federal public service
HEALTH, FOOD CHAIN SAFETY
AND ENVIRONMENT

SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

4,4'-(1,3-phenylene-bis(1-methylethylidene))bisphenol

EC No 428-970-4

CAS No 13595-25-0

Evaluating Member State(s): Belgium

Dated: 13 July 2016

Evaluating Member State Competent Authority

Belgian Federal Public Service Health, Food Chain Safety and Environment, Risk Management Service
Victor Horta Square 40/10
1060 Brussels
Belgium

Email: evaluation.reach@environment.belgium.be

Year of evaluation in CoRAP: 2014

The substance evaluation was terminated without requesting further information from the registrant under an Article 46(1) decision due to change in status of the registration dossier (cease manufacture in accordance with Article 50(3) of the REACH Regulation).

Further information on registered substances here:

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

DISCLAIMER

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

4,4'-(1,3-phenylene-bis(1-methylethylidene))bisphenol (Bisphenol M) was originally selected for substance evaluation in order to clarify concerns about:

- Suspected PBT/vPvB properties

- Exposure to the environment and consumer use

- Other: Possible ED properties

During the evaluation no other concerns were identified.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

NA

3. CONCLUSION OF SUBSTANCE EVALUATION

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

Table 1

CONCLUSION OF SUBSTANCE EVALUATION **Conclusions**	**Tick box**
Need for follow-up regulatory action at EU level *[if a specific regulatory action is already identified then, please, select one or more of the specific follow-up actions mentioned below]*	
Harmonised Classification and Labelling	
Identification as SVHC (authorisation)	
Restrictions	
Other EU-wide measures	
No need for regulatory follow-up action at EU level	x

After the first stage of evaluation the eMSCA concluded that further information was required to clarify the concerns regarding suspected PBT/vPvB properties, suspected ED properties and exposure for consumers/workers and the environment. A draft decision was prepared to request further data. By the end of the commenting period on the draft decision (11 June 2015) the registrant provided comments on the draft decision.

The registrant indicated his intention to withdraw the registration for this substance.
On 29 October 2015 the dossier was withdrawn and as there were no other active registrations, the substance evaluation was terminated.

The eMSCA is of the opinion that the concerns regarding suspected PBT/vPvB and ED properties remain unclarified.

4. FOLLOW-UP AT EU LEVEL

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

During the substance evaluation decision making process, the only registration has been revoked in accordance with article 50(3) of the REACH Regulation and the substance evaluation was terminated. Therefore, as there were no longer any uses within the scope of substance evaluation, the risk based concerns do not longer exist. At the time of finalising this report, there were no other active registrations.

The eMSCA is of the opinion that the concerns regarding PBT/vPvB and ED properties remain unclarified.

The eMSCA recommends that a new assessment of the PBT/vPvB properties, ED properties and the exposure data should be undertaken in the event of new registrations of 4,4'-(1,3-phenylene-bis(1-methylethylidene))bisphenol.

5.2. Other actions

Not applicable

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

4,4'-(1,3-phenylene-bis(1-methylethylidene))bisphenol was originally selected for substance evaluation in order to clarify concerns about:

- Suspected PBT/vPvB properties
- Exposure to the environment and consumer use
- Other: Possible ED properties

During the evaluation no other concerns were identified.

Table 3

EVALUATED ENDPOINTS Endpoint evaluated	Outcome/conclusion
Suspected PBT/vPvB	The eMSCA concluded that further information was required to clarify the concern regarding PBT/vPvB properties. However, due to termination of the substance evaluation process, no additional information was requested.
Exposure to the environment and consumer use	The eMSCA concluded that further information was needed to clarify this concern. However, due to termination of the substance evaluation process, no additional information was requested. Furthermore, there is no longer an active registration and therefore no longer any uses within the scope of substance evaluation.
Possible ED properties	The eMSCA concluded that further information was required to clarify the concern regarding ED properties. However, due to termination of the substance evaluation process, no additional information was requested.

7.2. Procedure

On 26 March 2014 the substance evaluation was started by the eMSCA on the basis of the registration data and public literature.

The evaluation was mostly targeted to the identification as PBT, and to the ED properties.

Limited data for human health were available, and these were also briefly evaluated.

Furthermore the exposure/use information was evaluated.

Based on the evaluation of the available data, the eMSCA concluded there was a need to request further information to clarify the concerns relating to PBT, exposure and ED

properties. The eMSCA prepared a draft decision pursuant to article 46(1) of the REACH Regulation to request further information.

On 11 May 2015 ECHA sent the draft decision to the registrant and invited him to comment by 11 June 2015. By that date ECHA received comments and forwarded them to the eMSCA.

On 29 October 2015 the status of the registration dossier for the substance was changed to 'inactive', as was indicated in the comments of the registrant.

As there were no other active registrations at that moment in time, the substance evaluation was terminated without a final decision requesting for additional information.

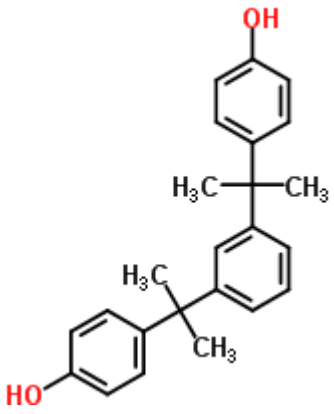
7.3. Identity of the substance

Table 4

SUBSTANCE IDENTITY	
Public name:	4,4'(1,3-phenylene-bis(1-methylethylidene))bisphenol
EC number:	428-970-4
CAS number:	13595-25-0
Index number in Annex VI of the CLP Regulation:	604-079-00-8
Molecular formula:	$C_{24}H_{26}O_2$
Molecular weight range:	346.46
Synonyms:	Bisphenol-M

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

Structural formula:



7.4. Physico-chemical properties

Table 5

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**
Physical state at 20°C and 101.3 kPa	White/off-white powder, solid
Melting/freezing point	OECD guideline 102: 136.5-138°C (at 1atm)
Boiling point	OECD guideline 103: >222°C (756 mm Hg)
Surface tension	NA (water solubility < 1mg/l at 20°C)
Vapour pressure	OECD guideline 104: 0.00059 Pa at 25°C
Water solubility	OECD guideline 105: <0.2 mg/l
Partition coefficient n-octanol/water (Log Kow)	OECD guideline 117: 4.3 (at 40°C)
Density	OECD guideline 109: 1.17

7.5. Manufacture and uses

7.5.1. Quantities

At the start of the substance evaluation process, the tonnage was reported to be 10-100 tonnes per annum. However, during the substance evaluation decision making process the registration was withdrawn in accordance with Article 50(3) of the REACH Regulation.

At the time of finalising this report, there were no active registrations for this substance.

7.5.2. Overview of uses

At the start of the substance evaluation process, the below mentioned uses were identified. However, during the substance evaluation decision making process the registration was withdrawn in accordance with Article 50(3) of the REACH Regulation.
At the time of finalising this report, there were no active registrations for this substance.

Table 6

USES	
	Use(s)
Uses as intermediate	/
Formulation	/
Uses at industrial sites	ERC 6c: Industrial use of monomers for manufacture of thermoplastics ERC 1: Manufacture of substances
Uses by professional workers	/
Consumer Uses	/

Article service life	AC 13: Plastic articles; articles used by workers

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

Index number: 604-079-00-8

H 317 : May cause an allergic skin reaction : Skin Sens. 1

H 361f: Suspected of damaging fertility of the unborn child: Repr. 2

H 411: Toxic to aquatic life with long lasting effects: Aquatic Chronic 2

7.6.2. Self-classification

- In the registration (before withdrawal)*:*

See harmonised classification

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

See harmonized classification

7.7. Environmental fate properties

7.7.1. Degradation

Hydrolysis

The study is not needed since Bisphenol M is highly insoluble in water.

Biodegradation in water:

Estimations by the evaluation member state (Biowin v4.10):

Biowin 2: 0.0282

Biowin 3: 2.1220

Biowin 6: 0.0150

A result for Biowin 2 and 6 lower than 0.5 means that the probability is low that the substance will biodegrade fast. Biowin 3 predicts the timeframe in which the substance will degrade. A result for Biowin 3 lower than 2.2 means that the substance will take months to biodegrade. The screening criteria for P defined in the R.11 REACH Guidance does only flag for 'persistency', not for 'not persistent'.

If Biowin 2 < 0.5 and Biowin 3 < 2.2 or Biowin 6 < 0.5 and Biowin 3 < 2.2 then the substance is persistent.

Therefore, on the basis of the predictions, Bisphenol M seems to be potentially persistent and further testing would be needed to confirm this.

Screening:

30.74% degradation was seen after 29 days (OECD Guideline 301B: Ready biodegradability: CO_2 evolution test) for a 10 mg OC/L sample, while 2.73% degradation was seen in the same test for a 20 mg OC/L sample.

On this basis, it was concluded in the registration dossier that Bisphenol M is inherently biodegradable.

The eMSCA however stated that such conclusion cannot be drawn from this ready biodegradability test and that further testing remains necessary since the study shows that the substance is not readily biodegradable.

Simulation test:

No data available in the registration dossier.

The registrant(s) provided a screening test as explained above. Since this test shows that Bisphenol M is not readily biodegradable, further information (simulation study) is needed to clarify whether Bisphenol M is persistent.

In addition, no information is available on possible breakdown products which can potentially be persistent (or PBT). Therefore it is necessary that not only the rate of transformation, but also the pathway of transformation is investigated.

Conclusion:
Bisphenol M is not readily biodegradable.

Further testing is needed to conclude whether the substance is persistent.

7.7.2. Environmental distribution

Adsorption/desorption:

The Log Kow for Bisphenol M was determined by the HPLC method: Log Kow = 4.3 at 40°C

The Log Koc was estimated on the basis of the Log Kow:

Log Koc = 0.827 x Log Kow + 0.292 = 3.8

Distribution modelling:

No data available in the registration dossier.

The eMSCA applied the Level III Fugacity Model (Episuite):

	Mass Amount (%)	Half life (hours)	Emissions (kg/hr)
Air	0.00087	2.84	1000
Water	1.18	1440	1000
Soil	41.9	2880	1000
Sediment	56.9	13000	0

In general, information is lacking on the environmental distribution. It seems however that Bisphenol M is mostly distributed to sediment and soil.

7.7.3. Bioaccumulation

The Log Kow for Bisphenol M was determined by the HPLC method: Log Kow = 4.3 at 40°C.

Furthermore, the eMSCA determined an estimated LogKow = 6.3 (KOWWIN v.1.68).

It is considered that the screening criterion for bioaccumulation is fulfilled if LogKow ≥ 4.5. The value of 4.3 as determined by the HPLC method is very close to the cut-off value and therefore, the eMSCA considers the substance to potentially fulfil the B criterion and further tests would be needed to conclude on this endpoint.

7.8. Environmental hazard assessment

7.8.1. Aquatic compartment (including sediment)

Acute toxicity

The acute toxicity in fish was tested according to OECD Guideline 203/EU C1 (semi-static).

96h LC50 = 3.8 mg/L

The acute toxicity to Daphnia magna was tested according to OECD Guideline 202 under static conditions. The 48 hour EC50 value was determined to be 10.6 mg/L.

An algae test according to OECD 201/EU C.3 is available showing:

72h EC50 > 100 mg/L

72h NOEC = 0.84 mg/L

Endocrine disruption

There are no data available in the registration dossier. However, the eMSCA identified a concern for the ENV due to the likely ED properties of Bisphenol M.

An initial concern regarding ED properties was identified given the substance belongs to the bisphenol family, for which there have been indications that they might have endocrine disrupting properties. Some clear indications were found in the public literature showing an estrogenic agonism of Bisphenol M. Furthermore, Bisphenol M is not readily biodegradable and might accumulate in the environment.

The eMSCA concluded that further testing is necessary based on the following triggers:

OECD QSAR toolbox result for Bisphenol M:

"Very strong binder, OH" - MW > 200 and MW =< 500 and with two non-impaired OH groups attached to two different 5 or 6 C-atoms ring

Very strong binder, OH:

Estrogen receptor binder due to two cyclic molecular structures each with a single non-impaired hydroxyl group.

Yamasaki *et al*., 2004 and Akahori *et al*., 2008 both compared the results of in vitro estrogen receptor binding assays and in vivo immature rat uterotrophic assays.

The receptor binding assay showed estrogenic activity of Bisphenol M (ER binding affinity). Based on the in vitro assay the relative binding affinity (RBA) to estrogen receptors was calculated for Bisphenol M. Bisphenol M has a LogRBA of -0.76 while the human hormone estradial (reference) has a logRBA of 2. In comparison, a logRBA of -2.26 was found for 4,4'-Sulfonyldiphenol (Bisphenol S; EC: 201-250-5) (Akahori *et al.*, 2008) and a LogRBA of -2.11 for 4,4'-isopropylidenediphenol (Bisphenol A; EC: 201-245-8) (Blair *et al.*, 2000).

It can be concluded from these reports that Bisphenol M has the highest RBA of these three bisphenol substances. Bisphenol M is considered as a moderate binder (log RBA between 0 and -2) whereas Bisphenol S and Bisphenol A are considered weak binders (log RBA < -2).

Furthermore, the uterotrophic assays in rat confirmed this estrogenic activity *in vivo:*

A significant increase in uterine weight was seen at the highest dose (50 mg/kg) (Yamasaki *et al.*, 2004).

The logLED (lowest effective dose) was 2.16 µmol/kg/day for Bisphenol M (Akahori *et al.*, 2008).

Conclusion:

Bisphenol M has a harmonised classification for the ENV as:

H 411: Toxic to aquatic life with long lasting effects: Aquatic Chronic 2

The substance is not readily biodegradable.

Log Kow ≥4

96h LC50 = 3.8 mg/L (Fish)
72h NOEC = 0.84 mg/L (Alage)

⇨ The eMSCA agrees to the harmonized classification.

Regarding the PBT concern, further information is needed to clarify whether Bisphenol M or any of its degradation products is persistent. If this is the case, then the B and T criterion are to be further evaluated.

Further information should also be requested to clarify the ED concern for the environment.

7.9. Human Health hazard assessment

The following available information was briefly evaluated by the eMSCA:

7.9.1. Toxicokinetics

No data available, while it would be useful to have data on the toxicokinetics for the following reasons:

An initial concern regarding ED properties was identified given the substance belongs to the bisphenol family, for which there have been indications that they might have endocrine disrupting properties. However, adequate toxicokinetics data are not available and would

be helpful to support the acceptability and applicability of comparison with analogous substances (read-across).

The phyisico-chemical properties of Bisphenol M are comparable to those of Bisphenol A and Bisphenol S. There are some differences in environmental distribution however: Bisphenol M is the least soluble (<0.2 mg/L) compared to 100-1000 mg/L for Bisphenol A and 1.1 g/L for Bisphenol S. Bisphenol A is more biodegradable than Bisphenol M and Bisphenol S. Moreover, Bisphenol M has a higher Log Kow (4.3) than Bisphenol S (1.6) and Bisphenol A (3.4).

Based on the structural similarity, Bisphenol M could possibly metabolise into another substance with endocrine disrupting properties (like for example Bisphenol A).

In general, an understanding of the toxicokinetics and the metabolism of bisphenol M could be usefull for its risk assessment and it could help to verify the mode of action of Bisphenol M on the metabolism and could explain any adverse effect seen in toxicological studies.

7.9.2. Acute toxicity and Corrosion/Irritation

Acute toxicity Oral

An OECD guideline 401 study is available (1986).

Mortality:

0 at 3162 mg/kg and 3976 mg/kg

3 males and 2 females our of 5 at 5000 mg/kg

3 males and 1 female out of 5 at 3288 mg/kg

LD50 males: 5465 mg/kg

LD50 females: 7443 mg/kg

Combined LD50: 6095 mg/kg

Acute toxicity Dermal

An OECD Guideline 402 (EU B.3) study is available (1997).

LD50 > 2000 mg/kg bw

Conclusion: No concern for acute toxicity identified based on the available information.

Skin irritation

An OECD Guideline 404 study is available in rabbits (1986). There was no dermal irritation response detected.

Eye irritation

An OECD guideline 405 study is available in rabbits (1986):

Animal	Corneal opacity	Iritis	Conj. redness	Chemosis

1	**1.7**	0.0	1.3	0.0
2	0.0	0.0	0.3	0.0
3	**1.0**	0.0	1.7	0.3

Based on the Corneal opacity, the substance can be classified as eye irritant (2 animals out of 3 with value ≥ 1), the evidence is however borderline and for the moment no further action was proposed.

7.9.3. Sensitisation

A study (EU Method B.6; skin) is available in guinea pig (1986).

Induction intradermal 10% showed no positive response.

The substance has a harmonised classification as Skin Sens. 1.

7.9.4. Repeated dose toxicity

A 28 day study (EU Method B.7; oral) is available in rats (1997).

No effect on body weight, but some slight modifications on hemato and biochemical parameters, but no effect on organ weight or necropsy.

Based on the available data, there was no concern identified for repeated dose toxicity.

7.9.5. Mutagenicity

In vitro data:

An OECD Guideline 473 study (chromosome aberration) is available. The results were negative.

An OECD Guideline 471 study (gene mutation) is available. The results were negative.

Based on the currently available information, no concern has been identified.

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

No data in the registration dossier, but Bisphenol M has a harmonized classification:

H 361f: Suspected of damaging fertility of the unborn child: Repr. 2

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

The substance has a harmonised classification and labelling (Index number: 604-079-00-8) for human health:

H 317 : May cause an allergic skin reaction : Skin Sens. 1

H 361f: Suspected of damaging fertility of the unborn child: Repr. 2

7.10. Assessment of endocrine disrupting (ED) properties

Publicly available data were analysed by the eMSCA.

An initial concern regarding ED properties was identified given the substance belongs to the bisphenol family, for which there have been indications that they might have endocrine disrupting properties.

OECD QSAR toolbox result for Bisphenol M:

"Very strong binder, OH" - MW > 200 and MW =< 500 and with two non-impaired OH groups attached to two different 5 or 6 C-atoms ring

Very strong binder, OH:

ER binder due to two cyclic molecular structures each with a single non-impaired hydroxyl group.

Yamasaki et al. (2004)

Yamasaki et al. (2004) performed both receptor binding assays and immature rat uterotrophic assays with 14 chemicals including Bisphenol M. For the description and the results of in vitro study see "OECD CF level 2[2]". For the description of the immature rat uterotrophic assay see "OECD CF Level3".

In an uterotrophic assay, immature 20-day-old female rats were subcutaneously injected with individual test chemicals once daily for 3 consecutive days. Estrogenic activity of the test chemicals was examined based on the absolute and relative uterine weight after necropsy. In similar treatments, ethinyl estradiol in olive oil was also subcutaneously injected into the back of the rats at a dose of 0.6 µg/kg per day for three consecutive days after administration of the test substance. A vehicle control group was injected with olive oil alone, and a positive control group was injected with ethinyl estradiol after administration of olive oil. A group injected with the estrogen antagonist chemical tamoxifen at a dose of 1 mg/kg per day plus ethinyl estradiol was also established to confirm the reliability of the study.

Bisphenol M was administered at doses of 2, 10, and 50 mg/kg. An apparent estrogenic effect was observed by increased absolute and relative uterine weight at 50 mg/kg. In the treatments with ethinyl estradiol administered after Bisphenol M, the low Bisphenol M treatment (2 mg/kg) showed significantly lower absolute and relative uterine weight compared to the vehicle control, whereas at the higher treatments no significant effects were observed.

In the human estrogen receptor binding assay, chemicals were tested over the $1E^{-11}$ to $1E^{-04}$ M concentration range and added to the test solution together with 17β-estradiol. The percent ratio (B/B0 (%)) of standard ligand (17β-estradiol) bound to the receptor was calculated from the radioactivities of the solutions with and without the test substance, subtracting the radioactivity due to nonspecifically bound standard ligand to the receptor. The B/B0 values as a function of the concentration were fit to the logistic equation and the fifty percent inhibitory value (IC50) of each chemical was calculated by the least-squares

[2] OECD Conceptual Framework for Testing and Assessment of Endocrine Disrupting Chemicals as included in the OECD Guidance Document No. 150

method using computer software. The binding abilities of test chemicals to the receptor were evaluated by relative binding affinity (RBA), ratio of IC50 values to 17β-estradiol.

The logRBA of Bisphenol M was -0.76 (relative to 17β-estradiol), which confirms that Bisphenol M has an estrogen activity.

The outcome of this assays was in agreement with that of the immature uterotrophic assay and indicated that Bisphenol M has an estrogen activity.

Akahori *et al*, 2008

The data provided in Akahori *et al*., 2008 seem to be a reassessment of the data from Yamasaki *et al*., 2004:

In a comparative study with 65 chemicals the relationship between the results of in vitro binding assay to human estrogen receptor α and in vivo immature rat uterotrophic assay was examined.

For the receptor binding assay, the recombinant human hERα ligand binding domain fused with gluthathione-S-transferase was expressed in E.Coli. Chemicals were tested between concentrations of 10^{-11} and 10^{-4}M. The relative binding affinity (RBA) was calculated as

$$RBA = \frac{(IC50 \text{ for } E2) \times 100}{(IC50 \text{ Bisphenol M})}$$

To evaluate estrogenic activity in the uterotrophic assay, immature non-ovariectomised 19-day old female rats were injected subcutaneous into their back with Bisphenol M for three consecutive days (4ml/kg/day). Three doses were used (6 rats/group), the highest dose set as maximum tolerance dose based on results of a range-finding test. The limit dose was 1000mg/kg/day.
Anti-estrogen activity was evaluated by using 17α-ethynylestradiol (0.6µg/kg/day) co-administered with Bisphenol M. The vehicle control group treated with olive oil and the positive control group for estrogen activity (0.6µg/kg/day 1717α-ethynylestradiol) were concurrently run. The positive control group for anti-estrogenicity was treated with 1mg/kg/day of tamoxifen co-administrated with 0.6µg/kg/day 17α-ethynylestradiol.
Estrogenic activity was indicated when uterine weights were significantly increased, anti-estrogen activity when uterine weights were significantly decreased. The lowest dose showing a statistically significant effect (The lowest effective dose LED, µmol/kg/day) was used as a quantitative parameter.

Log RBA of Bisphenol M was -0.76 (RBA=0.17%), compared to log RBA of 2.00 (RBA = 100) for 17β estradiol. In comparison, a logRBA of -2.26 was found for 4,4'-Sulfonyldiphenol (Bisphenol S; EC: 201-250-5) (Akahori *et al.*, 2008) and a LogRBA of -2.11 for 4,4'-isopropylidenediphenol (Bisphenol A; EC: 201-245-8) (Blair *et al.,* 2000).

Estrogenic and anti-estrogenic response was demonstrated for Bisphenol M. Log LED for estrogen activity was 2.16 µmol/kg/day (compared to <-2.43 µmol/kg/day for 17βestradiol, Padilla-Banks *et al*, 2001) and 0.76 µmol/kg/day for anti-estrogen activity.

7.11. PBT and VPVB assessment

Persistence

The substance is not readily biodegradable. Further testing would be needed to confirm whether the definite P criterion is fulfilled.

Bioaccumulation

The LogKow determined by the HPLC method is 4.3

The LogKow determined by KOWWIN v.1.68 is 6.3

Based on both results it can be concluded that more information would be needed to determine whether the B criterion is fulfilled for Bisphenol M .

Toxicity assessment

The T criterion is fulfilled since the substance has a harmonised classification as Repr.Cat.2.

Conclusion

The screening criteria for P and B can be considered fulfilled. Further tests would be needed to confirm whether the definite P and B criteria are fulfilled.

The T criterion is fulfilled since the substance has a harmonised classification as Repr. Cat. 2.

7.12. Exposure assessment

During the substance evaluation decision making process, the only registration has been revoked in accordance with article 50(3) of the REACH Regulation and the substance evaluation was terminated. Therefore, as there were no longer any uses within the scope of substance evaluation, the risk based concerns do not longer exist. At the time of finalising this report, there were no other active registrations.

7.13. Risk characterisation

During the substance evaluation decision making process, the only registration has been revoked in accordance with article 50(3) of the REACH Regulation and the substance evaluation was terminated. Therefore, as there were no longer any uses within the scope of substance evaluation, the risk based concerns do not longer exist. At the time of finalising this report, there were no other active registrations.

7.14. References

Akahori Y, Nakai M, Yamasaki K, Takatsuki M, Shimohigashi Y, Ohtaki M. Relationship between the results of in vitro receptor binding assay to human estrogen receptor alpha and in vivo uterotrophic assay: comparative study with 65 selected chemicals.Toxicol In Vitro. (2008), 22(1):225-31

Blair RM, Fang H, Branham WS, Hass BS, Dial SL, Moland CL, Tong W, Shi L, Perkins R, and Sheehan DM. 1999. The estrogen receptor relative binding affinities of 188 natural and xenochemicals: structural diversity of ligands. Toxicological sciences 54: 138-153

Yamasaki K, Noda S, Imatanaka N, Yakabe Y. Comparative study of the uterotrophic potency of 14 chemicals in a uterotrophic assay and their receptor-binding affinity. Toxicol Lett. (2004), 146(2):111-20.

7.15. Abbreviations

eMSCA: Evaluating Member State Competent Authority

ED: Endocrine disruptor

PBT: Persistence, Bioaccumulation and Toxicity

QSAR: Quantitative Structure Activity Relationship