >2000 mg a.s./kg bw (citrocil, a formulation containing a second a.s.). Due to the proposed indoor use, no exposure was expected for birds and mammals and therefore no risk assessment was conducted.

5.2. Risk to aquatic organisms

The lowest acute endpoint for fish was observed in a study with the active substance and *Oncorhynchus mykiss* (96h-LC_{50} = 4 mg a.s./L). The endpoint for invertebrate was 2.7 mg

a.s./L (*Daphnia magna*) and for algae 1.35 mg a.s./L (*Pseudokirch subcap.*). The experts discussed the proposal for classification of the active substance and the preparation. It was agreed to classify the substance on the basis of available data as R51 . However, EFSA noted after the meeting that according to the criteria of the Annex VI of the Directive 67/548 the R51 classification cannot set without R53. Since 2-phenylphenol was ready biodegradable and the BCF whole fish was 21.7, the criteria for R53 were not met. Therefore, EFSA agreed with the rapporteur Member State to retain the current ECB classification, which is R50 "**Very toxic to aquatic organisms**".

No classification was necessary for the product. The 21-day NOEC for fish was 0.036 mg a.s./L (*Pimephales promelas*). The chronic studies on daphnia were considered not valid (deviation from OECD 211 guideline). However the chronic study on chironomidae was considered enough to address the long-term effects on invertebrates and the NOEC was 1.85 mg a.s./L (*Chironomus riparius*).

A bioaccumulation study was available on *Danio rerio*: the BCF whole fish was 21.7.

No PEC_{sw} were used to calculate TER values. Indeed, the environmental fate and behaviour experts' meeting agreed that exposure of surface water via sewage systems is not expected because the product would be collected and transported to a management facility for chemical waste. No risk to aquatic organisms was expected.

5.3. Risk to bees

No data were submitted. Since 2-phenylphenol is used indoors the exposure of bees was not expected.

5.4. Risk to other arthropod species

No data were submitted. Since 2-phenylphenol is used indoors the exposure of non-target arthropods was not expected.

5.5. Risk to earthworms

The acute toxicity to earthworms was tested with a different formulation, 'preventol O-extra'. The 14d-LC_{50} was 198.2 mg a.s./kg. Since log P_{ow} is >2 the endpoint was divided by 2. Therefore the LC_{50corr} was 99.1 mg a.s./kg. Chronic testing was considered not necessary.

TER was not calculated since the exposure was not expected.

5.6. Risk to other soil non-target macro-organisms

No data were submitted. Since 2-phenylphenol is used indoors, exposure of non-target soil macro-organisms was not expected.

5.7. Risk to soil non-target micro-organisms

No data were submitted. Since 2-phenylphenol is used indoors, exposure of non-target soil micro-organisms was not expected.

5.8. Risk to other non-target-organisms (flora and fauna)

No data were submitted. Since 2-phenylphenol is used indoors, exposure of non-target organisms was not expected.

5.9. Risk to biological methods of sewage treatment

The effects of 2-phenylphenol on the respiration rate of activated sewage sludge were observed after a contact of 3 hours. The 3h-EC_{50} was 56 mg a.s./L. A risk assessment was provided by the notifier for sewage treatment plants based on the above EC_{50} and on the predicted environmental concentration in sewage treatment plant (PEC_{STP}). However, Member State experts considered the risk assessment not relevant.

6. Residue definitions

6.1. Soil

Definition for risk assessment:	2-phenylphenol
Definition for monitoring:	2-phenylphenol

6.2. Water

6.2.1. Ground water

Definition for exposure assessment:	2-phenylphenol
Definition for monitoring:	2-phenylphenol

6.2.2. Surface water

Definition for risk assessment

in surface water:	2-phenylphenol
in sediment:	2-phenylphenol
Definition for monitoring:	2-phenylphenol

6.3. Air

Definition for risk assessment:	2-phenylphenol
Definition for monitoring:	2-phenylphenol

6.4. Food of plant origin

Definition for risk assessment:	sum of 2-phenylphenol and 2-phenylhydroquinone and their conjugates, expressed as 2-phenylphenol (**provisional**, **for fruit crops only**)
Definition for monitoring:	sum of 2-phenylphenol and 2-phenylhydroquinone and their conjugates, expressed as 2-phenylphenol (**provisional**, **for fruit crops only**)

6.5. Food of animal origin

Definition for risk assessment:	proposal not possible as no metabolites could be identified in the metabolism study in ruminants; not required for the notified use on citrus fruit
Definition for monitoring:	proposal not possible as no metabolites could be identified in the metabolism study in ruminants; not required for the notified use on citrus fruit

6.6. Overview of the risk assessment of compounds listed in residue definitions for the environmental compartments

6.6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
2-phenylphenol	Very low persistence Single first-order DT_{50} = 0.11 day (20°C, 50% MWHC, n=1)	Due to the representative use (indoor), risk not assessed

6.6.2. Ground water

Compound (name and/or code)	Mobility in soil	>0.1 µg/L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
2-phenylphenol	Medium mobility K_{Foc} 252 to 393 mL/g[(a)]	Not calculated - not required		Yes	Yes

(a): The measured values reflect the reversibly adsorbed portion of 2-phenylphenol only with no equilibrium being reached after a short incubation period

6.6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology

2-phenylphenol	Toxic to aquatic organisms. Due to the representative use (indoor) risk not assessed.

6.6.4. Air

Compound (name and/or code)	Toxicology
2-phenylphenol	Not acutely toxic via inhalation

LIST OF STUDIES TO BE GENERATED, STILL ONGOING OR AVAILABLE BUT NOT PEER REVIEWED

- The efficiency of the hydrolysis step in the plant method must be validated (relevant for all uses evaluated, data gap identified by meeting of experts October 2008, proposed submission date unknown, refer to section 1).
- It must be demonstrated that the citrus method (Pollmann 2005a) can be used for pears (relevant for all uses evaluated, data gap identified by meeting of experts October 2008, proposed submission date unknown, refer to section 1).
- Validated method of analysis for air (relevant for all uses evaluated, data gap identified by meeting of experts October 2008, proposed submission date unknown, refer to section 1).
- Mammalian toxicity of PHQ to be addressed with regard to setting specific reference values (relevant for all uses evaluated, data gap identified by meeting of experts October 2008, proposed submission date unknown, refer to section 2).
- The potential for skin depigmentation for workers and consumers due to possible exposure to metabolite PHQ on citrus peel, based on its ability to cause depigmentation when applied to skin, to be clarified (relevant for all uses evaluated, data gap identified by meeting of experts October 2008, proposed submission date unknown, refer to section 2).
- Relevant historical control data for tumours in mice of the testing laboratory (relevant for all uses evaluated, data gap identified by meeting of experts October 2008, submitted in November 2008, refer to section 2.5).
- A valid freezer storage stability study on citrus (relevant for the use on citrus fruit evaluated; data gap identified by meeting of experts in October 2008; no submission date proposed by the notifier; refer to section 3.1.1).
- A valid freezer storage stability study on pear (relevant for the use on pears evaluated; data gap identified by meeting of experts in October 2008; no submission date proposed by the notifier; refer to section 3.1.1).
- Notifier to demonstrate that the analytical methods used in the residue trials and processing studies correctly quantify the residues of 2-phenylphenol, 2-phenylhydroquinone and their conjugates (relevant for all representative uses evaluated; data gap identified by meeting of experts in October 2008; no submission date proposed by the notifier; refer to section 3.1.1).
- Two further trials on oranges carried out in accordance with the notified cGAP and the proposed residue definition (relevant for the use on citrus fruit evaluated; data gap identified by meeting of experts in October 2008; no submission date proposed by the notifier; refer to section 3.1.1).
- A full data set of residue trials on pears carried out in accordance with the notified cGAP and the proposed residue definition (relevant for the use on pears evaluated; data gap identified by meeting of experts in October 2008; no submission date proposed by the notifier; refer to section 3.1.1).

CONCLUSIONS AND RECOMMENDATIONS

OVERALL CONCLUSIONS

This conclusion was reached on the basis of the evaluation of the representative use as a post harvest fungicide on citrus and pears (indoor use, closed drench chamber). Full details of the GAP can be found in the endpoints.

The representative formulated product for the evaluation was 'AGF/1-04', an emulsifiable concentrate (EC).

A partially validated method is available for citrus but there is currently no validated method for pears. Acceptable methods are available for soil and water but a method for air has been identified as a data gap. Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

Tested in mammals, 2-phenylphenol showed low acute oral, dermal and inhalation toxicity (oral LD_{50} 2733 mg/kg bw; dermal LD_{50} >2000 mg/kg, inhalation LC_{50} >0.036 mg/L). 2-Phenylphenol is irritating to skin (R38, "Irritating to skin proposed") and to eyes (R36, "Irritating to the eyes" and R41 "Risk of serious damage to eyes" proposed) and to respiratory system (R37 "Irritating to respiratory system"). 2-Phenylphenol is not a sensitising agent. The relevant short-term NOAEL is from a study in rats and is 391 mg/kg/day based on hyperplasia in the bladder urothelium and kidney damage in males. 2-Phenylphenol is not genotoxic. Systemic long-term and carcinogenicity NOAEL is 39 mg/kg bw/day, based on an increased incidence of urinary bladder papillomas, transitional cell carcinomas, and/or combined papillomas and/or transitional cell carcinomas. The mechanism of tumorigenesis in rats was assumed to be non-genotoxic, probably based on chronic irritation of the epithelium by a combination of high pH, high sodium-ion concentration and/or high concentration of free metabolites at high doses. In mice, 2-phenylphenol caused an increased incidence of liver adenoma, carcinoma and hepatoblastoma at 500 mg/kg bw/day and 1000 mg/kg bw/day. The NOAEL for systemic toxicity in mice was <250 mg/kg bw/day, whereas the NOAEL for tumours was 250 mg/kg bw/day. Considering the occurrence of liver tumours in mice and urinary bladder tumours in rats, where the mechanism is not known, R40 Carc. Cat 3 was proposed. Reproductive parameters were not affected at any dose level. The overall parental and offspring NOAEL was established at 100 mg/kg bw/day, and the reproductive NOAEL was 500 mg/kg bw/day. The relevant maternal and developmental NOAELs in rats were established at 150 mg/kg bw/day, whereas in rabbits the relevant maternal and developmental NOAEL were proposed to be 100 mg/kg bw/day and 250 mg/kg bw/day, respectively. 2-Phenylphenol did not show any evidence of neurotoxicity. The Acceptable Daily Intake (ADI) and the Acceptable Operator Exposure Level (AOEL) are 0.4 mg/kg bw/day (NOAEL 39 mg/kg bw/day) applying an SF of 100. An Acute Reference Dose (ARfD) was not allocated, based on the acute toxicological profile. The default dermal absorption value 100% was regarded as appropriate. Operator exposure was estimated to be below the AOEL even without the use of Personal Protective Equipment (PPE).

Metabolism of 2-phenylphenol was investigated in oranges and pears having received a post-harvest treatment. In oranges, substantial amounts of residues only penetrated into the peel and, in addition to 2-phenylphenol and its conjugates, 2-phenylhydroquinone and its conjugates were found. In pears, residues penetrated into the pulp and 2-phenylhydroquinone and its conjugates were not found.

Concern was raised with regard to the toxicological potential of the metabolite 2-phenylhydroquinone. Therefore, the experts meeting proposed a provisional residue definition for plant matrices including 2-phenylphenol, 2-phenylhydroquinone and its conjugates, expressed as 2-phenylphenol. This is pending information on the toxicological potential of 2-phenylhydroquinone which was requested from the notifier.

The notifier made a case that treated fruits are destined only for direct human consumption and will not be part of livestock diet. Therefore an assessment with regard to livestock exposure and residues in food of animal origin would not be necessary. However, consideration of the issue by risk managers is required. Therefore, as a precautionary measure, an assessment was carried out assuming livestock exposure to 2-phenylphenol residues from treated crops.

Intake of fruit pomace is only relevant for ruminants. A metabolism study on ruminants was submitted which showed only very low transfer of residues into milk and tissues. 2-Phenylphenol and metabolites could not be identified in the matrices analysed. Therefore, no residue definition for animal matrices could be proposed. Based on the intake calculation for pomace of citrus fruit treated with 2-phenylphenol according to the notified GAP, no significant residues are expected in milk or tissues of ruminants. However, this estimation might have to be re-addressed for pears when relevant data are available.

A provisional MRL for citrus fruit was proposed on the basis of four residue trials on mandarins and two residue trials on oranges. To confirm this MRL the notifier was asked to demonstrate that the analytical methods used in the residue trials and processing studies correctly quantify the residues of 2-phenylphenol, 2-phenylhydroquinone and their conjugates, and to provide two further residue trials and valid storage stability data. No MRL could be proposed for pears as no valid residue trials were available.

A provisional chronic dietary intake estimate for citrus fruit was carried out by the rapporteur Member State. The TMDI was below the ADI for all considered consumer groups. However, the risk assessment is provisional pending further information on the toxicological potential of the metabolite 2-phenylhydroquinone and on additional residue data for citrus fruit and a full set of residue data for pears.

With regard to the applied for representative uses and that waste water, including cleaning water, must be collected and handled as hazardous chemical waste, the contamination of the environment was deemed to be negligible and no calculation of predicted environmental concentrations was necessary. For unintended exposure of surface waters via sewage systems, Member States would need to have appropriate management practice in place to prevent such exposure or carry out a local risk assessment if release of waste water into the sewage system was to be permitted.

2-Phenylphenol was toxic to aquatic organisms (the proposal for classification was R50, "**Very toxic to aquatic organisms**"). Since the exposure of surface water was excluded by the environmental fate and behaviour expert meeting, the risk to aquatic organisms was not assessed. Due to the representative use (indoor), the risk was considered low for terrestrial vertebrates, bees, non-target arthropods, earthworms, soil macro and micro-organisms, other non-target organisms and biological methods for sewage treatment.

PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT TO MANAGE THE RISK(S) IDENTIFIED

Member States would need to have appropriate waste management practices in place to handle the waste solution remaining after application, including the cleaning water of the drenching system (e.g. to collect all the waste water, transport to a waste management facility and burn or handle as hazardous chemical waste). If release of waste water into the sewage system was to be permitted, a local risk assessment for the situation would be needed.

CRITICAL AREAS OF CONCERN

None.

APPENDICES

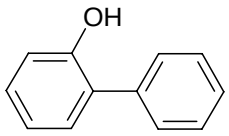
APPENDIX A – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	2-phenylphenol (ISO 765) (a common name is not required according to ISO) Synonyms: biphenyl-2-ol (EINECS name), *ortho*-phenylphenol, OPP
Function (*e.g.* fungicide)	Fungicide

Rapporteur Member State	Spain
Co-rapporteur Member State	

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	biphenyl-2-ol
Chemical name (CA) ‡	[1,1'-Biphenyl]-2-ol
CIPAC No ‡	246
CAS No ‡	90-43-7
EC No (EINECS or ELINCS) ‡	201-993-5
FAO Specification (including year of publication) ‡	No data available
Minimum purity of the active substance as manufactured ‡	998 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	None
Molecular formula ‡	$C_{12}H_{10}O$
Molecular mass ‡	170.2 g/mol
Structural formula ‡	

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	56.7 °C (99.9%)
Boiling point (state purity) ‡	287 °C (99.9%)
Temperature of decomposition (state purity)	No decomposition below the boiling point
Appearance (state purity) ‡	Pure material: Solid colourless flakes with slight phenolic odour (99.9 %)
	Technical material: Similar to pure active substance
Vapour pressure (state temperature, state purity) ‡	0.474 Pa at 20 °C and 0.906 Pa at 25 °C (>99%)
Henry's law constant ‡	Ratio between vapour pressure and water solubility: 0.15 $Pa \times m^3 \times mol^{-1}$ at pH 5 / 20 °C, 0.14 $Pa \times m^3 \times mol^{-1}$ at pH 7 / 20 °C, 0.13 $Pa \times m^3 \times mol^{-1}$ at pH 9 / 20 °C
Solubility in water (state temperature, state purity and pH) ‡	pH 5: 430 mg/L at 10°C 530 mg/L at 20°C 700 mg/L at 30°C pH 7: 450 mg/L at 10°C 560 mg/L at 20°C 730 mg/L at 30°C pH 9: 520 mg/L at 10°C 640 mg/L at 20°C 840 mg/L at 30°C (99.9 %)
Solubility in organic solvents ‡ (state temperature, state purity)	Solubility at 20 °C in g/L (100 %): n-heptane = 50.3 g/L acetone; 1,2-dichloroethane; ethyl acetate; methanol and p-xylene: > 250 g/L
Surface tension ‡ (state concentration and temperature, state purity)	58.72 mN/m at 20.1 °C (90 % saturated solution) (100 %)
Partition co-efficient ‡ (state temperature, pH and purity)	3.18 at 22.5 °C (pH = 6.3) (99.9 %)
Dissociation constant (state purity) ‡	pKa_1 = 9.4 ± 0.15 at 20ºC (99.89 %)

UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	acetonitrile solution: λ_{max} (nm); ε (L.mol^{-1}.cm^{-1}) 245 12800 287 8200 (100 %)
Flammability ‡ (state purity)	Not highly flammable, according to EC A.10 and EC A.12. (100 %)
Explosive properties ‡ (state purity)	Not explosive (expert statement)
Oxidising properties ‡ (state purity)	Not oxidising (expert statement)

Summary of representative uses evaluated (*o-phenylphenol*)*

Crop and/ or situation	Member State, Country or Region	Product name	F G or I	Pests or Group of pests controlled	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			DAT (days)	Remarks
(a)			(b)	(c)	Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	g as/hL (l) min – max	water L/ha min – max	g as/ha (l) min – max	(m)	
citrus fruit (CIDSS) pears (PYUCO) post-harvest treatment	Spain (RMS)	AGF/ 1-04	I	Fruit-rotting fungi	EC	100 g/L	drench (in a closed drenching chamber)	85 (citrus) 87 (pears)	1	not applicable	600 mg a.s./l treatment solution	not applicable	not applicable	Citrus fruit: 0 days Pears: 30 days	

* For uses where the column "Remarks" is marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s).

(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)

(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)

(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds

(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)

(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).**

(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application

(k) Indicate the minimum and maximum number of application possible under practical conditions of use

(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha

(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989	instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha
(f) All abbreviations used must be explained	(m) DAT Days after treatment
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench	
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated	

Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical as (analytical technique)	*2*-phenylphenol: CIPAC method 246 exists only as provisional Test Method A 02/0162/08 LEV: GC-FID Confirmation: not required
Impurities in technical as (analytical technique)	Not applicable
Plant protection product (analytical technique)	*2* -phenylphenol: Method 20041492/01-PCVE: reversed phase HPLC/UV Confirmation: not required

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		*2*-phenylphenol and 2-phenylhydroquinone and their conjugates expressed as *2*-phenylphenol
Food of animal origin		No residue definition (Not necessary)
Soil		*2*-phenylphenol
Water	surface	*2*-phenylphenol
	drinking/ground	*2*-phenylphenol
Air		*2*-phenylphenol

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	**Open**
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Nor required as no MRLs will be set.
Soil (analytical technique and LOQ)	**Method 00829** Höfchen and Laacher Hof soils LC/MS/MS LOQ: 0.005 mg/kg

Water (analytical technique and LOQ)	**Method 00828** For drinking and surface water. LC-MS/MS LOQ: 0.1 µg/L
Air (analytical technique and LOQ)	Open
Body fluids and tissues (analytical technique and LOQ)	A method for body fluids and tissues is not required, because 2-phenylphenol is not classified as toxic or highly toxic

Classification and proposed labelling with regard to physical and chemical data (Annex IIA, point 10)

	RMS/peer review proposal
2-Phenylphenol	None

Mammalian Toxicology

Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1)

Rate and extent of oral absorption ‡	Relatively rapid and almost complete, about 90 %, based on urinary (87.8%) fecal (2.9%) excretion within 24 h. after single oral dose of 160 mg/kg to male rats.
Distribution ‡	Widely distributed in rats.
Potential for accumulation ‡	No evidence of accumulation
Rate and extent of excretion ‡	Rapid and complete after a single dose of 500mg/kg. Mainly via urine (95.6%), faeces (6.%) at 96 hours. Bile and CO2 not estimated. Rapid and complete after repeated dose of 500 mg/kg. Mainly via urine (88.1%), faeces (3.3.%) at 96 hours
Metabolism in animals ‡	In rodents sulphation of 2-phenylphenol was the predominant metabolic pathway at the low dose levels, while glucuronidation gained significance high dose levels. Phenylhydroquinone formation increasing in dose-dependent mode and respective Phenylhydroquinone conjugates appears in urine. Cats and dogs: excrete the majority of 2-phenylphenol as the unmetabolised pared compound. Humans volunteers (2-phenylphenol dermally applied): in urine sulphate conjugated of 2-phenylphenol is the major metabolite, low levels of glucuronide conjugated of 2-phenylphenol and glucuronide conjugated of Phenylhydroquinone were also present.
Toxicologically relevant compounds ‡ (animals and plants)	2-phenylphenol; PHQ no data available
Toxicologically relevant compounds ‡ (environment)	Parent compound

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	LD_{50} : 2733 mg/kg bw	
Rat LD_{50} dermal ‡	LD_{50} > 2000 mg/kg bw	
Rat LC_{50} inhalation ‡	LC_{50} rat >0.036 mg/L (maximum attainable concentration Nose-only. Test material: aerosol	

Skin irritation ‡	Irritating to skin	R38
Eye irritation ‡	Irritating to eyes	R41
Skin sensitization ‡	No sensitizing (Buehler test)	
Respiratory system irritation	Irritating to respiratory system	R37

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Urinary bladder and kidney in male rats, Rat: abnormal growth in the in the bladder urothelium and kidney damage in males.	
Relevant oral NOAEL ‡	391 mg/kg bw/day (13-weeks rat).	
Relevant dermal NOAEL ‡	100 mg/kg bw/day (21 days rat).	
Relevant inhalation NOAEL ‡	No data - not required	

Genotoxicity ‡ (Annex IIA, point 5.4)

Genotoxic *in vitro* at cytotoxic doses. Overall, no genotoxic potential	

Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect ‡	Urinary bladder (rats), kidney (rats and mice) and liver (mice)	
Relevant NOAEL ‡	39mg/kg b.w/day (2-year rats) <250 mg/kg bw/day (2-year-mice)	
Carcinogenicity ‡	Rats: papillomas and transitional cell carcinomas in urinary bladder of male (at 200mg/kg b.w/day) Mice: hepatic tumors (adenoma, carcinomas and hepatoblastomas) in males at 500 mg/kg b.w./day.	Cat 3 R40

Reproductive toxicity (Annex IIA, point 5.6)

Multigeneration study

Reproduction target / critical effect ‡	Parental: Bw/bw gain depression (8-10%). Kidney, urinary bladder (hyperplasia of the transitional epithelium cells, chronic inflammation). Reproductive: No effects Offspring: Bw depression (11%)	

Relevant parental NOAEL ‡	100 mg/kg bw/day	
Relevant reproductive NOAEL ‡	500 mg/kg bw/day	
Relevant offspring NOAEL ‡	100 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Maternal: Bw/bw gain depression. Kidney (slight and focal tubule degeneration and inflammation) in rabbit. Developmental: Delayed ossification (sternebrae) and presence of skull bone island and foramen in rat. Slight decrease of foetal weight (rabbit)	
Relevant maternal NOAEL ‡	150 mg/kg bw/day - rat 100 mg/kg bw/day. Rabbit	
Relevant developmental NOAEL ‡	150 mg/kg bw/day - rat 250 mg/kg bw/day. Rabbit	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data-not required	
Repeated neurotoxicity ‡	No data-not required	
Delayed neurotoxicity ‡	No data-not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	Minimal potential to alter the immune system in mice. A battery of in vivo studies investigated the influence of urinary pH and Na+ concentration on the incidence of urinary bladder lesions. There was a positive correlation between urinary pH and the incidence of hyperplasic lesions of the bladder. 2-phenylphenol (20000 ppm) with or without BNN (tumor initiator) did not cause neoplasia of the urothelium during a treatment period of 36 weeks. Increased DNA synthesis can be detected in bladder epithelium , however there were no evidences of DNA adduct formation. 2-phenylphenol or its metabolites form protein adducts in bladder. 2-phenylphenol and PHQ stimulated PHGS (enzyme known to co-oxidise phenolic compounds, highly expressed in bladder) activity in vitro and were oxided in the presence of the enzyme. 2-phenylphenol, PHQ and PBQ inhibed PGHS at higher concentrations. PBQ induced hepatic and renal damage in male rats. 2-phenylphenol treatment led to GSH depletion. Based on these studies non-genotoxic mechanism of tumorigenesis in rats can be assumed. A probable mechanism could involve chronic irritation of the epithelium by a combination of high pH, high Na+, and high concentration of free metabolites after excessive dose of 2-phenylphenol.
Studies performed on metabolites or impurities ‡	-

Medical data ‡ (Annex IIA, point 5.9)

No reports of serious adverse effects on human health. Epidemiological studies showed a low sensitizing potential of 2-phenylphenol with positive reactions in 0.29% to 0.72% of the study subjects. There are no reports of intoxication with 2-phenylphenol in sources available to the applicant.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.4 mg/kg bw/day	2-year rat	100
AOEL ‡	0.4 mg/kg bw/day	2-year rat	100
ARfD ‡	Not allocated, not necessary		

Dermal absorption ‡ (Annex IIIA, point 7.3)

AGF/1-04 (10% 2-phenylphenol in water)	Dermal absorption for both concentrate and diluted: Default value of 100%

Exposure scenarios (Annex IIIA, point 7.2)

Operator	UK-POEM. No gloved used: 40% AOEL Gloves used: 2%
Workers	Specific worker study
PRE-SORTERS	35% AOEL (75 th percentile)
SORTERS	12% AOEL (75 th percentile)
PACKERS	6% AOEL (75 th percentile)
Bystanders	No exposure expected

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

	RMS/peer review proposal
2-phenylphenol	R37, R38, R41, R40 Carc. Cat. 3

Residues

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plant groups covered	Fruit/post-harvest treatment
Rotational crops	Not necessary
Metabolism in rotational crops similar to metabolism in primary crops?	Not necessary
Processed commodities	Hydrolysis studies simulating pasteurisation (pH 4, 90 °C, 20 min), baking and boiling (pH 5, 100 °C, 60 min) and sterilisation (pH 6, 120 °C, 20 min)
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes (no hydrolysis of 2-phenyl phenol takes place)
Plant residue definition for monitoring	**Provisional, for fruit crops only:** Sum of 2-phenylphenol and 2-phenylhydroquinone and their conjugates expressed as 2-phenylphenol
Plant residue definition for risk assessment	**Provisional, for fruit crops only:** Sum of 2-phenylphenol and 2-phenylhydroquinone and their conjugates expressed as 2-phenylphenol
Conversion factor (monitoring to risk assessment)	Not necessary

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	Lactating ruminant (goat)
Time needed to reach a plateau concentration in milk and eggs	Plateau was not reached within 5 days (duration of metabolism study)
Animal residue definition for monitoring	Proposal not possible as no metabolites could be identified / not required for notified use in citrus fruit
Animal residue definition for risk assessment	Proposal not possible as no radioactive compounds could be identified / not required for notified use in citrus fruit
Conversion factor (monitoring to risk assessment)	Not necessary
Metabolism in rat and ruminant similar (yes/no)	No metabolites identified in ruminants
Fat soluble residue: (yes/no)	Yes (partition coefficient 3.18)

Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

Not necessary for use for post-harvest treatment

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

Data gap (for citrus fruit and pears)

Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

Not necessary	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	[1] Yes Dairy cattle: 2 mg/kg feed (DM) (a) Beef cattle: 6 mg/kg feed (DM) (a)	[1] no	[1] no
Potential for accumulation (yes/no):	Not possible to conclude due to short duration of study.	Not required	Not required
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	No	Not required	Not required
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle	<0.001 mg/kg (b)	Not required	Not required
Liver	0.004 mg/kg (b)	Not required	Not required
Kidney	0.005 mg/kg (b)	Not required	Not required
Fat	<0.005 mg/kg (b)	Not required	Not required
Milk	Max. 0.008 mg/kg (b)		
Eggs		Not required	

[1] State whether intake by specified animals is ≥ 0.1 mg/kg diet/day or not, based on a dry weight basis as given in table 1 of Guidance Document Appendix G

[2] Fill in results from appropriate feeding studies at appropriate dose rates according to Guidance Document Appendix G. State 'not required' when the conditions of requirement of feeding studies according to directive 91/414/EEC are not met.

(a) Calculated by the PRAPeR 60 meeting on the basis of a processing factor for dry pomace (4.5) derived from one processing study on oranges. EFSA notes that the acceptability of the result is pending confirmation that the analytical method applied in the residue trials correctly quantify the residues of 2-phenylphenol, 2-phenylhydroquinone and their conjugates.

(b) Dose rate of 11 mg/kg feed (representing approximately 6 and 2 times the residue intake provisionally calculated for dairy and beef cattle respectively)

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Citrus fruit	Not relevant	OPP[1]: 1x 0.6; 1x0.8;1x 1.5; 2x 1.9; 1x 2.0; PHQ[1]: 6x <LOQ (0.2 mg/kg)	[1] Taking into account the highest residues values in the decline trials to calculate the MRL proposal and dietary risk assessment. (*)	[4] 5 mg/kg provisional value (**)	[7] 2.0 + 0.2 (**)	[5, 7] 1.7 + 0.2 (**)
Pears	Not relevant	-	Submitted residue trials were not regarded as valid, as they were performed using methods of analysis not including a hydrolysis step and therefore not in compliance with the residue definition. Data gap.	-	-	-

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17

(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the representative use

(c) Highest residue

[4] MRL proposal derived from supervised residue trials according to Guidance Document Appendix I. When the MRL is estimated at the LOQ, this should be annotated by an asterisk after the figure.

[5] STMR value from results of supervised residue trials.

[6] If several representative uses or European regions are foreseen for one crop, one row must be used for each specific situation

[7] For some crop/pesticide combinations, the residue definition for monitoring and RA may differ. If trials are reported in this table with analysis of the residues accordingly to both definitions, the results are reported in the format x(y), x being the result according to the definition for monitoring and y the result according to the definition for RA. The same applies for the HR and the STMR

(*)Pending confirmation that the analytical method applied in the residue trials correctly quantify the residues of 2-phenylphenol, 2-phenylhydroquinone and their conjugates and submission of valid storage stability studie

(**) Pending the submission of 2 additional residue trials oranges, confirmation that the analytical method applied in the residue trials correctly quantify the residues of 2-phenylphenol, 2-phenylhydroquinone and their conjugates and submission of valid storage stability studies

A. The same applies for the HR and the STMR

Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)[7]

EFSA notes that this risk assessment is only provisional and might underestimate the actual risk, and specifically that it does not take into account the use on pears. For details see EFSA conclusion.

ADI	0.4 mg/kg bw/d
TMDI (% ADI) according to WHO European diet	GEMS/Food Cluster Diet B: 1.95% ADI GEMS/Food Cluster Diet D: 0.58% ADI GEMS/Food Cluster Diet F: 1.41% ADI
TMDI (% ADI) according to national (S) diets	5.7% DE child 5.1% NL child 3.3% IE adult 2.9% ES child 2.9% FR toddler 2.9% UK Toddler 2.3% NL general 1.8% ES adult 1.7% SE general population 90th percentile 1.7% UK Infant 1.3% FR infant 1.0% PT General population 1.4% FI adult 0.9% IT toddler 1.3% UK vegetarian 0.4% DK child 0.7% IT adult 0.8% FR all population 0.9% UK Adult 0.3% DK adult 0.2% PL general population 0.1% LT adult
IEDI (WHO European Diet) (% ADI)	Not required.
NEDI (specify diet) (% ADI)	Not required.
Factors included in IEDI and NEDI	not applicable
ARfD	No acute reference dose was set by the expert meeting.
IESTI (% ARfD)	Not required
NESTI (% ARfD) according to national (to be specified) large portion consumption data	Not required.
Factors included in IESTI and NESTI	Not required.

[7] To be done on the basis of WHO guidelines and recommendations with the deviations within the EU so far accepted (especially diets).

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4) (a)

Crop/ process/ processed product	Number of studies	Processing factors	Amount transferred (%) (Optional)
orange	1	Dry pulp: 4.5 (b)	

(a) Processing studies on oranges and pears have been submitted. The meeting of experts discussed some details of the analytical methods used in these studies. As the TMDI does not exceed 10% of the ADI, the acceptability of these studies was not discussed in detail. EFSA notes, that it might be necessary to full evaluated for further uses. (For further details see EFSA conclusion on 2-phenylphenol).

(b) This processing factor derived from a single study was used by the meeting of experts to calculate a processing factor for wet pomace which was used for a provisional livestock burden calculation. In this study oranges were processed 0, 28 and 56 days after treatment. The processing factor derived from day 56 fruits was used as it was the highest. (For further details see EFSA conclusion on 2-phenylphenol).

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

Proposed MRLs	Citrus fruit: 5 mg/kg (provisional) (a) Pears: MRL proposal not possible as no acceptable residue trials have been submitted. Animal matrices: Proposal of MRLs not required for the intended use on citrus fruit (b)

(a) Pending confirmation that the analytical method applied in the residue trials correctly quantify the residues of 2-phenylphenol, 2-phenylhydroquinone and their conjugates, the submission of 2 additional residue trials and valid storage stability studies

(b) EFSA notes that the necessity of MRLs in animal matrices might need to be reassessed for pears or other further uses.

When the MRL is proposed at the LOQ, this should be annotated by an asterisk after the figure

Environmental fate and behaviour

Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)

Mineralization after 100 days ‡	8.4 % after 91 d and 9.6 % after 127 d, [phenyl-UL-^{14}C]-labelled ortho-phenylphenol (n= 1)
Non-extractable residues after 100 days ‡	80.0% after 91 d and 77.4% after 127 d, [phenyl-UL-^{14}C]-labelled ortho-phenylphenol (n= 1)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	no relevant metabolites

Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation ‡

Mineralization after 100 days	No data submitted/not required
Non-extractable residues after 100 days	No data submitted/not required
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No data submitted/not required

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No data submitted/not required

Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

Laboratory studies ‡

Parent	Aerobic conditions						
Soil type	OC	pH 0.01M $CaCl_2$ (1:1)	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam	2.5%	6.0	20/ 50%	0.11/ 0.36	0.11[5]	0.994	SFO

[5] Moisture correction factor > 1.00

Fate and behaviour in the Environment

Field studies ‡

No data submitted/not required

pH dependence ‡ (yes / no) (if yes type of dependence)	-
Soil accumulation and plateau concentration ‡	No data submitted/not required

Parent	Not relevant

Soil adsorption/desorption (Annex IIA, point 7.1.2)[1]

Parent ‡								
Soil Type	OC %	Soil pH 0.01M $CaCl_2$	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n	R^2
Clay Loam	1.9	7.1	not reported	not reported	7.47	393	0.809	0.999
Sandy loam	2.4	7.3	not reported	not reported	8.53	355	0.821	1.000
Sandy Silt Loam	3.0	5.2	not reported	not reported	11.66	389	0.870	0.996
Clay Loam	2.8	6.2	not reported	not reported	7.04	252	0.784	0.993
Arithmetic mean					8.68	347	0.82	-
pH dependence, Yes or No			No					

[1] these adsorption values represent short duration batch experiments of 1- 4 hours duration in which equilibrium was not reached with adsorption continuing to increase, so they are a low representation of true soil adsorption potential.

Mobilityin soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Column leaching ‡	No data submitted/not required
Aged residues leaching ‡	No data submitted/not required

Lysimeter/ field leaching studies ‡	No data submitted/not required

PEC (soil) (Annex IIIA, point 9.1.3)

Not relevant due to indoor use

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 5: stable at 50 °C pH 7: stable at 50 °C pH 9: stable at 50 °C (considered as additional information)
Photolytic degradation of active substance and metabolites above 10 % ‡	Experimental DT_{50}: 0.3 days Environmental DT_{50} [Phoenix, AZ, USA]: 1.7 days Environmental DT_{50} [Athens, Greece]: 2.6 days Diketohydroxy-compound (2-Hydroxy-1,2-dihydrodibenzo*[b,d]*furan-3,4-dione): 13.6 % AR at 1-DAT: Experimental DT50: 1.3 days Environmental DT50 [Phoenix, AZ, USA, lat: 33.26 N]: 7.2 days Environmental DT50 [Athens, Greece, lat: 38.03 N]: 11.1 days
Quantum yield of direct phototransformation in water at Σ > 290 nm	Direct photodegradation rate of 2-Phenylphenol: 0.13 d^{-1} and quantum yield of 0.044 (s = ± 0.001, n = 3) Direct-plus-indirect photolysis rate of 2-Phenylphenol: 0.15 d^{-1} Note: information in this box is considered as additional information
Readily biodegradable ‡ (yes/no)	Yes

Degradation in water / sediment

According to the notifier, not relevant exposure of aquatic organisms is expected due to indoor industrial use with no release of the pesticide to the environment. Any waste is collected and burnt. The information on this point is based on the results of the ecotox studies carried on sediment dwelling organisms and

regarded as only supplemental information. The waste derived from the proposed indoor treatment should be managed as a toxic residue according to the current national legislations in order to avoid OPP derived from the intended use in post harvest arrives to aquatic systems.

Parent	Distribution: not reported							
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	DT_{50} water	St. (r^2)	DT_{50}-DT_{90} sediment	Method of calculation
OECD 218 (spiked sed)	not reported	not reported	20	not reported	19 d	0.8998	not reported	SFO
OECD 219 (spiked water)	not reported	not reported	20	not reported	6.2 d	0.9685	not reported	SFO
Main test (spiked water)	7.6	not reported	20	not reported	**5.5 d**	0.996	not reported	SFO

PEC (surface water) and PEC sediment (Annex IIIA, point 9.2.3)

Not relevant. The product label includes statements about appropriate disposal.

PEC (ground water) (Annex IIIA, point 9.2.1)

No data submitted/not required

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

Direct photolysis in air ‡	Not studied - no data requested
Quantum yield of direct phototransformation	Not studied - no data requested
Photochemical oxidative degradation in air ‡	DT_{50} of 0.59 days derived by the Atkinson model (AOPWIN Program v1.91, 2000). OH (24 h) concentration assumed = 0.5 10^6 molecules/cm^3
Volatilisation ‡	Not studied - no data requested
Metabolites	Not studied - no data requested

PEC (air)

not calculated/not required for the environmental assessment

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: 2-phenylphenol Surface Water: 2-phenylphenol Sediment: 2-phenylphenol Ground water: 2-phenylphenol Air: 2-phenylphenol

Monitoring data, if available (Annex IIA, point 7.4)

Soil (indicate location and type of study)	No data provided
Surface water (indicate location and type of study)	Sampling time: Nov 1995; Sep and Nov 1996 **Surface water.** Daily composite samples were taken from rivers Lahn (Oberbiel), Kinzing (Hanau), Fulda (Wahnhausen), Werra (Heldra), Main (Bischofsheim), Rhein (Mainz), Nidda (Nied) as well as from the stream Schawrzbach (Trebur). Apart from these, random samples were screened from Ruhr (Essen), Mosel (Wehlen), Neckar (Heidelberg), Elbe (Hamburg) and several streams mostly located in the Heissian Ried (centre of Germany) Nº samples> LOD (0.01 µg/L): 28 of 31 Range: <0.01-0.25 µg/L Median: 0.023 µg/L 90th percentile: 0.079 µg/L **Municipal sewage treatment plant (STP).** 49 German municipal sewage treatment plant (STP) effluents were taken for analysis. All STP consisted of two commonly used main treatment steps: preliminary and final clarification as well as an aerator tank. Additionally, 43 STP are equipped with phosphate elimination and 25 STP with a nitrification treatment step and 13 with denitrification treatment step Nº samples> LOD (0.01 µg/L): 68 of 82 Range: <0.01-2.60 µg/L Median: 0.03 µg/L 90th percentile: 0.12 µg/L **Municipal sewage plant in Frankfurt/Main**: Two sampling periods in Nov 1995 and in Sep 1996. In Nov. 1996, daily 24 h composite samples were analyzed from the raw influent and the corresponding final effluent over 6 d Sampling was carried out by a flow proportional automatic sampler. The STP is connected to about

312,000 population equivalents and consisted of three commonly used main treatment steps: preliminary clarification, aerator tank by addition of Fe(II) chloride for phosphate elimination and final clarification.

Municipal STP close to Frankfurt/Main	µg/L	
	Influent average conc. over 6 d	Effluent average conc. over 6 d
	2.0± 0.8	0.04± 0.005

LOD: 0.01 µg/L.

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/denitrifcation), biological phosphate removal and final settlement tanks as main cleaning steps.
Concentrations of OPP in 24 h influent and effluent samples from 10/11 March 1998:

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

Concentrations of OPP in 24 h influent and effluent samples from 29/30 June 1998:

Substance (µg/L)	Influent 29/30 June	Effluent 29/30 June
OPP	3.64	n.d

LOD: 0.01 ng/L.

Ground water (indicate location and type of study)	No data provided
Air (indicate location and type of study)	No data provided

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

Readily biodegradable

Ecotoxicology

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Species	Test substance	Time scale	End point (mg a.i./kg bw/day)	End point (mg/kg feed)
Birds ‡				
Mallard duck	2-phenylphenol (99.2 % a.i)	Acute	LD_{50} > 2250	
Mallard duck	Preparation	Acute	No data	
Bobwhite quail	2-phenylphenol (99.2% a.i.)	Short-term	LC_{50} > 2810	> 5620
Mallard duck	2-phenylphenol (99.2% a.i.)	Short-term	LC50 > 1905	> 5620
Mallard duck	a.s.	Long-term	No data	
Mammals ‡				
Rat	2-phenylphenol	Acute	LD_{50} 2733	
Rat	Citrocil 8.70% (w/w) 2-phenylphenol 6.93% (w/w) Imazalil	Acute	LD_{50} > 2000 mg product kg/bw	
Rat	2-phenylphenol	Long term (Reproductive)	NOAEL = 500 mg a.s./kg/bw/d	
Rabbit	2-phenylphenol	Developmental	NOAEL = 100 mg a.s./kg bw/day	
Additional higher tier studies ‡				
No data available				

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Taking into account the slight low avian acute and short-term toxicity data of active substance OPP to birds and mammals and due to the indoor use of AGF/1-04 we can conclude that negligible risk to birds and mammals can be expected after AGF/1-04 use if it is applied according with Good Agriculture Practices and with the recommended use pattern.

7.

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg a.i./L)
Laboratory tests ‡				
Fish				
Oncorhynchus mykiss	2-phenylphenol (99.25%)	96 hr (flow-through)	Mortality, LC_{50}	4.0
Pimephales promelas	2-phenylphenol (99.9%)	21 d (flow-trough)	Growth NOEC	0.036
Oncorhynchus mykiss	AGF/1-04 (10% w/v)	96 hr (flow-through)	Mortality, LC_{50}	4.94
Aquatic invertebrate				
Daphnia magna	2-phenylphenol (99.25%)	48 h (static)	Mortality, EC_{50}	2.7
Daphnia magna	AGF/1-04 (10.1% w/v)	48 h (static)	Mortality, EC_{50}	2.42
Sediment dwelling organisms				
Chironomus riparius	2-phenylphenol (100%)	28 d (static)	NOEC	1.85
Chironomus riparius	Metabolite 2	28 d (static)	NOEC	
Algae				
Pseudokirch subcap.	2-phenylphenol (99.91%)	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	1.35 3.57
Higher plant				
Lemna gibba	a.s.	14 d (static)	Fronds, EC_{50}	Not required
Lemna gibba	Preparation	14 d (static)	Fronds, EC_{50}	Not required
Microcosm or mesocosm tests				
Not required				

[1] indicate whether based on nominal ($_{nom}$) or mean measured concentrations ($_{mm}$). In the case of preparations indicate whether end points are presented as units of preparation or a.s.

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

Disposal of 2-phenylphenol is through waste-water disposal and therefore the exposure is considered negligible
Crop and application rate: Post-harvest fungicide on citrus and pears. Maximum use rate 600 mg/L

Test substance	Organism	Toxicity end point (mg a.i./L)	Time scale	PEC_{sw} Notifier (mg a.i./L)	PEC_{sw} RMS (mg a.i./L)	TER	Annex VI Trigger[1]

[1]If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.
[2] only required for herbicides
[3] PEC_{sw} has been used

Bioconcentration				
	2-phenylphenol	Metabolite 1	Metabolite 2	Metabolite 3
$logP_{O/W}$	3.18 at 22.51 °C (provisional)			
Bioconcentration factor (BCF)[1] ‡	21.7			
Annex VI Trigger for the bioconcentration factor	1000			
Clearance time (days) (CT_{50})				
(CT_{90})				
Level and nature of residues (%) in organisms after the 14 day depuration phase				

[1] only required if log $P_{O/W}$ >3.

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
a.s. ‡	No data, not required	No data, not required
Preparation[1]	No data, not required	No data, not required
Metabolite 1		

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
Field or semi-field tests		
not required		

[1] for preparations indicate whether end point is expressed in units of a.s. or preparation

Hazard quotients for honey bees (Annex IIIA, point 10.4)

In the framework of Directive 91/414/EEC it is not relevant to calculate the risk of 2-phenylphenol to bees because preparations containing 2-phenylphenol are for exclusive use indoor where bees are not likely to be exposed. Therefore negligible risk to bees species can be expected after AGF/1-04 use if it is applied according with Good Agriculture Practices.

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g/ha[1])
Typhlodromus pyri ‡		Mortality	No data, not required
Aphidius rhopalosiphi ‡		Mortality	No data, not required

[1] for preparations indicate whether end point is expressed in units of a.s. or preparation

In the framework of Directive 91/414/EEC it is not relevant to calculate the risk of 2-phenylphenol to non-target arthropods because preparations containing 2-phenylphenol are for exclusive use indoor where not target arthropods species are unlikely to be exposed. Therefore negligible risk to not target arthropods species can be expected after AGF/1-04 use if it is applied according with Good Agriculture Practices and the recommended use pattern.

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	End point[1]
Earthworms			
Eisenia fetida	2-phenylphenol (100.2%)	Acute 14 days	$LC_{50corre}$ 99.1 mg a.s./kg d.w.soil (mg a.s/ha)
	a.s. ‡	Chronic 8 weeks	No data, no required
	Preparation	Acute	No data, no required
	Preparation	Chronic	No data, no required
Soil micro-organisms			
Nitrogen mineralisation	a.s. ‡		No data, no required
Carbon mineralisation	a.s. ‡		No data, no required

Test organism	Test substance	Time scale	End point[1]
Field studies[2]			
Indicate if not required			

[1] indicate where end point has been corrected due to log Pow >2.0 (e.g. LC_{50corr})
[2] litter bag, field arthropod studies not included at 8.3.2/10.5 above, and earthworm field studies

Toxicity/exposure ratios for soil organisms

Acute negligible risk to earthworms can be expected after AGF/1-04 use if it is applied according with Good Agriculture Practices and the recommended use pattern. Chronic risk from the 2-phenylphenol use can not be expected on earthworms because of indoor use of the AGF/1-04 (likely not exposure situation) and the low bioaccumulation potential.

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

Preliminary screening data

Not required for herbicides as ER_{50} tests should be provided

Laboratory dose response tests

Most sensitive species	Test substance	ER_{50} (g/ha)[2] vegetative vigour	ER_{50} (g/ha)[2] emergence	Exposure[1] (g/ha)[2]	TER	Trigger
		Not required	Not required		Not required	

[1] explanation of how exposure has been estimated should be provided (e.g. based on Ganzelmeier drift data)
[2] for preparations indicate whether dose is expressed in units of a.s. or preparation

Additional studies (e.g. semi-field or field studies)

Effects on biological methods for sewage treatment (Annex IIA 8.7)

Test type/organism	end point
Activated sludge	EC_{50} = 56 mg a.i./L
Pseudomonas sp	

Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

Compartment	
soil	Parent: 2-phenylphenol
water	Parent: 2-phenylphenol

sediment	Parent: 2-phenylphenol
groundwater	Parent: 2-phenylphenol

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Active substance	R50, S60, S61, N

	RMS/peer review proposal
Preparation	S60, S61

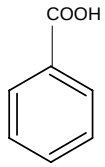
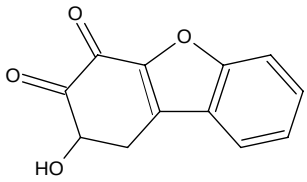
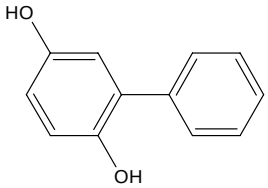
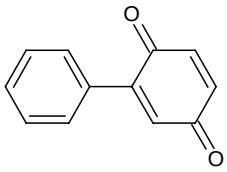
APPENDIX B – LIST OF ABBREVIATIONS

ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AR	applied radioactivity
ARfD	acute reference dose
AV	avoidance factor
BCF	bioconcentration factor
bw	body weight
CAS	Chemical Abstract Service
cGAP	critical good agricultural practice
CI	confidence interval
CIPAC	Collaborative International Pesticide Analytical Council Limited
CL	confidence limits
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
EU	European Union
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FIR	Food intake rate
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
GAP	good agricultural practice
GC	gas chromatography
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HQ	hazard quotient
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry

kg	kilogram
K_{foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M/L	mixing and loading
MAF	multiple application factor
mg	milligram
mL	millilitre
mm	millimetre
MRL	maximum residue limit or level
MS	mass spectrometry
MWHC	maximum water holding capacity
NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OM	organic matter content
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in ground water
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
PEC_{STP}	predicted environmental concentration in sewage treatment plant
pH	pH-value
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between n-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
r^2	coefficient of determination
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
STP	sewage treatment plant
TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure

TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TWA	time weighted average
UV	ultraviolet
W/S	water/sediment
WG	water dispersible granule
WHO	World Health Organisation
yr	year

APPENDIX C – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
Benzoic acid	Benzoic acid	
Diketohydroxy-compound	2-Hydroxy-1,2-dihydrodibenzo[b,d]furan-3,4-dione	
Phenylhydroquinone PHQ	2-Phenylhydroquinone 2,5-Dihydroxybiphenyl	
Phenylbenzoquinone PBQ	–	
2-Methoxybiphenyl 2-MBP	–