SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

biphenyl

EC No 202-163-5

CAS No 92-52-4

Evaluating Member State(s): Portugal

Dated: 30 September 2019

Evaluating Member State Competent Authority

Portuguese Environment Agency
Rua da Murgueira, 9 – Bairro Zambujal - Alfragide
2610-124 Amadora
Portugal
Tel: (+351) 21 472 82 00
Email: geral@apambiente.pt

Year of evaluation in CoRAP: 2013

Before concluding the substance evaluation a Decision to request further information was issued on: 1 October 2015

Further information on registered substances here:

http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

DISCLAIMER

This document has been prepared by the evaluating Member State as a part of the substance evaluation process under the REACH Regulation (EC) No 1907/2006. The information and views set out in this document are those of the author and do not necessarily reflect the position or opinion of the European Chemicals Agency or other Member States. The Agency does not guarantee the accuracy of the information included in the document. Neither the Agency nor the evaluating Member State nor any person acting on either of their behalves may be held liable for the use which may be made of the information contained therein. Statements made or information contained in the document are without prejudice to any further regulatory work that the Agency or Member States may initiate at a later stage.

Foreword

Substance evaluation is an evaluation process under REACH Regulation (EC) No. 1907/2006. Under this process the Member States perform the evaluation and ECHA secretariat coordinates the work. The Community rolling action plan (CoRAP) of substances subject to evaluation, is updated and published annually on the ECHA web site[1].

Substance evaluation is a concern driven process, which aims to clarify whether a substance constitutes a risk to human health or the environment. Member States evaluate assigned substances in the CoRAP with the objective to clarify the potential concern and, if necessary, to request further information from the registrant(s) concerning the substance. If the evaluating Member State concludes that no further information needs to be requested, the substance evaluation is completed. If additional information is required, this is sought by the evaluating Member State. The evaluating Member State then draws conclusions on how to use the existing and obtained information for the safe use of the substance.

This Conclusion document, as required by Article 48 of the REACH Regulation, provides the final outcome of the Substance Evaluation carried out by the evaluating Member State. The document consists of two parts i.e. A) the conclusion and B) the evaluation report. In the conclusion part A, the evaluating Member State considers how the information on the substance can be used for the purposes of regulatory risk management such as identification of substances of very high concern (SVHC), restriction and/or classification and labelling. In the evaluation report part B the document provides explanation how the evaluating Member State assessed and drew the conclusions from the information available.

With this Conclusion document the substance evaluation process is finished and the Commission, the Registrant(s) of the substance and the Competent Authorities of the other Member States are informed of the considerations of the evaluating Member State. In case the evaluating Member State proposes further regulatory risk management measures, this document shall not be considered initiating those other measures or processes. Further analyses may need to be performed which may change the proposed regulatory measures in this document. Since this document only reflects the views of the evaluating Member State, it does not preclude other Member States or the European Commission from initiating regulatory risk management measures which they deem appropriate.

[1] http://echa.europa.eu/regulations/reach/evaluation/substance-evaluation/community-rolling-action-plan

Contents

Part A. Conclusion

1. CONCERN(S) SUBJECT TO EVALUATION

Biphenyl was originally selected for substance evaluation in order to clarify concerns about:

- Environment: Potential PBT

- Exposure: High aggregated tonnage

During the evaluation also other concern was identified. The additional concern was:

- Reproductive toxicity.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

A targeted Compliance Check was performed and concluded and a testing proposal examination is ongoing.

3. CONCLUSION OF SUBSTANCE EVALUATION

Based on the outcome of the ready biodegradation test performed and other available information, the substance can be concluded not to fulfil the criteria for P/vP, Annex XIII of REACH. Furthermore, based on the available information on bioaccumulation the criterion for B/vB is likely not met, neither the criteria for toxicity (T), according to the PBT criteria.

During the evaluation, a concern on reproductive toxicity was also identified. From the assessment of the requested extended one-generation reproductive toxicity study in rats it was concluded that there was no evidence of treatment related reproductive toxicity.

Therefore, it is concluded that both the initial concern on potential PBT properties and the reproductive toxicity concern are removed and no follow-up action is needed.

After the exposure assessment based on the aggregated tonnage, the eMSCA concluded that the identified uses of the substance have acceptable risks (RCRs <1) for the environmental compartments assessed.

The evaluation of the available information on the substance has led the evaluating Member State to the following conclusion, as summarised in the table below.

Table 1. Conclusion of substance evaluation

CONCLUSION OF SUBSTANCE EVALUATION	
Conclusions	**Tick box**
Need for follow-up regulatory action at EU level	
Harmonised Classification and Labelling	
Identification as SVHC (authorisation)	
Restrictions	
Other EU-wide measures	
No need for regulatory follow-up action at EU level	x

4. FOLLOW-UP AT EU LEVEL

4.1. Need for follow-up regulatory action at EU level

4.1.1. Harmonised Classification and Labelling

Not applicable.

4.1.2. Identification as a substance of very high concern, SVHC (first step towards authorisation)

Not applicable.

4.1.3. Restriction

Not applicable.

4.1.4. Other EU-wide regulatory risk management measures

Not applicable.

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

5.1. No need for regulatory follow-up at EU level

Table 2. Reason for removed concern

REASON FOR REMOVED CONCERN	
The concern could be removed because	**Tick box**
Clarification of hazard properties/exposure	x
Actions by the registrants to ensure safety, as reflected in the registration dossiers (e.g. change in supported uses, applied risk management measures, etc.)	

The evaluation of the available information regarding suspected PBT properties of biphenyl, allowed to conclude that the substance is not persistent (P/vP) and likely is not bioaccumulative (B/vB), neither toxic (T criteria), according to the PBT criteria in Annex XIII of REACH.

During the evaluation, a concern on reproductive toxicity was also identified. From the assessment of the requested extended one-generation reproductive toxicity study in rats it was concluded that there was no evidence of treatment related reproductive toxicity.

It is considered that the information provided by the Registrant(s) is enough to remove the identified concerns on potential PBT properties and reproductive toxicity. Therefore, no follow-up action at EU level is needed at this time.

5.2. Other actions

The eMSCA doesn’t consider necessary any other actions as a relevant follow-up for the substance evaluation performed.

6. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS (IF NECESSARY)

Not applicable.

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

Biphenyl was originally selected for substance evaluation in order to clarify concerns about:

- Environment: potential PBT

- Exposure: high aggregated tonnage

During the evaluation also other concern was identified. The additional concern was:

- Reproductive toxicity.

Table 3. Evaluated Endpoints

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Potential PBT	Concern not substantiated. No further action.
High aggregated tonnage	Concern not substantiated. No further action.
Reproductive toxicity	Concern not substantiated. No further action.

7.2. Procedure

The substance evaluation of biphenyl was initiated on 20 March 2013.

A targeted assessment of endpoints related to PBT properties (including relevant human health endpoints) was performed. Also environmental exposure information was evaluated. During the evaluation, the eMSCA identified an additional concern regarding reproductive toxicity.

The evaluation included relevant information from the aggregated registration dossier and information from literature search. The environmental exposure assessment has been performed using the EUSES default release factors unless stated otherwise.

During the evaluation, informal contacts were held between the eMSCA and the Registrant(s), namely two telephone conferences in November 2013 and May 2014 and a face to face meeting in February 2014, to discuss the process and the preliminary conclusions.

Full reports and additional information were provided by the Registrant(s) regarding the biodegradability, but conclusions on the relevant studies could not be confirmed by the eMSCA due to lack of detailed information.

Based on the evaluation of the available information, the eMSCA concluded that it was necessary to request additional data, and therefore, a draft decision was submitted to ECHA on 17 March 2014.

The Registrant(s), the Competent Authorities of other Member States and ECHA were invited to provide comments and proposals for amendments to the draft decision in accordance with the procedure described in the REACH Regulation. A detailed description

of the commenting phase, including the dates, can be found in the Substance Evaluation Decision of the substance[2]. Unanimous agreement of the Member State Committee on the draft decision was reached on 11 June 2015.

On 1 October 2015 the Substance Evaluation Decision requesting a ready biodegradability test, sediment simulation test (dependent on the outcome of the ready biodegradability test) and an extended one-generation reproductive toxicity study in rats was sent to the Registrant(s).

An updated registration dossier with all the requested information was submitted on 8 October 2018, namely the data from a ready biodegradability test and an extended one-generation reproductive toxicity study.

Based on the evaluation of the newly generated data and the previously available information, the substance evaluation was concluded on 30 September 2019 and this Conclusion document prepared.

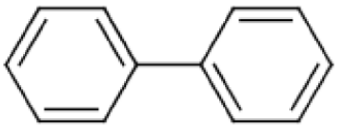
7.3. Identity of the substance

Table 4. Substance identity

SUBSTANCE IDENTITY	
Public name:	Biphenyl
EC number:	202-163-5
CAS number:	92-52-4
Index number in Annex VI of the CLP Regulation:	601-042-00-8
Molecular formula:	$C_{12}H_{10}$
Molecular weight range:	154.2
Synonyms:	-

Type of substance ☒ Mono-constituent ☐ Multi-constituent ☐ UVCB

Structural formula:



7.4. Physico-chemical properties

Biphenyl is a mono-constituent substance having the following physico-chemical properties.

[2] The Decision is publicly available at: https://echa.europa.eu/documents/10162/a24ebfd3-9287-4a00-9db1-21cd21b50c48

Table 5. Overview of relevant physico-chemical properties

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**
Physical state at 20°C and 101.3 kPa	Solid
Melting point	69.5 °C (342.6 K)
Vapour pressure	1.19 Pa at 25 °C
Water solubility	7.35 mg/L at 25 °C
Partition coefficient n-octanol/water (Log Kow)	Log Kow (Pow): 4.008 at 25 °C
Flammability	Non flammable
Explosive properties	Non explosive

7.5. Manufacture and uses

Biphenyl is manufactured/or imported in the EU in a range of 1000 – 10,000 tonnes/year. The substance is mainly used in different industrial settings and by professional workers as heat transfer fluid and laboratory chemical. Based on the information provided by the Registrant(s) following exposure scenarios have been considered for the exposure assessment.

ES1: Manufacture of the substance
ES2: Formulation
ES3: Heat transfer fluids
ES4: Intermediate/solvent/process medium
ES5: Laboratory chemicals

7.5.1. Quantities

The aggregated tonnage per year in the European Economic Area is in the range of 1000 - 10,000 ton/year.

Table 6. Tonnage range

AGGREGATED TONNAGE (PER YEAR)				
☐ 1 – 10 t	☐ 10 – 100 t	☐ 100 – 1000 t	☒ **1000- 10,000 t**	☐ 10,000-50,000 t
☐ 50,000 – 100,000 t	☐ 100,000 – 500,000 t	☐ 500,000 – 1000,000 t	☐ > 1000,000 t	☐ Confidential

7.5.2. Overview of uses

Based on a report on biphenyl by the Danish Environmental Protection Agency (Danish EPA, 2015), the use as intermediate in the manufacture of other chemicals is a minor use and most of the substance in the EU is used as a component in heat transfer fluids. Other uses mentioned in the report include use in dyestuff carriers for textiles, dyestuff carriers for copying paper, solvents for pharmaceutical production, non-agricultural pesticides and preservatives as well as in fuel additives.

The uses reported at the ECHA website[3] are summarised in Table 7.

Table 7. Identified uses

USES	Use(s)
Uses as intermediate	Use as intermediate in the manufacture of other chemicals ERC 6a: Industrial use resulting in manufacture of another substance (use of intermediates)
Formulation	Formulation into mixtures (heat transfer fluids, intermediates) and repackaging Charging and recharging of mixtures of substances (e.g. mixing during transport) PROC 1: Use in closed process, no likelihood of exposure PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 3: Use in closed batch process (synthesis or formulation) PROC 4: Use in batch and other process (synthesis) where opportunity for exposure arises PROC 5: Mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact) PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing) PROC 15: Use as laboratory reagent ERC 2: Formulation of preparations ERC 8b: Wide dispersive indoor use of reactive substances in open systems
Uses at industrial sites	Use in industrial chemical processes Use in formulation of preparations Use in charging and discharging of substances during transport Use in heat transfer fluids Use as processing solvent Use in electrolyte fluids in the production of batteries Use in laboratories PROC 1: Use in closed process, no likelihood of exposure PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 3: Use in closed batch process (synthesis or formulation) PROC 4: Use in batch and other process (synthesis) where opportunity for exposure arises PROC 5: Mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact) PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing) PROC 15: Use as laboratory reagent PROC 22: Potentially closed processing operations with minerals/metals at elevated temperature. Industrial setting ERC 2: Formulation of preparations ERC 4: Industrial use of processing aids in processes and products, not becoming part of articles ERC 7: Industrial use of substances in closed systems
Uses by professional workers	Use as a laboratory chemical PROC 15: Use as laboratory reagent ERC 8a: Wide dispersive indoor use of processing aids in open systems

[3] Information published on 16-11-2018.

Consumer Uses	No consumer uses
Article service life	No article service life
Uses advised against	No uses advised against

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

The harmonised classification of the substance included in table 3.1 in Annex VI of the CLP Regulation (Regulation (EC) 1272/2008) is shown in Table 8.

Table 8. Harmonised classification

HARMONISED CLASSIFICATION ACCORDING TO ANNEX VI OF CLP REGULATION (REGULATION (EC) 1272/2008)							
Index No	**International Chemical Identification**	**EC No**	**CAS No**	**Classification**		**Spec. Conc. Limits, M-factors**	**Notes**
				Hazard Class and Category Code(s)	**Hazard statement code(s)**		
601-042-00-8	Biphenyl, diphenyl	202-163-5	92-52-4	Skin Irrit. 2 Eye Irrit. 2 STOT SE 3 Aquatic Acute 1 Aquatic Chronic 1	H315 H319 H335 H400 H410		-

Labelling:

Signal word: warning

Hazard pictogram:

GHS07: Exclamation mark
GHS09: Environment

7.6.2. Self-classification

- In the registration(s)*:*

The registration dossier refers a proposal related to the Environmental hazards, however no additional information is available.

- The following hazard classes are in addition notified among the aggregated self-classifications in the C&L Inventory[4]:

Asp. Tox. 1, H304

Acute Tox. 2, H330

[4] Information searched on 19-09-2019.

7.7. Environmental fate properties

Only the relevant information on fate properties, agreed by the eMSCA, has been compiled in this report. Additional studies on biphenyl can be found at the ECHA dissemination webpage.

7.7.1. Degradation

7.7.1.1. Abiotic degradation

Hydrolysis:

The Registrant(s) have waived this test based on the expected ready biodegradability of the substance. Hydrolysis is not expected to be an important process in the environment as the substance does not contain water-reactive or hydrolysable groups.

Phototransformation in air:

Results from a published study, not following a test guideline, are included in the registration dossier. There was no observed reaction with ozone or nitrate radicals, the rate constant for ozone is < 2E-19 cm^3/molecule/s. Second-order rate constant for reaction with OH radical is 8.06E-12 cm^3/molecule/s at 294 K (21°C) (Atkinson *et al*., 1984).

AOPWIN v1.92 was used to estimate a half-life for indirect phototransformation in air through reaction with OH radicals. The OH rate constant predicted by AOPWIN results in a half-life of 19 h. This is very similar to an experimental database match value cited in the AOPWIN program, which was a half-life of 18 h.

Thus, the indirect photolysis with OH radical is the dominant process affecting fate of biphenyl in the atmosphere.

Phototransformation in water:

No reliable information has been identified on phototransformation of biphenyl in water. A study using a method equivalent or similar to OECD Guideline draft "Phototransformation of Chemicals in Water - Direct and Indirect Photolysis" shows no significant photolysis after 29 days exposure to direct sunlight at 32 °C and an initial measured concentration of 20 ppm. The absorbance at 290 nm was 0.03 for biphenyl, which is very low. Another study with the same method, showed 9% degradation after 28 days of exposure to direct sunlight compared to dark controls. However, the reduction in test substance concentration appeared to be at least partially due to other processes, of which volatilization is most likely the most important.

Although these two studies were considered not reliable, they were used in a weight of evidence approach to indicate that phototransformation of biphenyl in water is not a significant process in the environment.

Phototransformation in soil:

No information available.

7.7.1.2. Biodegradation

7.7.1.2.1. Biodegradation in water

Screening tests:

A ready biodegradation screening test with the registered substance according to OECD Guideline 301D was requested in the Substance Evaluation decision and the choice of the

test method was justified based on the water solubility and volatility of the substance. However, the Registrant(s) provided information from a study following OECD Guideline 301F (unnamed, 2015). The eMSCA accepted the study as valid and reliable as this guideline is also applicable for poorly soluble substances and losses of the test substance by volatilisation were prevented by using an appropriate test system. In this test, activated sludge (30 mg/L) and the test substance at a concentration of 18 mg/L (equivalent to 54 mg ThOD/L), introduced to the test system using silica gel, were incubated in a mineral medium for 28 days. Oxygen consumption was continuously recorded at 6 h intervals, using an electrolytic respirometer system. Based on the measured oxygen consumption, 68.4% of the test substance was degraded after 28 days, and the criterion for 10-day window was met. Therefore, the criteria for ready biodegradability indicated in the OECD Guideline 301F are fulfilled.

It is noted that the amount of CO_2 produced was also measured, at the end of the test. Based on the CO_2 measurement, 45.3% degradation of the test substance after 28 days was determined. Hence, the results determined based on oxygen consumption and evolved CO_2 are somehow conflicting. The O_2 measurements were done throughout the test, with results very similar and the degradation determined based on that data follows a typical degradation curve observed for readily biodegradable substances with the exception of a small inhibition observed at the beginning of the test, even though no toxicity is shown in controls. Since CO_2 was only measured at the end of the test and there is no further information on the evolution of the CO_2 formation during the test, it is not possible to assess what might have caused the observed differences.

The concentration tested in the OECD Guideline 301F test was 18 mg/L, which is slightly above the NOEC applied in this SEV Report for STP microorganisms (NOEC of 3.2 mg/L and LOEC of 5.6 mg/L, see section 7.8.3). Then, it cannot be excluded that the lower CO_2 production compared to the oxygen consumption could be related to an initial period of small inhibition of the inoculum. If so, it would be expected that the lag period for the recovery of the inoculum result in a delay in its optimum activity and a decrease in the CO_2 production.

Considering that according to the OECD Guideline 301F the degradation is determined based on oxygen consumption and that the CO_2 is an optional endpoint, to be measured only once at the test termination and there is no guidance on how to interpret the CO_2 results, the eMSCA concluded that more weight should be given to the results based on O_2 consumption.

The original registration dossier included several screening studies that were not considered fully reliable or whose reliability could not be evaluated due to lack of detailed information. However, these studies can be used as supporting information.

The results of a modified MITI test (no GLP) (unnamed, 1992) similar to OECD Guideline 301C, were available. However the test substance concentration (100 mg/L) was far above the water solubility (7.35 mg/L) of the substance, and no information was given on how the substance was mixed with the test medium and to what extent the substance was dissolved in the test medium. There is no detailed description of the test procedure. In this study, with inoculum 30 mg/L activated sludge, 66% BOD was observed after a 14-d incubation period at a level significantly exceeding the water solubility of the substance. Due to lack of information ready biodegradability cannot be concluded nor confirmed on this assay.

A supporting study (unnamed, 1994), conducted under method similar to EU Method C.5. Degradation Biochemical Oxygen Demand reports a 5-day BOD of 67% and 48.8% of the theoretical oxygen demand for non-acclimated and acclimated seeds, respectively. It seems that similar degradation percentages are obtained for non-acclimated and acclimated organisms, with very different volume of inoculum (x20) used as seed of acclimated (0.05 mL) and non-acclimated (1 mL). A lower concentration is referred regarding the acclimated seed, but no other information is provided, i.e. cellular density.

Therefore, the yield of both systems cannot be compared and no conclusion can be made. This assay does not allow a conclusion on ready biodegradability.

One study similar to OECD Guideline 302A (Inherent Biodegradability: Modified SCAS Test), (no GLP) is available (unnamed, 1983). In this study, activated sludge microorganisms were exposed in a SCAS unit to a step-wise increase (from 1 up to 50 mg/L) of biphenyl concentrations for over 20 weeks, the suspended solids concentration was around 3000 mg/L and the test was performed in the dark. Samples taken at the beginning and end of each 24-h aeration cycle were analysed for biphenyl. The results of the test indicate > 95 % primary biodegradation within 24 h up to initial concentrations of 50 mg/L. Some limitations were reported in this study: mean volatility loss was 2.4 % (analysis after scrubbing of off-gases); some information is missing (e.g., several details on materials and methods, no information on controls); test concentrations were increased step-wise; biodegradation was only monitored through test material analysis. This study can be considered supporting on potential biodegradability but not on ready biodegradability.

Another study reported the results of a CO_2 evolution test (Adapted Sturm test) equivalent to OECD Guideline 301B (no GLP) (unnamed, 1983), in which pre-adapted activated sludge microorganisms were exposed to 20 mg/L biphenyl for 43 days. Monitoring of CO_2 evolution indicated that biphenyl is ultimately degraded by 88 % after 43 days and around 69 % after 28 days. Because of pre-adapted sludge and the longer test duration this study was considered a screening study for inherent biodegradability.

Additionally the SVHC Support Document of terphenyl, hydrogenated, which is a UVCB substance containing, among other constituents, three-ring analogues of biphenyl, indicates in the PBT assessment that "the 2-ring compounds seem to be more readily biodegradable as compared to the three ring compounds" which has been used for its SVHC identification (ECHA, 2018).

Simulation tests (water and sediment):

An Aerobic Mineralisation in Surface Water study (Bailey *et al*., 1980) is included as additional supporting information on rapid biodegradability. This river die-away study, which is to some extent similar to OECD Guideline 309 - Aerobic Mineralisation in Surface Water - Simulation Biodegradation Test (GLP), was performed in a closed system and using microorganisms present in natural river water. Biphenyl was eliminated with half-lives of around 2-3 days depending on the initial concentrations (nominal: 1-100 µg/L). Based on measurements of trapped $^{14}CO_2$, > 70% biphenyl is ultimately biodegraded in 28 days. The highest half-life reported in these studies (i.e., 3 days at 20°C) can be used as key value for biodegradation in water in the chemical safety assessment.

In a water/sediment study (Saeger *et al.*, 1988a), biodegradation of biphenyl was examined during 10 days in a natural lake sediment/water system with naturally present microorganisms. Analysis of trapped $^{14}CO_2$ indicates ultimate biodegradation of 17.7% at 1 mg/L and 37.8% at 0.077 mg/L. For the active ecocores sacrificed at 10 days, biphenyl volatility losses accounted for 5.7 - 49.8% of total ^{14}C activity at 1 mg/L and 5.0 - 9.3% at 0.077 mg/L. Biphenyl volatility losses before acidification were 2.7-5.6% at 1 mg/L and 2.6-3.1% at 0.077 mg/L but volatility that occurred in ecocores sacrificed at previous sampling times were not specified in the dossier. The half-life of biphenyl was estimated to be 6-10 days in the lake sediment/water system.

In another study (Saeger *et al.*, 1988b) biodegradation of biphenyl was examined during 10 days in a natural river water/sediment system with naturally present microorganisms. Analysis of trapped $^{14}CO_2$ indicates ultimate biodegradation of 38.5 % at 1 mg/L (volatility losses were 4.3-8.6% of total ^{14}C activity) and 42.4 % at 0.077 mg/L (volatility losses were 4.6-5.9% of total ^{14}C activity). In this study the half-life for biphenyl was determined to be 2-3 days for primary biodegradation.

Several limitations are identified in the water/sediment studies: slightly lower water:sediment ratio; not fully conducted in the dark but with a photoperiod of 12h light:12h dark; volatility losses; low number of ecocores replicates; test duration of 10 days instead of 28 days; material balance of the system under 90% in the river water/sediment study.

The photoperiod indicated in both studies is considered relevant since a DT_{50} photolysis of 19h is stated in the dossier, therefore, high disappearance (c.a. 31%) can be expected under each 12-hour light photoperiod applied in the tests. At the end of the test the ultimate biodegradation achieved was c.a. 40% on the river water/sediment test and 18% and 38% (depending on the concentration used) on the lake water/sediment test. Estimations for ultimate degradation half-life were not provided.

The registration dossier includes also a study (Saeger *et al.*, 1988c) where anaerobic biodegradation of biphenyl was examined during 12 weeks in a water/sediment system obtained from a sewage lagoon. Analysis of trapped $^{14}CO_2$ and $^{14}CH_4$ indicated no significant biodegradation of biphenyl via methanogenic or denitrifying processes. The study was considered by the Registrant(s) equivalent or similar to OECD Guideline 308, but not enough information is provided to confirm this point. Anaerobic biodegradation is not expected to play an important role in the elimination of biphenyl from natural sediment/water systems. However it is considered that the anaerobic biodegradation could be relevant for risk assessment purposes.

In a published study (Pruell & Quinn, 1985), surface sediments were collected from locations along a PAHs polluted gradient in a bay and tested over a period of 394 days in controlled seawater mesocosms with controlled 27 days turnover time and simulated turbulence. The concentrations of total PAHs and specifically biphenyl decreased significantly with time in the contaminated sediments. Calculated half-life for biphenyl in sediment was 333 days. This study is not considered reliable for the determination of biphenyl half-life and raised a concern for the biodegradability in sediments of the substance. However, this concern was overruled by the new data available and through the application of the persistency testing strategy established in Chapter R.11 (ECHA, 2017) of the REACH Guidance on IR&CSA.

7.7.1.2.2. Biodegradation in soil

There is one available study, a simulation test in soil similar to OECD Guideline 307 (Aerobic and Anaerobic Transformation in Soil) (unnamed, 1992) in which biphenyl was tested with phenol at an initial concentration of 1 ppm in the soil/groundwater mixture. The test was performed in two series: with and without addition of N and P.

In the series without addition of nutrients, DT_{50} values for mineralization ranged from 5 to 22 days, and monitoring of $^{14}CO_2$ evolution indicated ultimate biodegradation of 40-90% after 28 days, depending on the soil used. But in the series with addition of nutrients, DT_{50} values for mineralization ranged from 1.5 to 3.5 days, and monitoring of $^{14}CO_2$ evolution indicated ultimate biodegradation of 40-50% after 36 days, depending on the soil used. With addition of nutrients, ultimate biodegradation was lower as well as DT_{50} for mineralization.

The limitations of this test are: use of soil/groundwater system from site contaminated with hydrocarbons; biphenyl tested in mixture with phenol may affect individual test results; no mass balance presented; details on the methods missing.

In the dossier a data waiving argument was presented for this endpoint.

7.7.1.3. Summary and discussion on degradation

Based on data on oxygen consumption from the recent ready biodegradability test (OECD Guideline 301F) the criterion for ready biodegradation is fulfilled. It is noted that the results of the OECD Guideline 301F test based on O_2 consumption and CO_2 evolution are

somehow conflicting. The eMSCA considers that the O_2 measurements should be given more weight, since they were done throughout the test whereas CO_2 was only measured at the end, additionally O_2 consumption is the parameter indicated in the Guideline for determining degradation.

The conclusion on ready biodegradability of biphenyl is also supported by the results of an earlier OECD Guideline 301C test where 66% degradation after 14 days based on BOD was determined, although detailed information on this test is missing.

Additionally, most of the information available on the degradation of biphenyl, although not considered fully reliable, indicate that the substance has potential to be degraded in the environment, and that the substance most probably is not persistent to the level that it fulfils the P/vP criteria of Annex XIII.

Taking into account all the available biodegradation data in a weight-of-evidence analysis, the eMSCA concluded that biphenyl can be considered not persistent.

7.7.2. Environmental distribution

Adsorption/desorption

Based on the available information (Southworth and Keller, 1986), a Koc of 1546 (at 20 ºC) and a log Koc of 3.19 (at 20 °C) are considered for the substance, which indicates moderate soil adsorption. This is an average value of eight well-documented measured Koc values obtained in two key studies using a method equivalent or similar to OECD Guideline 106 (Adsorption-Desorption using a batch equilibrium method). The measured Koc values in widely varied soils were in the range of 870 - 3,300 (log Koc ranging from 2.94 - 3.52). The average log Koc value from these studies is in accordance with the estimated log Koc of 3.15 predicted by a QSAR model for neutral organics reported by Schüürmann *et al*. (2006). The EPIsuite KOCWIN model predicts a log Koc of 3.71 based on first-order molecular connectivity index, and a log Koc of 3.47 based on log Kow.

Volatilisation

There is no experimental information on Henry's Law constant in the registration dossiers.

The calculated Henry's Law Constant is 25 $Pa \cdot m^3/mol$ at 25 °C and 12 $Pa \cdot m^3/mol$ at 12ºC (EUSES). Henry´s Law constant estimated with EPISuite HENRYWIN v3.20 model is 43 $Pa \cdot m^3/mol$. In the EPISuite's experimental database a Henry's Law Constant of 31.2 $Pa \cdot m^3/mol$ at 25 °C is reported for biphenyl. This value is used in the risk assessment of the substance.

The available Henry's Law constant values indicate that moderate evaporation of the substance from water into the atmosphere is expected.

Distribution modelling

The distribution estimated by EPISuite Level III Fugacity model is 3.35%, 17.4%, 76.5% and 2.73% in air, water, soil and sediment, respectively. Hence, based on the modelling soil and water would be the most relevant compartments. However, due to the moderate adsorption potential (log Koc 3.19), part of the substance may adsorb to particulate material in water and end up in the sediment.

7.7.3. Bioaccumulation

Bioaccumulation of biphenyl is assessed on the basis of a measured log Kow of 4.008 (at 25 °C) and available BCF values measured in fish and oysters. Three studies were selected from the available information on bioconcentration in aquatic organisms, from the registration dossier.

In an aqueous exposure study (unnamed, 1974) using a method to some extent similar to the OECD Guideline 305 (Bioconcentration: Flow-through Fish Test) (no GLP), *Oncorhynchus mykiss* (rainbow trout) was exposed for 96h/4 days to concentrations between 1 and 10 µg/L of biphenyl. A 96h depuration period was also included in the study. The test solutions were prepared containing 218.7 µg ^{14}C-biphenyl/mL and 4.66 µg ^{14}C-biphenyl/mL using acetone. Fish samples were taken at 6 h, 12 h, 24 h, 48 h and 96 h during the uptake and depuration phases. Test water was sampled at 6 h, 12 h, 24 h, 48 h and 96 h of the uptake phase. According to the Registrant(s) steady-state was reached in the test. Whole-body fish BCF was calculated using a one-compartment model and based on total radioactivity using kinetic analysis (ratio of uptake rate (k1) and clearance rate constant (k2). A kinetic BCF of 1900 L/kg (w/w) for the fish whole-body, a depuration half-life of 64 hours and a depuration rate constant of 0.0108/h are reported.

In the registration dossier relatively limited details are available on this study. Therefore, it is not possible to assess whether the validity criteria indicated in the current OECD guideline 305 are fulfilled. Based on the available information there seems to be some deviations from the current guideline and other factors that add uncertainty to the study. E.g. according to the OECD Guideline 305, to demonstrate that the steady-state was reached, three successive analyses of concentration in fish done at intervals of at least two days should be within ±20% of each other, and there was no significant increase in C_{fish} between the first and last successive analysis. The available fish bioconcentration study had an uptake phase that lasted only 96 hours and the fish were sampled at 6 h, 12 h, 24 h, 48 h, 96 h. Therefore, the three last analyses were not made at intervals of at least two days, and hence, the determination of steady state does not follow the instructions of the OECD Guideline 305. In addition, there is no information on the concentrations of the substance in fish at different sampling points, and thus, it is not possible to confirm whether the three last measurements of the uptake phase were within ±20% of each other. Therefore, it is not possible to confirm that steady state was reached in the study.

Furthermore, the available information does not allow to confirm whether 95% loss was achieved during the depuration phase.

Other deviations from the guideline include e.g. lack of information on test medium, water parameters and fish lipid content. Furthermore, based on the information on the fish weights, there was a significant variation in fish size both at the start and end of the test. In addition, the measured concentrations of the test substance at the end of the test were significantly lower than the nominal and measured concentrations at its start. It is not clear which concentrations were used in the calculation of BCF.

In conclusion, there are uncertainties in the reliability of the study and in the determination of the BCF value, namely it is not clear which test concentrations were used in the calculations. The reported BCF of 1900 L/kg (w/w) was calculated based on total radioactivity, however is not lipid normalised nor growth corrected.

A study by Neely *et al.* (1974) using a method similar to OECD Guideline 305 and rainbow trout with an exposure of 5 days at 10-12 °C was followed by a 28 days depuration study. Steady-state BCF based on biphenyl concentration in exposure water and in edible fillet tissue (wet weight) was considered. The results are BCF of 438 (dimensionless) for the fish edible fraction. As the BCF is not determined for whole fish, this information can only be used as supporting information.

In a study (unnamed, 1989) using a method equivalent to EPA OTS 797.1830 – presently EPA 850.1710 - (Oyster Bioconcentration Test) in GLP accordance, the saltwater bivalve *Crassostrea virginica* (oyster) was exposed for 28 days in a flow-through system to a mean measured concentration of 0.058 mg/L, followed by a 14 days depuration phase. Mortality in the solvent control was too high, but mortality in negative control and exposure concentrations was acceptable. A steady-state was attained at 7 days. Transformation products associated with oyster tissues were 3'-4'-hydroxybiphenyl (less than 1%), non-polar compounds (5.4%) and highly polar compounds (31.5%). Oysters

did not eliminate significant amounts of ^{14}C from soft tissues in the depuration phase. The BCF for the total ^{14}C activity was 2422 $\pm$ 515.6 L/kg (w/w) for the mollusc edible fraction. Based on HPLC analysis of tissues sampled at the end of the uptake phase (on day 28), the BCF of the parent biphenyl was calculated to be 110 L/kg (w/w).

7.7.3.1. Summary and discussion on bioaccumulation

The log Kow of 4.008 is below the screening criterion for B/vB but it is indicative of moderate potential for bioaccumulation.

In a bioconcentration in fish study that is not considered fully reliable, a kinetic BCF of 1900 L/kg (w/w) is reported based on total radioactivity. The result is not lipid-normalised nor growth corrected and there are uncertainties regarding the exposure concentration used in the calculations. However, it is noted that in the oyster bioconcentration study significant metabolism of biphenyl was observed and the BCF of biphenyl in oysters (110 L/kg) was well below the BCF based on total ^{14}C in oysters (2422 L/kg), it can be expected that the substance is also metabolised in fish. Therefore, since the available fish BCF of 1900 L/kg (w/w) is determined based on total radioactivity, the BCF of biphenyl is likely to be lower than that.

Based on the available results from bioconcentration tests in fish and oysters, biphenyl seems to be easily taken up by organisms but may not be highly bioaccumulative. This appears to be due to the ability of organisms to metabolise the substance to more polar and excretable substances. However, as the available fish BCF study is not fully reliable, and a BCF close to 2000 is reported, some uncertainty remains regarding the bioaccumulation.

The BCF value of 1900 L/kg (wwt based) for total bioaccumulation in fish will be used in the chemical safety assessment.

7.8. Environmental hazard assessment

Only the information for the environmental hazard assessment considered relevant by the eMSCA has been compiled in this report. Additional studies on biphenyl can be found in ECHA dissemination website.

7.8.1. Aquatic compartment (including sediment)

7.8.1.1. Fish

Short-term toxicity testing on fish:

Several studies on acute toxicity to fish are presented in the registration dossier.

A study (Unnamed, 1975) considered to be the key study, is a freshwater 96-h flow-through fish test equivalent to OECD Guideline 203, conducted at 10 °C on fathead minnow *(Pimephales promelas*). This temperature is lower than the guideline recommended range of 21-25 °C. At lower temperature fish may have a lowered metabolism, and it cannot be excluded that a higher toxicity could be observed at higher temperatures. Acetone was used as a carrier solvent. Concentrations were measured and analytical monitoring was performed. There were no replicates and it is not clear whether a vehicle control was performed. At the highest tested concentration - 3.6 mg/L - 100% mortality was observed, and a 96h LC_{50} of 3.0 mg/L was obtained. These data are considered in the freshwater aquatic hazard assessment taking into consideration that adequate long-term test on fish is available and a ratio of 10 is obtained from acute to chronic data.

Long-term toxicity testing on fish:

An 87 days early-life stage test started with newly fertilized rainbow trout eggs (*Salmo gairdneri*) is available. This was flow-through test conducted at 10 °C in accordance with an in-house SOP of the Dow Chemical Company (equivalent to OECD Guideline 210 Fish, Early-Life Stage Toxicity Test) and GLP (unnamed, 1988). The temperature used is in the recommended range according to OECD Guideline 210. Acetone was used as a carrier solvent and vehicle control was also included. Concentrations were measured and analytical monitoring was performed. Test conditions have been described and four vessels per treatment were included. NOEC was determined using analysis of variance and Dunnett's two-tailed t-test. A NOEC value of 0.229 mg/L (based on arithmetic mean of the measured concentrations) is reported based on length measurements of surviving larvae. This study is selected and used in the freshwater aquatic hazard assessment.

7.8.1.2. Aquatic invertebrates

Short-term toxicity testing on aquatic invertebrates:

Several studies on acute toxicity to aquatic invertebrates are presented in the registration dossiers. The following study (unnamed, 1988) is considered to be the key study and is used in the freshwater aquatic hazard assessment.

The study is a 48-h flow-through with *Daphnia magna* performed according to an internal SOP of the DOW Chemical Company and GLP. Test conditions are well described in the registration dossier. Acetone was used as carrier and vehicle control was included. Three replicates per treatment were used. This study resulted in a 48-h LC_{50} of 0.36 mg/L based on the arithmetic mean of measured concentrations.

Long-term toxicity testing on aquatic invertebrates:

A 21-d flow-through reproduction toxicity test with juveniles (<24h old) of *Daphnia magna* conducted in accordance with an in-house SOP of the Dow Chemical Company 2004 and GLP is provided (unnamed, 1988). Test conditions well described in the registration dossier. Four replicates with 5 animals per treatment were used. Acetone was used as carrier and a vehicle control was included. Concentrations were measured and analytical monitoring were included. A 21-d NOEC of 0.17 mg/L for both reproduction and mortality is reported. NOEC and LOEC were determined using analysis of variance followed by Dunnett's t-test ($\alpha = 0.05$). This study is used in the freshwater aquatic hazard assessment.

7.8.1.3. Algae and aquatic plants

The registration dossier includes five algal toxicity studies, four on biphenyl and one on a read-across substance, but these studies are not considered reliable also by the Registrant(s). Briefly,

- The first study (Unnamed, 1980) was conducted with a read-across substance diphenyl oxide. The test concentrations were not measured, and hence, the test is not considered reliable.

- Two studies on *Chlamydomonas angulosa* and *Chlorella vulgaris* assessed the inhibition of the photosynthesis after an exposure period of 3h (Hutchinson *et al.*, 1980). These studies resulted in EC_{50} of 1.28 mg/L and EC_{50} of 3.86 mg/L, respectively. The test concentrations were not measured and the duration of the tests was short and there is no information on controls. Therefore, the studies are considered not reliable (Klimisch 3).

- The fourth study on *Pseudokirchneriella subcapitata* was performed with a mixture containing 26.3% biphenyl and had a duration of 96h (unnamed, 1979). The test

concentrations were not measured, and hence, the test is not considered reliable (Klimisch 3).

- The fifth study, included in the Japan CHEmicals Collaborative Knowledge database, report results from existing chemicals survey program conducted by the Japanese Government (Unnamed, 1998). This study is indicated to be conducted according to OECD Guideline 201 and GLP. However, reliability of the results could not be evaluated because a robust study summary or full study report are not available. No information on testing conditions nor test procedures, apart from the reference to the OECD guideline is provided. The results are a 72h EC_{50} of 0.78 mg/L and NOEC of 0.007 mg/L on growth rate and 72h EC_{50} of 0.28 mg/L and NOEC of 0.0072 mg/L on areas under the growth curves for *Pseudokirchneriella subcapitata*.

There are some concerns on the result of latter test since the calculated acute to chronic ratio is 100, instead of 10 which is the general accepted value, and no further information on the study, namely on the concentrations used in the test, is available to evaluate its reliability.

Since the available studies are either not reliable or their reliability cannot be assessed, QSAR estimations were performed. Toxicity values for algae were predicted using US EPA's ECOSAR v1.11 QSAR model (log Kow = 4.0, melting point = 69.5 °C and water solubility = 7.35 mg/L used as input values) and within the applicability domain of the model. The predicted toxicity values are a 96-h EC_{50} of 2.211 mg/L and a chronic value of 0.874 mg/L. The NOEC was estimated to be 0.58 mg/L, considering that the chronic value given by ECOSAR represents the geometric mean of NOEC and LOEC and assuming a maximum spacing factor of 2 between adjacent test concentrations. These predicted values suggest that algae are not expected to be the most sensitive group. However, it is noted that some uncertainty remains regarding the toxicity to algae since there is no reliable experimental data or the reliability cannot be assessed. The Danish QSAR database[5] was also searched for toxicity of biphenyl, however the substance is out of the models' domain.

7.8.1.4. Sediment organisms

No relevant information available.

7.8.1.5. Other aquatic organisms

No relevant information on other aquatic organism is available.

7.8.2. Terrestrial compartment

No reliable information has been presented in the registration dossier.

7.8.3. Microbiological activity in sewage treatment systems

Five studies on aquatic micro-organisms are available in the registration dossier as supporting studies, and although considered not reliable, they are used as weight of evidence. The determined NOEC and effect concentrations are near the water solubility limit of the substance (7.35 mg/L).

Taking into consideration all available information, in a weight of evidence approach, the reasonable worst case is used, LOEC of 5.6 mg/L (Dive *et al.*, 1980) from exposure of the ciliate *Colpidium campylum* to a series of biphenyl concentrations during 43 hours in an open system. The effect concentrations were based on growth (cell number) and in the

[5] Available at http://qsar.food.dtu.dk

study no NOEC was reported. However, based on the information in the publication, it can be assumed that the test concentration series of 1.8 – 3.2 – 5.6 – 10.0 mg/L was used, and thus, a NOEC of 3.2 mg/L was considered. This value is used for the hazard assessment.

7.8.4. PNEC derivation and other hazard conclusions

In Table 9 are provided the PNECs derivation for the different environmental compartments.

Table 9. PNECs derivation

PNEC DERIVATION AND OTHER HAZARD CONCLUSIONS		
Hazard assessment conclusion for the environment compartment	**Hazard conclusion**	**Remarks/Justification**
Freshwater	Hazard assessment conclusion (freshwater): PNEC aqua (freshwater): 3.4 x 10^{-3} mg/L	Assessment factor: 50 Reliable acute and chronic data is available only for fish and aquatic invertebrates (data on algae was considered not reliable or reliability could not be assessed). Assessment factor of 50 is used for the lowest reliable and confirmed chronic value, i.e. the NOEC of 0.17 mg/L of *Daphnia magna*.
Marine water	Hazard assessment conclusion (marine waters): PNEC aqua (marine water): 3.4 x 10^{-4} mg/L	Assessment factor: 500
Intermittent releases to water	Hazard assessment conclusion (intermittent releases): PNEC aqua (intermittent releases):3.6 x 10^{-3} mg/L.	Assessment factor: 100
Sediments (freshwater)	Hazard assessment conclusion (sediment freshwater): PNEC sediment (freshwater): 9.66 x 10^{-2} mg/kg	Extrapolation method: equilibrium partitioning method (PNEC aqua 3.4 x 10^{-3} mg/L; Koc 1546)
Sediments (marine water)	Hazard assessment conclusion (sediment marine water): PNEC sediment (freshwater): 9.66 x 10^{-3} mg/kg	Extrapolation method: equilibrium partitioning method (PNEC aqua 3.4 x 10^{-4} mg/L; Koc 1546)
Sewage treatment plant	Hazard assessment conclusion (STP): PNEC STP: 3.2 mg/L	Assessment factor: 1
Soil	Hazard assessment conclusion (soil): PNEC soil: 0.0766 mg/kg	Extrapolation method: equilibrium partitioning method (PNECaqua 3.4 x 10^{-3} mg/L; Koc 1546; Henry's Law Constant

		12 Pa·m^3/mol at 12 °C calculated by EUSES*)
Secondary poisoning	Hazard assessment conclusion: PNEC oral: 16.7 mg/kg food	Assessment factor: 30 No data on avian toxicity available. The lowest available NOAEL value of 25 mg/kg bw/day for female rats from a EOGRTS was used for deriving PNECoral. The NOAEL was converted to NOEC of 500 mg/kg using a conversion factor of 20 (rats, exposed > 6 weeks)

*Due to the moderately volatility of the substance, a refinement has been applied by using the Henry´s Law constant at 12ºC.

7.8.5. Conclusions for classification and labelling

The harmonised classification of biphenyl as N; R50-53 was agreed under the Dangerous Substances Directive (Directive 67/548/EEC) and it was converted to Regulation (EC) No. 1272/2008 (CLP Regulation). According to the Table 3.1. of Annex VI of CLP Regulation, biphenyl has a harmonised classification as Aquatic Acute 1 and Aquatic Chronic 1.

The available information supports the harmonised classification for acute aquatic hazards as the 48h LC_{50} for *Daphnia magna* is below 1 mg/L (0.36 mg/L). The acute M-factor is 1.

Regarding chronic classification, based on the available information, the substance is considered to be rapidly biodegradable and the key ecotoxicity data considered reliable is on fish and aquatic invertebrates with a measured 87d-NOEC of 0.229 mg/L for *Onchorhynchus mykiss* and a measured 21d-NOEC of 0.17 mg/L for *Daphnia magna.* The available data on algae was not considered reliable or reliability could not be assessed. Therefore, considering that there is no sufficient data on all three trophic levels for classification purposes, the substance could be classified for chronic hazards according to both Tables 4.1.0.(b)(ii) and 4.1.0.(b)(iii) of CLP Regulation and the most stringent outcome is selected.

According to the Table 4.1.0.(b)(ii) the substance receives a chronic classification of Aquatic Chronic Category 3 (based on the NOEC of 0.17 mg/L for *Daphnia magna*).

According to Table 4.1.0.(b)(iii) and based on the LC_{50} of 0.36 mg/L for *Daphnia magna* and the BCF of 1900 L/kg (w/w) in fish, the substance is classified as Aquatic Chronic Category 1. This supports the harmonized classification and is more stringent than the classification obtained based on the chronic data. The chronic M-factor based on the acute data is 1.

In conclusion, based on the available chronic toxicity data a classification as Aquatic Chronic Category 1 is adequate.

7.9. Human Health hazard assessment

The eMSCA screened only repeated dose toxicity for the assessment of secondary poisoning and human health relevant endpoints for PBT properties. Other human health related endpoints were not assessed as being outside the scope of this targeted substance evaluation.

7.9.1. Toxicokinetics

Not assessed.

7.9.2. Acute toxicity and Corrosion/Irritation

Not assessed.

7.9.3. Sensitisation

Not assessed.

7.9.4. Repeated dose toxicity

The registration dossier includes 18 studies on repeated dose toxicity, most of them considered as not reliable with Klimisch 3-4 assigned. A summary of all studies is shown below.

Table 10. Summary of repeated dose toxicity studies

Test	Reference (Guideline)	GLP	Reliability	LOAEL (mg/kg bw/day)	NOAEL (mg/kg bw/day)
				General Toxicity (organ)	General Toxicity
Combined repeated dose/carcinogenicity - oral – rats	Unnamed, 2002 (OECD 453)	yes	2	114 (kidney)	38
90 day - oral exposure - mice	Unnamed, 2004 (OECD 408)	no	2	608 (liver)	304
Combined Chronic Toxicity / Carcinogenicity Studies – oral exposure - mice	Unnamed, 2005 (OECD 453)	yes	2	300 (kidney)	100
1 year study - oral exposure – monkeys	Unnamed, 1953 (OECD 452)	no	3	insufficient information	
28 day - oral exposure – rats	Unnamed, 1989b (no GD)	no	3	insufficient information	
90 day - oral exposure – rats	Unnamed, 1953 (OECD 408)	no	3	insufficient information	
90 day - oral exposure -rats	Ohnishi et al. 2001 (no GD)	no	4	insufficient information	
26 day - oral exposure -rabbits	Unnamed, 1938 (no GD)	no	4	100 (kidney)	< 100
Oral exposure – rabbits	Unnamed, 1939 (no GD)	no	4	insufficient information	
5-20 weeks - oral exposure – rabbits	Unnamed, 1947 (no GD)	no	4	insufficient information	
165 days -oral exposure - rats	Unnamed, 1961 (no GD)	no	4	375 (kidney)	75
1 year - oral exposure – rats	Pecchiai & Saffiotti 1957 (no GD)	no	4	250 (kidney & liver)	< 250
Oral exposure – mice	Sunouchi et al. 1999 (no GD)	no	4	insufficient information	
56 days - oral exposure - rats	Unnamed, 1989a (no GD)	no	3	insufficient information	
2 year -oral exposure – rats	Ambrose et al. 1960 (no GD)	no	4	0.5%* (kidney)	0.10%*

Test	Reference (Guideline)	GLP	Reliability	LOAEL (mg/kg bw/day)	NOAEL (mg/kg bw/day)
				General Toxicity (organ)	General Toxicity
90 day- inhalation exposure - rabbits, rats & mice	Unnamed, 1947 (no GD)	no	4	insufficient information	
42 day - dermal exposure – rabbits	Unnamed, 1953 (OECD 410)	no	4	> 2000	2000
Dermal exposure – rabbits	Unnamed, 1947 (no GD)	no	4	insufficient information	

* % in diet

The key study (Unnamed, 2002) is performed on rats with 6 weeks of age at the initiation of the study and according to OECD Guideline 435 (1991). Fifty animals per dose were exposed during 105 weeks at 500, 1500 and 4500 ppm (concentrations of biphenyl in the diet). Adverse effects were mainly observed in the kidney, both in male and female rats, and neoplastic lesions (tumours) were observed in the male urinary bladder. The relative kidney weight showed a statistically significant increase at and above 1500 ppm (males and females). Females dosed at 1500 ppm had simple transitional cell hyperplasia of renal pelvis and deposit of hemosiderin. At the next dose level, significant damage to the kidney was evident as well as to the urinary bladder.

Bladder tumours were induced in male rats dosed with 4500 ppm biphenyl. Induction was associated with calculus formation and haematuria, and regenerative lesions in the urinary system. The sustained mechanical damage caused by the bladder calculi plays an important role in tumorigenesis. This effect is considered a secondary mode of action exhibited in high test concentrations only. No neoplastic lesions were found in female rats dosed at 4500 ppm.

A no observed adverse effect level (NOAEL) of 500 ppm (concentration in diet) was thus determined based on the adverse effects on the kidney at the next dose levels. This is recalculated to a NOAEL value of 38 mg/kg bw/day and the lowest observed adverse effect level (LOAEL) in this study is set at 1500 ppm (equivalent to 114 mg/kg bw/day).

7.9.5. Mutagenicity

Not assessed.

7.9.6. Carcinogenicity

Not assessed.

7.9.7. Toxicity to reproduction (effects on fertility and developmental toxicity)

Six oral exposure studies are available, as summarised below.

Table 11. Summary of reproductive toxicity studies

Test	Reference (Guideline)	GLP	Reliability	LOAEL (mg/kg bw/day)		NOAEL (mg/kg bw/day)		
				General Toxicity (organ)	Reproductive	General Toxicity	Fertility	Developmental toxicity
EOGRTS	Unnamed, 2018 (OECD 443)	yes	1	75 (kidney)	215 (reduced pup bw)	25	215	75

Test	Reference (Guideline)	GLP	Reliability	LOAEL (mg/kg bw/day)		NOAEL (mg/kg bw/day)		
				General Toxicity (organ)	Reproductive	General Toxicity	Fertility	Developmental toxicity
Reproduction/ Developmental Toxicity screening	Unnamed, 2017 (OECD 421)	yes	2	100 (kidney)	200 (reduced pup bw)	< 100	400	100
Teratogenic study -oral exposure - rabbits	Unnamed, 1979 (OECD 414)	no	2	no information	500 (increased missing/ unossified sternebrae)	no information	1000	250
One generation fertility study - oral exposure - rats	Unnamed, 1960 (no GD)	no	3	not assessed	888 (reduced litter size)	not assessed	444	not assessed
3 generation reproductive toxicity - oral exposure - rats	Unnamed, 1953 (no GD)	no	4	not assessed	887 (reduced bw & litter size)	not assessed	88	88
Prenatal Developmental Toxicity Study - oral exposure - mice	Unnamed, 1988 (EPA OPP 83-3 (1984))	yes	4	no information	1000 (reduced bw, pregnancy, litter size)	no information	500	500

Three studies were assessed and considered reliable with Klimisch 1-2 and are discussed in more detail.

An extended one-generation reproductive toxicity study (EOGRTS) according to OECD Guideline 443 is available as the key study. This is a GLP compliant study and was assigned Klimisch 1 by the eMSCA. In this study, groups of 26 male and 26 female young adult rats were fed control or biphenyl containing diets supplying 0, 300, 1000, and 2800 ppm biphenyl (equivalent to 25, 75, and 215 mg biphenyl/kg/day, respectively, as nominal doses) for approximately ten weeks prior to breeding, and continuing through breeding (two weeks). An additional satellite group of P1 females (4/dose) was included primarily for assessments of kidney function in adult non-pregnant females during the pre-breeding period. The satellite female group was given biphenyl-containing diets concurrent with the P1 animals during pre-breeding. Satellite females were removed from study/terminated at the end of the pre-breeding period. After breeding, P1 males continued on the test diets for an additional 7-8 weeks (19-20 weeks total exposure). After breeding, P1 females continued on the test diets through gestation and lactation (16-18 weeks total exposure).

F1 offspring were divided into Cohorts 1A, 1B, 2A, 2B and 3 at weaning (postnatal day (PND) 21) as follows:

- Cohort 1A (22-24/sex/dose, 1 pup/sex/litter) were used to evaluate reproductive/ endocrine toxicity, which included oestrous cycle evaluation and post-mortem evaluations focused on reproductive organs, sperm assessment, and ovarian follicle counts on PND 90. This group also was used to assess general systemic and thyroid toxicity, which included clinical chemistry/haematology parameters, thyroid hormone assessment, and urinalysis. Post-mortem evaluations in Cohort 1A (PND 90) also included gross pathology, organ weights, and histopathology on a wide range of tissues, including thyroids.
- Cohort 1B animals (21-24/sex/dose, 1 pup/sex/litter) were known as the endocrine group and designated to clarify any equivocal responses seen in the Cohort 1A animals. This group was used to generate a second generation of offspring, based on equivocal incidences of dystocia in the P0 animals.

  - Additional in-life parameters evaluated in the Cohort 1B P1 animals included an oestrous cycle evaluation, litter and fertility data, thyroid hormone measurements, clinical chemistry/haematology parameters, and urinalysis. Post-mortem evaluations in Cohort 1B P1 animals occurred in males after approximately 19 weeks of postnatal exposure (PND 138-148) and in females on Lactation day 22 (after approximately 21 weeks of postnatal exposure). Evaluations included sperm assessment, gross pathology, organ weights, and histopathology with a primary focus on tissues affected in Cohort 1A, including kidney, liver and urinary bladder.
- The Cohort 2A and 2B animals (21-22/sex/dose, 1 pup/sex/litter) were used to assess potential developmental neurotoxicity (DNT) as follows:
  - Cohort 2A (11-12/sex/dose, 1 pup/sex/litter) were used for DNT assessments, which included functional observational battery (FOB), motor activity, and acoustic startle response (ASR). On PND 78, Cohort 2A F1 animals were perfused for central nervous system (CNS) and peripheral nerve neuropathology evaluation and brain morphometry.
  - Cohort 2B (10/sex/dose, 1 pup/litter) underwent necropsy on PND 22, which included brain weight collection in these weanlings and immersion fixation of tissues for examination of neuropathology.
- Cohort 3 (10/sex/dose, 1 pup/litter) were used for developmental immunotoxicity (DIT) assessments.

This biphenyl extended one-generation reproduction study identified kidney, urinary bladder and liver as target organs for biphenyl-induced toxicity, resulting in systemic NOAELs in both generations with the NOAEL of 1000 ppm (75 mg/kg bw/day) for males based on bladder and kidney toxicity, and the NOAEL of 300 ppm (25 mg/kg bw/day) for females based on kidney toxicity.

There was no evidence of treatment-related reproductive toxicity, including an absence of effects on reproductive and litter parameters in both generations up to the highest dose tested (NOAEL of 2800 ppm or 215 mg/kg bw/day).

For developmental neurotoxicity, there were no treatment-related effects on neurobehavior or neuropathology at any dose levels in either Cohort 2A or 2B animals. Biphenyl exposure did not result in developmental immunotoxicity at any dose level. However, transient decrease in pup body weight at 2800 ppm during lactation period (from PND 7) is recorded. This effect appeared to be secondary to decreased maternal feed consumption. Consequently, a developmental NOAEL is set at 1000 ppm (75 mg/kg bw/day). In the F2 generation this effect was not reproduced.

In this study there were no effects on the estrogen-, androgen-, or thyroid-related endocrine pathways at any dose of biphenyl.

In addition, a GLP compliant OECD Guideline 421 (Reproduction/developmental toxicity screening) study is also available. This study was assigned Klimisch 2 by the eMSCA since no clinical biochemistry data was examined and incomplete data collection of parameters linked to female oestrous cycle. In this study groups of 10 male and 10 female Crl:CD(SD) rats were administered biphenyl via the diet at concentrations of 0, 1375, 2750, or 5500 ppm (equivalent to 0, 100, 200 and 400 mg/kg bw/day biphenyl respectively). Females were dosed daily for two weeks prior to breeding, through breeding (up to two weeks), gestation (three weeks), lactation (three weeks) and until necropsy on post-partum days 22-24. The males were dosed for two weeks prior to breeding, through breeding (up to two weeks), and until necropsy (test day 36). Effects on reproductive as well as general toxicity were evaluated.

Based upon the kidney histopathological findings at 1375 ppm (100 mg/kg bw/day) in females, a no-observed-adverse effect level (NOAEL) for systemic toxicity could not be determined for females. The NOAEL for systemic toxicity in males was 1375 ppm (100

mg/kg bw/day). The NOAEL for reproductive toxicity was 5500 ppm (400 mg/kg bw/day), the highest dose tested. The NOAEL for toxicity in the offspring was 1375 ppm (100 mg/kg bw/day) based on a transient decrease in pup body weights 2750 ppm (200 mg/kg bw/day). No effects indicative of endocrine mediated toxicity was observed.

Two additional studies are available to assess developmental effects, as indicated below:

As a key study (Unnamed, 1979), assigned Klimisch score 2, by the Registrant(s), a test similar to OECD Guideline 414 - Prenatal Developmental Toxicity Study (no GLP) by oral route/gavage was available. It presents incomplete or no information on environmental conditions and animals. Rats were administered 0, 125, 250, 500 or 1000 mg/kg bw/day biphenyl on gestation days 6–15. The maximum dosing volume exceeded recommended volume and there is limited information on clinical observations. Foetal toxicity, including non-significant increases in foetuses with missing or non-ossified sternebrae and maternal toxicity at 1000 mg/kg bw/day were referred in the registration dossier. Considering the statistically significant increasing trend of missing and unossified sternebrae with dose and that this anomaly was more severe than the other anomalies, US EPA (2013) estimated a LOAEL of 500 mg/kg bw/day for increased incidence of foetuses with missing and unossified sternebrae and a NOAEL of 250 mg/kg bw/day, based on data from the publication (Unnamed, 1979).

A summary of a mouse study (Unnamed, 1988) according to EPA OPP 83-3 - Prenatal Developmental Toxicity Study (GLP) was assigned Klimisch 4 by the Registrant(s) since a full report was not available. Mice were administered 0, 125, 250, 500 or 1000 mg/kg bw/day. There was a high incidence of non-pregnancy in all groups. Food consumption was similar in exposed animals and control, maternal mortality and reduction in maternal weight gain was increased at the high-dose level (1000 mg/kg bw/day). Regarding litter effects, the total resorptions were significantly increased and mean litter size reduced at 1000 mg/kg bw/day. In this study it was concluded that biphenyl is fetotoxic and maternally toxic at 1000 mg/kg bw/day causing mortality of both dams and early-pregnancy loss including complete resorptions. The 500 mg/kg bw/day dose level was statistically a NOAEL for both dams and foetuses. The incidence of malformations was not increased.

A pre-natal developmental toxicity study (OECD Guideline 414) in a second species (rabbit), oral (feed) route using the registered substance was requested under a Testing proposal Decision issued by ECHA[6].
In addition, two fertility studies are available as supporting evidence:

- A one-generation fertility study in rats, by oral route (Unnamed, 1960) (no GLP), with pre-mating, mating and until weaning treatments with administered doses of 5000 or 10000 ppm is available. This study was assigned Klimisch 3 by the Registrant(s). Endpoints recorded were limited to litter observations. Reduced number of pups and litter size were observed at 10000 ppm.
- In a three-generation dietary exposure study (Unnamed, 1953) (equivalent to an extended OECD Guideline 422) (no GLP) assigned Klimisch 4 by the Registrant(s), rats were orally administered 100, 1000 or 10000 mg/kg of biphenyl. At the highest dose tested (estimated 887 mg/kg bw/day in males and 1006 mg/kg bw/day in females), poor fertility, decreased litter size and poorer growth of the young (decreased body weights) was observed, compared to the controls. Data on food consumption and breeding rat weight are not available. The estimated effect concentrations (887 mg/kg bw/day and 1006 mg/kg bw/day) were similar to the dose that caused maternal

[6] The Decision is publicly available at: https://echa.europa.eu/documents/10162/a7fa7627-74c5-0c66-65af-464c67f9d048

toxicity in a developmental toxicity study (Unnamed, 1979). In this study a NOAEL of 500 ppm for fertility and developmental toxicity is determined.

Both fertility studies listed above have limited information on experimental design and a small number of animals were tested.

In conclusion, the following critical target values are determined based on the six studies submitted.

Table 12. Summary of general toxicity, fertility and developmental toxicity

	General Toxicity	Fertility	Developmental Toxicity
LOAEL (mg/kg bw/day)	75 (kidney)	215 (highest dose no effects)	200 (reduced pup bw)*
NOAEL (mg/kg bw/day)	25	215	75#
Key study	EOGRTS (OECD 443)	EOGRTS (OECD 443)	# EOGRTS (OECD 443) * Reproduction/ Developmental Toxicity screening (OECD 421)

7.9.8. Hazard assessment of physico-chemical properties

Not relevant for the assessment.

7.9.9. Selection of the critical DNEL(s)/DMEL(s) and/or qualitative/semi-quantitative descriptors for critical health effects

Not relevant for the assessment.

7.9.10. Conclusions of the human health hazard assessment and related classification and labelling

According to Table 3.1. of Annex VI of CLP Regulation, biphenyl has a harmonised classification for human health as Skin Irrit. 2, Eye Irrit. 2 and STOT SE 3.

Since the focus of this substance evaluation was on effects leading to PBT properties and reproductive toxicity, the eMSCA assessed available repeated-dose toxicity and reproductive toxicity studies to compare with CLP criteria.

In conclusion, the following critical target values and CLP classifications are determined based on the long-term submitted data.

Table 13. Summary of general toxicity, fertility, developmental toxicity and CLP classification

	General Toxicity	Fertility	Developmental Toxicity
LOAEL (mg/kg bw/day)	75 (kidney)	215 (highest dose no effects)	200 (reduced pup bw)*
NOAEL (mg/kg bw/day)	25	215	75#
Key study	EOGRTS (OECD 443)	EOGRTS (OECD 443)	# EOGRTS (OECD 443) * Reproduction/ Developmental Toxicity screening (OECD 421)
Potential CLP Classification	None	None	None

Taking the mammalian repeated-dose and the reproductive toxicity studies available into consideration the eMSCA considers the EOGRTS (OECD TG 443) as the key study. In this study a general toxicity LOAEL of 75 mg/kg bw/day is set. The value of 75 mg/kg bw/day corresponds to the guidance values for category STOT RE 2 (10 < C ≤ 100 - oral), thus the substance might cause damage to kidney through prolonged or repeated exposure. However, as the observed effects are very slight to slight and only in females, the substance is unlikely to meet the criteria to be classified as STOT RE 2.

7.10. Assessment of endocrine disrupting (ED) properties

7.10.1. Endocrine disruption – Environment

Not assessed.

7.10.2. Endocrine disruption - Human health

During the evaluation the eMSCA noticed indications of potential endocrine activity.

The concern for potential endocrine disruption is based on the study by Petit *et al.* (1997) in which a competitive bioassay was performed to determine direct interaction between rtER and xenobiotics. The estrogenic potency of xenobiotics was observed when the yeast cells and trout hepatocytes aggregated cultures were treated. Biphenyl and its metabolites (hydroxylated compounds) showed a dose-dependent induction of lacZ gene.

Biphenyl showed less estrogenic activity than the evaluated metabolites (20H-Biphenyl; 2,2 'OH-Biphenyl; 3OH-Biphenyl; 4OH-Biphenyl and 4,4OH-Biphenyl) which exhibited clear estrogenic activity in the two bioassays. The results suggest that biphenyl is more than four orders of magnitude less active than 17β-Estradiol, which represents the maximum induction (reference unit). The maximal activity obtained with biphenyl metabolites is three orders of magnitude lower than 17β-Estradiol. In this study, biphenyl metabolites 3-hydroxybiphenyl, 4-hydroxybiphenyl, 4,4*-dihydroxybiphenyl, showed a relative binding affinity for ER 1700- to 6700-fold lower than E2 but in the same range that several Aroclors and nonylphenol diethoxylate.

Supporting evidence is available from the US EPA report (2013) that also includes indications of endocrine activity of biphenyl and its metabolites. This report concludes that compounds without an hydroxyl group (e.g. biphenyl) were inactive estrogenically but estrogenic activity of the hydroxylated metabolites (4-hydroxybiphenyl, 3-hydroxybipehnyl, 2-dydroxybiphenyl, 4,4´-dihydroxybiphenyl) is in the same order of magnitude than Bisphenol-A regarding relative gene activation of the Lac-Z gen of *Saccharomyces cerevisiae* based and estrogenic activity in MCF-7 cells and rat liver microsomes.

In the registration dossier two *in vivo* studies, GLP compliant, are available that allow for a more detailed endocrine disruption assessment. In a reproduction/developmental toxicity screening (OECD 421) study no adverse effects resulted on the reproductive indices, nor on weights and histopathology examinations in reproductive organs. Thus, no ED effects were observed in this study. In an EOGRTS (OECD 443) rat study ED relevant parameters were assessed in detail. Parameters investigated included: reproductive organ and thyroid weights and histopathology, sperm parameters (motility, counts, morphology) as well as reproductive performance and the oestrous cycle. In addition, thyroid hormone (T3, T4 and TSH) levels were also investigated. In both generations, no adverse effects resulted in any of the ED parameters assessed in this study. Thus, no ED effects were observed.

In conclusion, the *in vivo* tests do not indicate that biphenyl exposure results in an adverse effect on the endocrine system.

7.10.3. Conclusion on endocrine disrupting properties (combined/separate)

Based on the mammalian *in vivo* studies presented biphenyl exposure does not result in an adverse effect on the endocrine system.

7.11. PBT and vPvB assessment

1) Persistence

Based on the outcome of the requested ready biodegradation test and other available screening information, the eMSCA concluded that biphenyl is readily biodegradable and thus the screening criterion for P/vP is not met.

The available simulation studies in surface water, water/sediment systems and soil are not fully reliable but they can be used as supporting information on the degradation potential. Based on these studies it seems that the substance is likely to degrade in the environment, although some uncertainty remains regarding the degradation in water/sediment systems, especially under anaerobic conditions. However, it is considered that anaerobic persistency is not likely to occur, since the substance would be initially biodegraded within the aerobic water layer and the sediments' aerobic upper layer.

Taking into account all the available information in a weight-of-evidence analysis, it is concluded that biphenyl is not persistent to the level that it fulfils the P/vP criteria of Annex XIII.

2) Bioaccumulation

The measured log Kow of the substance is 4.008 (at 25 °C), and thus, the screening criterion for bioaccumulation is not met.

In a fish bioconcentration study, considered not fully reliable, a kinetic BCF of 1900 L/kg (w/w) is reported based on total radioactivity. The result is not lipid-normalised nor growth corrected and there are uncertainties regarding the exposure concentration used in the calculations. Additionally, it is noted that in an oyster bioconcentration study significant metabolism of biphenyl was observed and the BCF of biphenyl in oysters (110 L/kg)) was well below the BCF based on total ^{14}C in oysters (2422 L/kg). It can be expected that the substance is also metabolised in fish, at least to some extent. Therefore, since the available fish BCF of 1900 L/kg (w/w) is determined based on total radioactivity, the BCF of biphenyl is likely to be lower than that.

In conclusion, based on the available results from bioconcentration tests in fish and oysters, biphenyl seems to be easily taken up by organisms but may not be highly bioaccumulative. This appears to be due to the ability of organisms to metabolise the substance to more polar and excretable substances. Therefore, biphenyl is not likely to fulfil the criteria for B/vB in Annex XIII of REACH. However, as the available fish BCF study is not fully reliable, and a BCF close to 2000 is reported, some uncertainty remains regarding the bioaccumulation. But as the substance is not considered to be P/vP, no further information is needed.

3) Toxicity

The lowest reliable chronic aquatic toxicity value for the substance is a 21-d NOEC of 0.17 mg/L for *Daphnia magna* based on both reproduction and mortality. This value does not fulfil the criterion for T in Annex XIII of REACH. Regarding aquatic toxicity, it should be noted that some uncertainty remains regarding the chronic toxicity to algae.

Additionally, based on the available data, biphenyl does not fulfil the criteria for classification as carcinogenic (category 1A or 1B), germ cell mutagenic (category 1A or

1B), toxic for reproduction (category 1A, 1B or 2), STOT RE 1 according to the CLP Regulation.

However, taking the mammalian repeated-dose and the reproductive toxicity studies available into consideration the eMSCA considers the EOGRTS (OECD TG 443) as the key study. In this study a general toxicity LOAEL of 75 mg/kg bw/day is set. Although, the value of 75 mg/kg bw/day corresponds to the guidance values for category STOT RE 2 (10 < C ≤ 100 - oral), as these effects were very slight to slight and only in females, the substance is unlikely to meet the criteria to be classified as STOT RE 2.

Therefore, based on the available data is not likely that biphenyl meets the T criterion.

4) Overall conclusion

Based on the available information biphenyl does not meet the criteria for persistence (P/vP) in Annex XIII of REACH. Additionally, based on the available information the criterion for bioaccumulation (B/vB) is likely not met, neither the criteria for toxicity (T), according to the PBT criteria, in Annex XIII of REACH

In conclusion, biphenyl should not be considered as a PBT/vPvB substance.

7.12. Exposure assessment

The main focus of the Substance Evaluation of biphenyl was to clarify the concern on potential PBT properties, potential reproductive toxicity and the high aggregated tonnage for environmental exposure.

Biphenyl is manufactured and/or imported in the EU in a range of 1000 – 10,000 tonnes/year. The substance is mainly used in different industrial settings and also by professional workers as heat transfer fluid and laboratory chemical. Based on the information provided by Registrant(s) following exposure scenarios have been considered for the exposure assessment.

ES1: Manufacture
ES2: Formulation
ES3: Heat transfer fluids
ES4: Intermediate/solvent/process medium
ES5: Laboratory chemicals

Exposure scenarios have been developed on the basis of the latest version of the chapters R.12 (ECHA, 2015) and R.16 (ECHA, 2016) of the REACH Guidance on IR&CSA, the EUSES 2.1.2 programme, Specific Environmental Releases Categories (SPERC) (CEFIC, 2012; ESIG, 2018) and site-specific monitoring information when provided by Registrant(s).

The outcomes and results of this assessment have been calculated by the eMSCA considering tonnage and uses provided by the Registrant(s) in the registration dossier. Confidential information has been included in a Confidential Annex.

The exposure assessment and final RCRs were calculated by applying conditions which cover tonnage and scenarios of the registration dossiers. Only two scenarios are presented, covering all the conditions, tonnage and uses:

- Assessment 1, covering production sites with specific environmental conditions;
- Assessment 2, using generic scenarios for other uses.

For ES2, ES3, ES4 and ES5 release fraction to soil is selected from the SPERCs scenarios. Since application of the STP sludge on agricultural soils cannot be excluded for all the registrants, the agricultural soil compartment has been considered in the assessment.

In the next sections the characteristics of the five exposure scenarios considered in this assessment are summarised.

ES1 MANUFACTURE

This scenario covers, the synthesis, material transfers, cleaning, storage, waste treatment, sampling, maintenance, (un)coupling, packing of flaked biphenyl and tanker loading with liquid biphenyl.

This exposure scenario is defined based on the conditions described by the Registrant(s) and written in site-specific terms which cover the whole process of production.

Duration, frequency and volume for Manufacture (ES1) is included in the confidential annex.

Environmental surrounding characteristics

Environmental surrounding characteristics are considered only for marine water as follows:

Fresh water flow rate: - (no emission to freshwater environment)

Municipal Sewage Treatment plant discharge: 3E+03 m^3/d (specific value).

Marine water flow rate: A site specific dilution factor for discharges to a coastal zone (marine environment) of 200 is considered for the assessment.

Operational conditions

Production processes take place in closed systems with dedicated equipment.

Estimated release factors based on the SPERC ESVOC 1.1.v1 have been applied in calculations. ESVOC 1.1.v1 describes the manufacture or use as a process chemical or extraction for petroleum substances.

Wastes are considered as hazardous residues and will be treated accordingly, e.g. by means of incinerated. External treatment and disposal of waste comply with applicable local and/or national regulations.

The site-specific characteristics considered in the assessment can be consulted in the confidential annex.

Release fraction to air from process	see confidential annex
Release fraction to wastewater from process	see confidential annex
Release fraction to soil from process	see confidential annex
Fraction tonnage to region	10%
Fraction used at main source	100%

Based on the information provided by Registrant(s) regarding the consideration of waste as hazardous and incinerated, no emissions to soil are expected. No emissions to soil are considered for calculations regarding the agricultural use of the soil compartment.

Risk Management Measures

The local releases are summarized in the confidential annex.

ES2 FORMULATION

Formulation and packing of mixtures in batch or continuous operations, includes storage, materials transfers, mixing, large and small scale packing, sampling, and maintenance.

The maximum concentration of biphenyl in the final formulated products, either liquid or solid, can be consulted in the confidential annex. Duration, frequency and volume for ES2 is also included in the confidential annex.

Environmental surrounding characteristics

Site-specific environmental conditions were used when available and the following generic EU conditions have been used in calculations, for other cases:

Fresh water flow rate: 1.8E+04 m^3/d (default value)

Municipal Sewage Treatment plant discharge: 2E+03 m^3/d (default value)

Marine water flow rate: A default dilution factor for discharges to a coastal zone (marine environment) of 100 is assumed to be representative for a realistic worst case.

Operational conditions

Formulation takes place in the closed production equipment, in a continuous process.

Estimated release factors based on the SPERC ESVOC 2.2.v1 have been applied in calculations. ESVOC 2.2.v1 describes the formulation and (re)packaging of substances and mixtures for petroleum substances and petrochemicals in industrial process.

The following specific characteristics are considered based on the information regarding formulation:

Release fraction to air from process	2.5E-03
Release fraction to wastewater from process	2E-05
Release fraction to soil from process	1E-04
Fraction tonnage to region	10%
Fraction used at main source	100%

External treatment and disposal of waste comply with applicable local and/or national regulations.

Risk management Measures

There is no information on the risk management measures applied. Therefore, the calculated local emissions are provided based on the worst-case information.

Table 14. Estimated local worst-case release rates for the scenario ES2 (Formulation).

Environmental compartment	Measure	Effectivity
Risk management measures (air)	-	Local release to air (kg/d): 8E+1
Risk management measures (water)	Waste disposal according to regulations	Local release to sewage (kg/d): 3
Risk management measures		Local release to soil (kg/d): -

(soil)		

ES3 HEAT TRANSFER FLUIDS

Heat transfer fluids scenario covers the processing of the substance and its mixtures includes storage, filling, circulation, heating, materials transfers, mixing, large and small scale packing, loading, waste collection, waste incineration, and maintenance.

It was considered that major part of the total EU tonnage is formulated into heat transfer fluids. Therefore a worst-case scenario assuming the tonnage from formulation has been applied.

Duration, frequency and volume for ES3 of individual registrants can be consulted at the confidential annex.

Environmental surrounding characteristics

Site-specific environmental conditions were used when available and the following generic EU conditions have been used in calculations.

Specific site environmental conditions were used when available and the following generic EU conditions have been used in calculations, for other cases:

Environmental surrounding characteristics are considered as follows:

Fresh water flow rate: 1.8E+04 m^3/d (default value)

Municipal Sewage Treatment plant discharge: 2E+03 m^3/d (default value)

Marine water flow rate: A default dilution factor for discharges to a coastal zone (marine environment) of 100 is assumed to be representative for a realistic worst case.

Operational conditions

Release factors by SPERC ESVOC 7.13a.v1 have been applied in calculations for ES3. ESVOC 7.13a.v1 describes the environmental releases for functional fluids in industrial processes and estimates are based on the substance water solubility. Release to water is highly unlikely as heat transfer fluids are used in closed systems. Thus, exposure would only arise during filling.

The following specific characteristics are considered based on the information regarding heat transfer fluids.

Release fraction to air from process	5E-04
Release fraction to wastewater from process	3E-06
Release fraction to soil from process	5E-03
Fraction tonnage to region	10%
Fraction used at main source	100%

Risk Management Measures

There is no information on the risk management measures applied. Therefore, the calculated local emissions are provided based on the specific information applied.

Table 15. Estimated local worst-cases releases rates for the scenario ES3 (Heat transfer fluids).

Environmental compartment	Measure	Effectivity
Risk management measures (air)	-	Local release to air (kg/d): 1.67
Risk management measures (water)	Waste disposal according to regulations	Local release to sewage (kg/d): 1E-2
Risk management measures (soil)		Local release to soil (kg/d): -

ES4 INTERMEDIATE/SOLVENT/PROCESS MEDIUM

This scenario covers chemical processing of substances including filling, circulating, heating, storage, sampling, maintenance, (un)coupling, and loading.
Duration, frequency and volume for ES4 of individual registrants can be consulted at the confidential annex.

Environmental surrounding characteristics

Site-specific environmental conditions were used when available and the following generic EU conditions have been used in calculations, for other cases.

Environmental surrounding characteristics are considered as follows:

Fresh water flow rate: 1.8E+04 m^3/d (default value),

Municipal Sewage Treatment plant discharge: 2E+03 m^3/d (default value).

Marine water flow rate: A default dilution factor for discharges to a coastal zone (marine environment) of 100 is assumed to be representative for a realistic worst case.

Operational conditions

The following specific characteristics are considered based on the specific information regarding Intermediate/Solvent/process medium scenario.

Release factors by the SPERC ESVOC 6.1a.v1 have been applied for rest of uses of the ES4 (intermediate). ESVOC 6.1a.v1 describes the environmental releases for Petroleum substances and petrochemicals used as an intermediate in industrial processes.

Release fraction to air from process	1.5E-04
Release fraction to wastewater from process	3E-06
Release fraction to soil from process	1E-03
Fraction tonnage to region	10%
Fraction used at main source	100%

In this scenario environmental discharges are prevented, consistent with regulatory requirements. The use of closed production equipment, with no extraction, except when opening vessels for additions or sampling is indicated.

Risk Management Measures

There is no information on the risk management measures applied. Therefore, the calculated local emissions are provided based on the specific information applied.

Table 16 summarizes the local worst-case releases.

Table 16. Estimated local worst-case releases rates for the scenario ES4 (Intermediate/solvent/process medium).

Environmental compartment	Measure	Effectivity
Risk management measures (air)	-	Local release to air (kg/d): 1.92E-1
Risk management measures (water)	Waste disposal according to regulations	Local release to sewage (kg/d): 3.85E-3
Risk management measures (soil)		Local release to soil (kg/d):

ES5 LABORATORY CHEMICALS

This scenario covers laboratory activities including quality control and research and development in which biphenyl is used in liquid, solid or mixtures at a concentration up to 100% of biphenyl.

Duration, frequency and volume for ES5 of individual registrants is included in the confidential annex.

Environmental surrounding characteristics

Site-specific environmental conditions were used when available and the following generic EU conditions have been used in calculations, for other cases.

Environmental surrounding characteristics are considered for only marine water as follows:

Fresh water flow rate: 1.8E+04 m^3/d (default value)

Municipal Sewage Treatment plant discharge: 2E+03 m^3/d (specific value)

Marine water flow rate: A site specific dilution factor for discharges to a coastal zone (marine environment) of 200 is considered for the assessment.

Operational conditions

EUSES 2.1 release factors have been applied for calculations for ES5 (laboratory chemicals). The following specific characteristics are considered:

Release fraction to air from process	1.00E+00
Release fraction to wastewater from process	1.00E+00
Release fraction to soil from process	0.00E+00
Fraction tonnage to region	10%
Fraction used at main source	100%

Based on the information provided by Registrant(s) regarding the consideration of waste as hazardous and incinerated, no emissions to soil are expected. No emissions to soil are considered for calculations regarding the agricultural use of the soil compartment.

Risk management Measures

There is no information on the risk management measures applied. Therefore, the calculated local emissions are provided based on the specific information applied.

Table 17 summarized the local worst-case releases rates.

Table 17. Estimated local worst-case releases rates for the scenario ES5 (laboratory chemicals).

Environmental compartment	Measure	Effectivity
Risk management measures (air)	-	Local release to air (kg/d): 2
Risk management measures (water)	Waste disposal according to regulations	Local release to sewage (kg/d): 2
Risk management measures (soil)		Local release to soil (kg/d): -

7.12.1. Human health

7.12.1.1. Worker

Not assessed.

7.12.1.2. Consumer

Not assessed.

7.12.2. Environment

7.12.2.1. Aquatic compartment (incl. sediment)

In Table 18 are included the aquatic PECs calculated for ES1 (Manufacture), ES2 (Formulation), ES3 (Heat transfer fluids), ES4 (Intermediate, Solvent, Process medium) and ES5 (Laboratory chemicals) scenarios.

The Assessment 1 corresponds to the Production Sites (marine compartments and specific environmental conditions) and Assessment 2 corresponds to the rest of the uses considering a worst-case tonnage covering all the registrants under generic environmental conditions.

Table 18. PECs* for the aquatic compartment and the different scenarios considered.

	Protection target	ES1	ES2	ES3	ES4	ES5
Assessment 1	Fresh Water (mg/L)	-	-	-	-	-
	Fresh Water sediment (mg/kgwwt)	-	-	-	-	-
	Marine Water (mg/L)	*	*	*	*	*
	Marine sediment (mg/kgwwt)	*	*	*	*	*
	STP (mg/L)	*	*	*	*	*
Assessment 2	Fresh Water (mg/L)	-	4.44E-04	3.43E-05	2.05E-05	2.12E-05
	Fresh Water sediment (mg/kgwwt)	-	1.28E-02	9.76E-04	5.80E-04	6.03E-04
	Marine Water (mg/L)	-	3.65E-05	1.43E-06	4.57E-07	3.13E-07
	Marine sediment (mg/kgwwt)	-	1.26E-03	4.92E-05	5.81E-05	6.04E-05
	STP (mg/L)	-	4.45E-03	3.42E-04	2.02E-04	2.1E-04

*PECs for Manufacture are included in the confidential annex.

7.12.2.2. Terrestrial compartment

In Table 19 are included the terrestrial PECs calculated for ES2 (Formulation), ES3 (Heat transfer fluids), ES4 (Intermediate, Solvent, Process medium) and ES5 (Laboratory chemicals) scenarios.

No exposure has been considered for the local industrial soil, because it has been specified that wastes are considered as hazardous residues and managed accordingly to national legislation regarding hazardous waste or incineration, exposure to agricultural soil is unlikely. Since the application of the STP sludge on agricultural soils cannot be excluded for all the registrants, the agricultural soil compartment has been considered in the assessment.

The Assessment 1 corresponds to production sites (marine compartments and specific environmental conditions) and Assessment 2 corresponds to the rest of uses considering a worst-case tonnage covering all the Registrants under generic environmental conditions.

Table 19. PECs for the terrestrial compartment and the different scenarios considered.

	Protection target	ES1	ES2	ES3	ES4	ES5
Assessment 1	Agricultural soil (mg/kgwwt)	-	-	-	-	-
Assessment 2	Agricultural soil (mg/kgwwt)	-	1.16E-02	9.05E-04	5.14E-04	5.32E-04

7.12.2.3. Atmospheric compartment

Not assessed.

7.12.3. Combined exposure assessment

Not assessed.

7.13. Risk characterisation

In Tables 20 and 21 are presented the RCRs for the aquatic and terrestrial compartments, respectively for the scenarios assessed.

Table 20. RCRs* for the aquatic compartment and the different scenarios considered.

	Protection target	ES1	ES2	ES3	ES4	ES5
Assessment 1	Fresh Water	-	-	-	-	-
	Fresh Water sediment	-	-	-	-	-
	Marine Water	RCR <1	RCR <1	RCR <1	RCR <1	RCR <1
	Marine sediment	RCR <1	RCR <1	RCR <1	RCR <1	RCR <1
	Sewage Treatment Plant	RCR <1	RCR <1	RCR <1	RCR <1	RCR <1
Assessment 2	Fresh Water	-	1.34E-01	1.01E-02	6E-03	6.24E-03
	Fresh Water sediment	-	1.31E-01	1.01E-02	6E-03	6.24E-03
	Marine Water	-	1.31E-01	5.09E-03	6.02E-03	6.25E-03
	Marine sediment	-	1.31E-01	5.0E-03	6.02E-03	6.25E-03
	Sewage Treatment Plant	-	1.39E-03	1.07E-04	6.32E-05	6.58E-05

*RCRs values for Assessment 1 are included in the confidential annex.

Table 21. RCRs for the terrestrial compartment and the different scenarios considered.

	Protection target	ES1	ES2	ES3	ES4	ES5
Assessment 1	Agricultural soil	**-**	**-**	**-**	**-**	**-**
Assessment 2	Agricultural soil	-	1.52E-01	1.18E-02	6.71E-03	6.94E-03

In Table 22 are presented the regional RCRs estimated by the eMSCA for the relevant environmental compartments.

Table 22. Regional RCRs for the aquatic and terrestrial compartments.

Protection target	Regional
Fresh Water	1.30E-04
Fresh Water sediment	1.09E-04
Marine Water	1.36E-04
Marine sediment	7.69E-05
Agricultural soil	4.58E-06

The above detailed assessment results in RCR below 1 for local and regional environmental compartments. Therefore, the eMSCA concludes that there is no need for further actions or risk management measures to be implemented.

7.14. References

(Remark: This list doesn't include the references in the publicly available registration dossier updated on 11-Feb-2019: https://echa.europa.eu/registration-dossier/-/registered-dossier/14948/1)

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7.15. Abbreviations

B/vB	Bioaccumulative/very Bioaccumulative
BCF	Bioconcentration factor
bw	Body Weight
BOD	Biochemical oxygen demand
C&L	Classification & Labelling
CMR	Carcinogenic, Mutagenic or Toxic to Reproduction
CoRAP	Community Rolling Action Plan
dwt	dry weight
EC_{50}	Median Effective Concentration
ECHA	European Chemicals Agency
eMSCA	evaluating Member State Competent Authority
EPM	Equilibrium Partitioning Method
EOGRTS	Extended One-Generation Reproduction Toxicity Study
ERC	Environmental Release Categories
ES	Exposure Scenario
ESVOC	European Solvents Volatile Organic Compounds Committee
EUSES	European Union System for the Evaluation of Substances
GLP	Good Laboratory Practice
IR&CSA	Information Requirements and Chemical Safety Assessment
Koa	Octanol-air partition coefficient
Koc	Organic carbon normalised adsorption coefficient
Kow	Octanol / water partition coefficient
LC_{50}	Median Lethal Concentration
LOAEL	Lowest Observed Adverse Effect Level
LOEC	Lowest Observed Effect Concentration
NOAEL	No Observed Adverse Effect Level
NOEC	No Observed Effect Concentration
OECD	Organisation for Economic Co-operation and Development
P/vP	Persistent/very Persistent
PBT	Persistent, Bioaccumulative and Toxic
PEC	Predicted Environmental Concentration

PND	Postnatal Day
PNEC	Predicted No Effect Concentration
PROC	Process Categories
QSAR	Quantitative Structure–Activity Relationship
RCR	Risk Characterization Ratio
SOP	Standard Operational Procedure
SPERC	Specific Environmental Release Category
STOT RE	Specific Target Organ Toxicity - Repeated Exposure
SVHC	Substance of Very High Concern
T	Toxic
ThOD	Theoretical Oxygen Demand
EPA	United States Environmental Protection Agency
UVCB	Substances of Unknown or Variable composition, Complex reaction products or Biological materials
vPvB	very Persistent and very Bioaccumulative
WS	Water solubility
wwt	wet weight