federal public service
HEALTH, FOOD CHAIN SAFETY AND ENVIRONMENT

SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

Mono-and/or di-and/or tri(1-phenylethyl)-m-cresol and p-cresol

EC No 700-427-9

CAS No NA

Evaluating Member State: Belgium

Dated: 30 September 2015

Evaluating Member State Competent Authority

Belgian Federal Public Service Health, Food Chain Safety and Environment, Risk Management Service
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Year of evaluation in CoRAP: 2013

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

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

Mono-and/or di-and/or tri(1-phenylethyl)-m-cresol and p-cresol was originally selected for substance evaluation in order to clarify concerns about:

- Suspected PBT/vPvB properties

- Wide dispersive use and consumer use

During the evaluation also other concerns were identified. The additional concerns were:

- Inconsistencies regarding some of the physico-chemical properties

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

The dossier was updated following the testing proposal evaluation (TPE) final decision (TPE-D-0000001585-71-05/F) which was issued on 24-10-2011.

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 Belgian Competent Authority (BE CA) concluded that further information was required to clarify the concerns regarding suspected PBT/vPvB properties, exposure for consumers and the environment and inconsistencies regarding some physico-chemical properties. A draft decision was prepared to request further data. By the end of the commenting period on the draft decision (5 June 2014) the registrant provided comments on the draft decision.
During the decision-making process the BE CA noted that the status of the registration dossier for the substance was changed to 'inactive'.
On 28 July 2015 ECHA sent a 'Request for clarification' letter to the registrant who was given the opportunity to consider whether they intended to cease manufacture according to Art. 50(3) or to indicate that they did not intend to cease manufacture. As the

registrant did not communciate anything different within the provided deadline, the registration has been revoked.
As there were no other active registrations, the substance evaluation was terminated.

The BE CA is of the opinion that the concerns regarding suspected PBT/vPvB properties and physico-chemical 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 BE CA is of the opinion that the concerns regarding PBT/vPvB and physico-chemical properties remain unclarified.

The BE CA recommends that a new assessment of the PBT/vPvB properties, the physico-chemical data and the exposure data should be undertaken in the event of new registrations of Mono-and/or di-and/or tri(1-phenylethyl)-m-cresol and p-cresol.

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

Mono-and/or di-and/or tri(1-phenylethyl)-m-cresol and p-cresol was originally selected for substance evaluation in order to clarify concerns about:

- Suspected PBT/vPvB properties

- Wide dispersive use and consumer use

During the evaluation also other concerns were identified. The additional concerns were:

- Inconsistencies regarding some of the physico-chemical properties

Table 4

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Suspected PBT/vPvB	The BE CA 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.
Wide dispersive use and consumer use	The BE CA 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.
Inconsistencies regarding physico-chemical properties	The BE CA concluded that further information was required to clarify the concern regarding inconsistencies for physico-chemical properties. However, due to termination of the substance evaluation process, no additional information was requested.

7.2. Procedure

On 20 March 2013 the substance evaluation was started by the BE CA.

The evaluation was mostly targeted to the P, B and T properties, but also the relevant physico-chemical properties were looked at in detail.

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 evaluating MSCA concluded there was a need to request further information to clarify the concerns relating to PBT, exposure

and physico-chemical properties. The BE CA prepared a draft decision pursuant to article 46(1) of the REACH Regulation to request further information.

On 5 May 2014 ECHA sent the draft decision to the registrant and invited him to comment by 5 June 2014. By that date ECHA received comments and forwarded them to the BE CA.

During the decision-making process the status of the registration dossier for the substance was changed to 'inactive'.

On 28 July 2015 ECHA sent a 'Request for clarification' letter to the registrant who was given the opportunity to consider whether they intended to cease manufacture according to Art. 50(3) of the REACH Regulation or to indicate that they did not intend to cease manufacture. As the registrant did not comment on this letter within the provided deadline, the registration has been revoked.

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

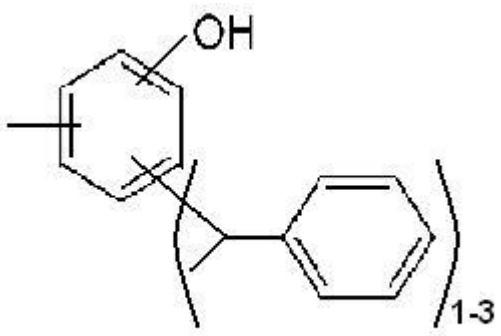
7.3. Identity of the substance

Table 5

SUBSTANCE IDENTITY	
Public name:	Mono- and/or di- and/or tri(1-phenylethyl)-m-cresol and p-cresol
EC number:	700-427-9
CAS number:	NA
Index number in Annex VI of the CLP Regulation:	NA
Molecular formula:	CnHn+1O; n=15, 23 or 31
Molecular weight range:	>=212.0 and <=421.0
Synonyms:	Atlen SK

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

Structural formula:



Multiconstituent/UVCB substance/others

Table 6

Constituent **Constituents**	**Typical concentration**	**Concentration range**	**Remarks**
Di(1-phenylethyl)-m-cresol and p-cresol	confidential	confidential	/
Tri(1-phenylethyl)-m-cresol and p-cresol	confidential	confidential	/
Mono(1-phenylethyl)-m-cresol and p-cresol	confidential	confidential	/
Benzenesulfonic acid, 4-C10-13-sec-alkyl derivs. EC: 287-494-3	confidential	confidential	/
Styrene EC: 202-851-5	confidential	confidential	/

The BE CA indicates that in total, 24 possible constituents could be identified in mono- and/or di- and/or tri(1-phenylethyl)-m-cresol and p-cresol:

Di-constituents group (C_{23} H_{24} O)

6 m-cresols:

2,4-di-pe-3-cresol: Oc1c(C(C)c2ccccc2)c(C)c(C(C)c3ccccc3)cc1

2,5-di-pe-3-cresol: Oc1c(C(C)c2ccccc2)c(C)cc(C(C)c3ccccc3)c1

2,6-di-pe-3-cresol: Oc1c(C(C)c2ccccc2)c(C)ccc1(C(C)c3ccccc3)

4,5-di-pe-3-cresol: Oc1cc(C)c(C(C)c2ccccc2)c(C(C)c3ccccc3)c1

4,6-di-pe-3-cresol: Oc1cc(C)c(C(C)c2ccccc2)cc1(C(C)c3ccccc3)

5,6-di-pe-3-cresol: Oc1cc(C)cc(C(C)c2ccccc2)c1(C(C)c3ccccc3)

4 p-cresols:

2,3-di-pe-4-cresol: Oc1c(C(C)c2ccccc2)c(C(C)c3ccccc3)c(C)cc1

2,5-di-pe-4-cresol: Oc1c(C(C)c2ccccc2)cc(C) c(C(C)c3ccccc3)c1

2,6-di-pe-4-cresol: Oc1c(C(C)c2ccccc2)cc(C)cc1(C(C)c3ccccc3)

3,5-di-pe-4-cresol: Oc1cc(C(C)c2ccccc2)c(C)c(C(C)c3ccccc3)c1

Tri-constituents group (C_{31} H_{32} O)

4 m-cresols:

2,4,5-tri-pe-3-cresol:
Oc1c(C(C)c2ccccc2)c(C)c(C(C)c3ccccc3)c(C(C)c4ccccc4)c1

2,4,6-tri-pe-3-cresol:
Oc1c(C(C)c2ccccc2)c(C)c(C(C)c3ccccc3)cc1(C(C)c4ccccc4)

2,5,6-tri-pe-3-cresol:
Oc1c(C(C)c2ccccc2)c(C)cc(C(C)c3ccccc3)c1(C(C)c4ccccc4)

4,5,6-tri-pe-3-cresol:
Oc1cc(C)c(C(C)c2ccccc2)c(C(C)c3ccccc3)c1(C(C)c4ccccc4)

2 p-cresols:

2,3,5-tri-pe-4-cresol:
Oc1c(C(C)c2ccccc2)c(C(C)c3ccccc3)c(C)c(C(C)c4ccccc4)c1

2,3,6-tri-pe-4-cresol:
Oc1c(C(C)c2ccccc2)c(C(C)c3ccccc3)c(C)cc1(C(C)c4ccccc4)

Mono-constituents group (C_{15} H_{16} O)

4 m-cresols :

2-pe-3-cresol	Oc1c(C(C)c2ccccc2)c(C)ccc1
4-pe-3-cresol	Oc1cc(C)c(C(C)c2ccccc2)cc1
5-pe-3-cresol	Oc1cc(C)cc(C(C)c2ccccc2)c1
6-pe-3-cresol	Oc1cc(C)ccc1(C(C)c2ccccc2)

2 p-cresols :

2-pe-4-cresol	Oc1c(C(C)c2ccccc2)cc(C)cc1
3-pe-4-cresol	Oc1cc(C(C)c2ccccc2)c(C)cc1

The BE CA (as clarified further in the document) noted a high similarity in properties within the mono-, di and tri cresol constituent groups. However, between these different constituent groups significant differences in properties were noted (based on preliminary QSAR data).

7.4. Physico-chemical properties

Table 7

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**
Physical state at 20°C and 101.3 kPa	Atlen SK is a (homogeneous), transparent and brown liquid of honey like consistency and characteristic odour
Vapour pressure	1.22 hPa at 20°C extrapolated from measured vapour pressure at 70 and 80°C
Water solubility	Experimentally measured 0.0103 g/L at pH 7 (20°C) 0.0153 g/L at pH 4 (20°C) 0.0167 g/L at pH 10 (20°C)
Partition coefficient n-octanol/water (Log Kow)	Experimentally measured LogPow is 4.45 at 20°C
Dissociation constant	10.04 – 12.00 (SPARC calculation)
Viscosity	584676 mPa.s (20°C, dynamic)

The BE CA identified the following concerns regarding the vapour pressure, water solubility and partition coefficient n-octanol/water:

Vapour pressure:

The vapour pressure of 1.22 hPa at 20°C was extrapolated from two measured vapour pressures, at 70°C and 80°C (difficulties in testing due to high viscosity).

The BE CA noted that vapour pressures of other cresol-type substances indicate significant increase of vapour pressure with temperature.

The BE CA estimated vapour pressure values with EPIWIN which are at least 3 orders of magnitude lower than 1.22 hPa:

Compound	Antoine Method (Pa)	Modified Grain Method (Pa)	Mackay Method (Pa)
Mono-1-phenylethyl cresols	0.00123	0.00224	0.0148
Di-1-phenylethyl cresols	9.50E-08	1.11E-07	1.46E-05
Tri-1-phenylethyl cresols	8.93E-13	3.57E-10	1.03E-08
m-cresol	24.3	20.3	64.3
p-cresol	19.9	16.6	51.3
Styrene	730	618	887

No information was provided on the constituent inducing the experimentally measured vapour pressure. It is likely that the vapour pressure of the individual mono/di/tri-1-phenylethyl-m/p-cresols is much lower than the reported vapour pressure of 122 Pa (at 20 °C) for the UVCB substance.

Therefore, it is considered that no reliable information on the vapour pressure of the substance (or its constituants) is available while this information is needed to reliably evaluate the fate in the environment.

Water solubility

In the registration data, the shake flask method was used to experimentally determine the water solubility of the UVCB substance. The water solubility was determined at 3 pH levels:

The solubility at pH 4 is 15.3 mg/l

The solubility at pH 7 is 10.3 mg/l

The solubility at pH 10 is 16.7 mg/l

The test results however are difficult to interpret because it is unclear which molecules/constituents have been detected in the water.

The BE CA determined water solubility with QSAR estimations (EPISuite):

Compound	WSKow v1.42 (mg/l)	WATERNT v1.01 (mg/l)
Mono-1-phenylethyl cresols	35.98	16.45
Di-1-phenylethyl cresols	0.13-0.72	0.013
Tri-1-phenylehtyl cresols	0.00045-0.0024	9.26E-6

WSKow accepts experimental logKow and melting point values and its accuracy greatly improves if an experimental melting point (MP) is entered. In this case no experimental data on the melting point nor for logKow were available for the individual constituents. The Kow was estimated by the Kowwin QSAR and no MP was entered. WATERNT is a fragment-based method and like all fragment-based methods the accuracy of its estimates is influenced by the relative number of fragments covered by the model. In this case, the identified fragments were: -CH3, -CH, aromatic C (C-H type), -OH and an aromatic carbon (C-substituent type). These fragments represent quite well the fragments of the different mono/di/tri-1-phenylethyl-m/p-cresols. Therefore, preference is given to the results obtained from WATERNT compared to WSKOW.

According to the QSAR results, the mono-1-phenylethyl cresols are slightly soluble in water (16.45-35.98 mg/l) while the water solubility is significantly lower for the tri-1-phenylethyl cresols (9.26E-6 – 0.0024 mg/l). The reported solubility from the experimental test with the UVCB was ca. 0.0103 g/l. The solubility found during the test could thus mainly be explained by the solubility of the most soluble constituent, i.e. the mono-1-phenylethyl constituent group or other impurities.

Therefore, it is considered that no reliable information on the water solubility of the substance (or its constituants) is available while this information is needed to reliably evaluate the fate in the environment.

Partition coefficient n-octanol/water

The log Kow value presented in the registration data is 4.45. This value was estimated using the solubilities of the test substance in pure solvents which were determined during HPLC analysis.

The BE CA determined LogKow values with EPIWIN estimations.

Estimated Log Kow values (EPISuite):

Compound	LogKow
Mono-1-phenylethyl cresols	4.22
Di-1-phenylethyl cresols	5.52-6.37
Tri-1-phenylehtyl cresols	7.68-8.53

It is considered that the Log Kow values for the di- and tri- constituents are likely to be higher than 4.45, but no information was provided on the individual Log Kow values.

Information on the Log Kow values of the various constituents is however needed to reliably evaluate the fate of the substance in the environment.

7.5. Manufacture and uses

7.5.1. Quantities

At the start of the substance evaluation process, the tonnage was reported to be 100-1000 tonnes per annum. However, during the substance evaluation decision making process the registration was revoked 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 revoked 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 9

USES Use(s)	
Uses as intermediate	
Formulation	PROCs 1, 2, 3, 4 and 8b
Uses at industrial sites	Manufacture of rubber products with subsequent service life PROCs 5, 6, 8b, 9, 14 and 21
Uses by professional workers	
Consumer Uses	Consumer indoor and outdoor use of rubber products (also

	waste disposal)
Article service life	Rubber articles (worker and consumer use)

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

Not applicable

7.6.2. Self-classification

- In the registration (before revocation)*:*

Skin Sens. 1; H317: May cause an allergic skin reaction

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

NA

7.7. Environmental fate properties

7.7.1. Degradation

Hydrolysis

There are no available experimental data, but the substance is not expected to undergo hydrolysis in the environment due to a lack of hydrolysable functional groups in its structure.

Biodegradation in water:

BE CA determined the following values through QSAR estimations:

Biowin results for the different constituent groups based on EPISuite (US EPA, 2012a)

Compound	Biowin 2	Biowin 3	Biowin 6
Mono-1-phenylethyl cresols	0.9793	2.6587	0.1730
Di-1-phenylethyl cresols	0.9915	2.3757	0.0217
Tri-1-phenylethyl cresols	0.9965	2.0927	0.0023

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 biodegradation will take

months. The screening criteria for P defined in the R.11 REACH Guidance 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 potentially persistent.

Screening criteria test according to table R.11-2 (R.11 REACH Guidance)

Compound	Biowin 2 < 0.5 and Biowing 3 < 2.2	Biowing 6 < 0.5 and Biowing 3 < 2.2	Persistent?
Mono-1-phenylethyl cresols	No	No	Unknown
Di-1-phenylethyl cresols	No	No	Unknown
Tri-1-phenylethyl cresols	No	Yes	Yes

In the registration dossier an OECD 301B guideline study (CO_2 evolution) was used to determine the ready biodegradability of the substance. The test showed that the substance is not readily biodegradable after direct addition and ultrasonification (7% degradation in 28 days). On the contrary, when the substance was first dissolved in acetone (to increase bioavailability), it was found to be readily biodegradable. The BE CA however does not consider this last result to be reliable since acetone itself also biodegrades and some unexplained inconsistencies in the study report were detected regarding the solvent.

The BE CA does not agree with the conclusion in the registration dossier that the substance is readily biodegradable and noted that based on the available QSAR data and the available result from the screening test without solvent, the screening criterion for P is fulfilled (at least for 1 constituents group). There were no simulation tests available.

The BE CA is of the opinion that the concern for persistency remains, since no additional information was requested to clarify the concern due to the termination of the substance evaluation decision making process.

The BE CA also concluded that it is most likely that the various constituents (mono, di or tri) would show divergent biodegradation rates.

7.7.2. Environmental distribution

In the registration dossier, the adsorption/desorption study was waived.

The BE CA applied KOCWIN v2.00:

Compound	Log Koc estimate from MCI	Log Koc estimate from Log Kow estimate
Mono-1-phenylethyl cresols (2-pe-3-cresol)	4.5164	3.4262

Di-1-phenylethyl cresols (2,4-di-pe-3-cresol)	6.5462	4.6154
Tri-1-phenylethyl cresols (2,4,5-tri-pe-3-cresol)	8.5761	5.8101

BE CA is of the opinion that more information on adsorption/desorption is needed to reliably evaluate the distribution of the various constituents in the environment since no additional information was requested to clarify the concern due to the termination of the substance evaluation decision making process.

No data were available on the distribution of the substance in the environment.

The BE CA applied the Level III Fugacity Model (Episuite) on a tri-constituent:

	Mass amount (%)	Half-life (hr)	Emissions (kg/hr)
Air	0.0116	1.24	1000
Water	1.32	1.44E+003	1000
Soil	30.2	2.88E+003	1000
Sediment	68.5	1.3E+004	0

The BE CA applied the Level III Fugacity Model (EPISuite) on a di-constituent:

	Mass amount (%)	Half-life (hr)	Emissions (kg/hr)
Air	0.0226	1.84	1000
Water	2.03	900	1000
Soil	31.2	1800	1000
Sediment	66.8	8100	0

7.7.3. Bioaccumulation

BE CA notes that the LogKow is 4.45 (for Mono- and/or di- and/or tri(1-phenylethyl)-m-cresol and p-cresol) and that exposure to the environment is likely due to its applications (use in rubber articles).

Based on QSAR data, the Log Kow values for the di and tri constituents are likely to be higher than 4.45.

The reported BCF value was calculated on the basis of the octanol/water partition coefficient using bilinear equation proposed by Kubinyi (BCF = 1767).

The BE CA is of the opinion that the concern regarding bioaccumulation remains since no additional information was requested to clarify the concern due to the termination of the substance evaluation decision making process.

The BE CA also concluded that it is most likely that the various constituents (mono, bis or tris) would show divergent bioaccumulation potential.

7.8. Environmental hazard assessment

7.8.1. Aquatic compartment (including sediment)

A WAF 96h LC50 of >100 mg/l or a 96h LC50 of >0.001 mg/l was obtained for fish using static exposure conditions according to EU Method C.1. (Acute Toxicity Fish). In the acute fish test 0% mortality was observed in the tested loading of 100 mg/l.

A WAF 48h EC50 of >100 mg/l or a 48h EC50 of >0.001 mg/l was obtained for invertebrates using static exposure condictions according to EU Method C.2 (Acute Toxicity Daphnia). In the acute Daphnia test 0% immobilisation was observed in the tested loading of 100 mg/l.

A WAF 72h EC50 of >100 mg/l was obtained for algae using static exposure conditions according to EU method C.3 (Algal Inhibition Test). The algae test also resulted in a NOEL ≥ 100 mg/l.

The BE CA noted that the toxicity of some constituents could be higher and should hence be further investigated.

No experimental acute or chronic toxicity data are available for the individual constituents of the substance. The following assessment of the T-criterion by the BE CA is therefore based on data obtained from QSARs.

The following QSARs have been applied by the BE CA in order to assess the aquatic acute/chronic toxicity to freshwater species:

- TEST (Toxicity Estimation Software Tool; US EPA, 2012)
- ECOSAR (Ecological Structure Activity Relationships; US EPA 2012)
- VEGA using EPA, version 1.0.6 and DEMETRA version 1.0.3-DEV

TEST searches for similar chemicals in the training set. Such chemicals are available for Mono-and/or di-and/or tri(1-phenylethyl)-m-cresol and p-cresol substance (similarity above 0.5), which means that it falls into the Applicability Domain (AD) of the QSAR.

The substance was divided in 3 constituent groups with similar physico-chemical properties, e.g. water solubility and log Kow. The compounds are grouped as follows:

- Group 1: mono-1-phenylethyl cresol constituent group characterized by log Kow of 4.22 and water solubility of 35.98 mg/l (according to ECOSAR)
- Group 2: di-1-phenylethyl cresol constituent group characterized by log Kow of 5.52-6.37 and water solubility of 0.1347-0.7164 mg/l (according to ECOSAR)
- Group 3: Tri-1-phenylethyl cresol constituent group characterized by log Kow of 7.68-8.53 and water solubility of 0.002391-0.0004494 mg/l (according to ECOSAR)

According to ECOSAR, the different constituent groups are linked to both the chemical class of the "phenols" and "neutral organics".

A summary of predicted acute toxicity data is presented hereunder. The different QSARs predict the acute toxicity of the different compounds as follows (in decreasing order): tri-1-phenylethyl compounds > di-1-phenylethyl compounds > mono-1-phenylethyl compounds.

The QSAR predictions using TEST, ECOSAR and VEGA for acute aquatic toxicity indicate that group 3 (tris-1-phenylethyl compounds) and group 2 (bis-1-phenylethyl compounds) fulfill the screening criteria for T, i.e. L(E)C50 < 0.1 mg/L.

Acute toxicity to freshwater organisms of the different groups using QSARs

QSAR	Group	Toxicity (L(E)C50 (mg/l))			Acute criterion? <0.1 mg/l
		Fish	Daphnia	Algae	
TEST	1	1.18-2.5	0.26-0.55	/	N
	2	0.033-0.13	0.00394-0.00894	/	Y
	3	0.0059-0.0318	0.0031-0.00637	/	Y
ECOSAR (phenols)	1	0.761	0.615	2.281	N
	2	0.026-0.115	0.055-0.167	0.165*-0.544	Y
	3	0.000794*-0.004*	0.004*-0.013*	0.011*-0.035*	Y
ECOSAR (neutral organics)	1	1.78	1.434	1.347	N
	2	0.031-0.178	0.037-0.184	0.035-0.174	Y
	3	0.000471*-0.003*	0.000861*-0.004*	0.000829*-0.004*	Y
VEGA (EPA)	1	1.22-1.65**	1.61-2.04**	/	N
	2	0.04-0.05***	0.21-0.31**	/	Y
	3	0****	0.03-0.04****	/	Y
VEGA (DEMETRA)	1	/	0.66-0.87****	/	N
	2	/	0.13-0.22****	/	N
	3	/	0.05-	/	Y

			0.06****		

*: toxicity values are above water solubility and should therefore be carefully considered
**: data of moderate quality and should therefore be carefully considered
***: data of moderate/low quality and should therefore be very carefully considered
****: data of low quality and should therefore be very carefully considered

Chronic toxicity

ECOSAR predicts the chronic toxicity of the different compounds as follows (in decreasing order): tri-1-phenylethyl compounds > di-1-phenylethyl compounds > mono-1-phenylethyl compounds.

The QSAR predictions using ECOSAR for chronic aquatic toxicity indicate that group 3 (tri-1-phenylethyl compounds) and group 2 (di-1-phenylethyl compounds) fulfill the screening criteria for T, i.e. NOEC < 0.01 mg/L.

Table: Chronic toxicity to freshwater organisms of the different groups using QSARs

QSAR	Group	Toxicity (mg/l) ChV			Chronic criterion? (<0.01 mg/l)
		Fish	Daphnia	Algae	
TEST		/	/	/	/
ECOSAR (phenols)	1	0.106	0.117	1.042	N
	2	0.005-0.019	0.01**-0.032	0.073-0.245	Y
	3	0.000208-0.000815	0.000824*-0.003*	0.005*-0.015*	Y
ECOSAR (neutral organics)	1	0.222	0.214	0.890	N
	2	0.005-0.026	0.008-0.034	0.066-0.216	Y
	3	0.0000938-0.000496	0.000255-0.0011	0.004*-0.014*	Y

*: toxicity values are above water solubility and should therefore be carefully considered
**: the chronic NOEC value is expected to be lower than the ChV of 0.01 mg/L

BE CA Conclusion:

According to the above QSAR results, the long-term no-observed effect concentrations (NOEC) for the tri-1-phenylethyl compounds and di-1-phenylethyl compounds are less than 0.01 mg/L, indicating that these constituents of Mono- and/or di- and/or tri(1-phenylethyl)-m-cresol and p-cresol fulfill the toxicity screening criterion T.

The QSAR results cannot provide us with a final conclusion regarding the aquatic toxicity of the substance or its constituents, but it provides sufficient indications that further investigation on the tri-1-phenylethyl compounds and the di-1-phenylethyl compounds is needed.

The BE CA is of the opinion that the concern for environmental toxicity remains since no additional information was requested to clarify the concern due to the Registrant's cease of manufacture and the consequent termination of the substance evaluation decision making process.

The BE CA also concluded that it is most likely that the various constituents (mono, di or tri) would show a divergent environmental toxicity potential.

7.9. Human Health hazard assessment

The following available information was briefly evaluated by the BE CA:

7.9.1. Toxicokinetics

The substance is expected to undergo dermal and oral/GI absorption and to exhibit high bioaccumulation potential.

7.9.2. Acute toxicity and Corrosion/Irritation

Oral LD50 > 2000 mg/kg

Dermal LD50 > 2000 mg/kg

The substance didn't induce eye irritation.

BE CA concluded that the available data show no concern for skin or eye irritation.

7.9.3. Sensitisation

EC_3 = 1,75% => LOAEL = 4375 µg/cm^2

The substance is self-classified as:

Skin Sens 1; H317: May cause an allergic skin reaction

BE CA agrees with the proposed self-classification

7.9.4. Repeated dose toxicity

Oral 28 day repeated dose toxicity study: NOAEL ≥ 300 mg/kg bw/day

Dermal 28 day repeated dose toxicity: NOAEL = 1000 mg/kg

BE CA concluded that the available data show no concern for repeated dose toxicity.

7.9.5. Mutagenicity

In vitro data:

Mammalian chromosome aberration: all results are negative

Bacterial reverse mutation assay: all results are negative

Mammalian cell gene mutation assay: all results are negative

BE CA concluded that the available data show no concern for mutagenicity

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

Fertility

An OECD 421 screening study dermal route is available: NOAEL (P and F1) = 1000 mg/kg.

Developmental toxicity

An OECD 414 pre-natal developmental toxicity study is available.

NOAEL (teratogenicity) = 1000 mg/kg

NOAEL (embryo-foetal toxicity) = 300 mg/kg

NOAEL (maternal) = 550 mg/kg

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

The BE CA agreed with the proposed self-classification of the registrant based on the currently available information:

Skin Sens 1; H317: May cause an allergic skin reaction

7.10. Assessment of endocrine disrupting (ED) properties

Not evaluated.

7.11. PBT and VPVB assessment

The guidance on PBT assessment states that:

The process of assessing multi-constituent substances and UVCB substances is made up of several stages, including identification of the main constituents (10-80% of the substance) and significant impurities (in the range 0.1 – 10% of the substance). It also involves gathering available data, relating these to the P, B and T properties of constituents and impurities and, where necessary, generating new information.

Based on QSAR generated data, it is expected that the tri-1-phenylethyl cresols are more likely to be PBT than the di-1-phenylehtyl cresols and the mono-1-phenylethyl cresols.

Benzenesulfonic acid, 4-C10-13-sec-alkyl derivs. and styrene are probably not PBT.

Overall conclusion

QSAR results were generated by the BE CA.

The table underneath reports the different QSAR estimated parameters. The BE CA concluded that the mono-1-phenylethyl cresols are the most soluble in water and that water solubility is lower for the other two groups. The estimated vapour pressure for the different groups is very low. We can conclude that the main constituents of the UVCB are

not volatile. The log K_{ow} increases with the increase of phenylethyl groups attached on the cresol.

	Mono-1-phenylethyl cresols	**Di-1-phenylethyl cresols**	**Tri-1-phenylethyl cresols**
Water solubility QSAR (mg/l)	16.45	0.013	9.26E-6
Vapour pressure QSAR (Pa)	0.00224	1.11E-07	3.57E-10
Log Kow QSAR	4.22	5.52-6.37	7.68-8.53
Persistent QSAR screening	Unknown	Unknown	Yes
Bioaccumulation QSAR screening	No	Probably	Probably
Toxic QSAR screening	Unknown	Yes	Yes
Screening PBT	**No**	**Potentially**	**Likely**

According to the QSAR results, an increasing PBT probability with increasing phenylethyl groups attached on the cresols is detected. The mono-1-phenylethyl cresols can be excluded from further PBT testing. The di- and tri-1-phenylethyl cresols should be further investigated for their PBT properties, but also their behavior in the environment will need some further clarification.

During the substance evaluation process however, the status of the registration for Mono- and/or di- and/or tri(1-phenylethyl)-m-cresol and p-cresol was changed such that the registration was revoked. As there were no other registrants of the substance at that time, there was subsequently no valid registration. Therefore, the substance evaluation decision making process was terminated and no further information was requested. The identified concerns therefore remain unresolved.

7.12. Exposure assessment

After a preliminary assessment the BE CA identified the need for some clarifications regarding the use of certain values deviating from the defaults, both for consumer exposure and exposure to the environment.

The registrant responded to the original requests in his response to the draft decision (dated 5 June 2014) and indicated that he had updated the dossier with the provided information.

During the substance evaluation process however the status of the registration for Mono- and/or di- and/or tri(1-phenylethyl)-m-cresol and p-cresol was changed as the registration was revoked. The provided information was not further evaluated and as there were no other registrants of the substance at that time, there was subsequently no valid registration. Therefore, the substance evaluation decision making process was terminated and no further information was requested.

7.13. Risk characterisation

Not evaluated.

7.14. References

Information from the registration dossier.

7.15. Abbreviations

AC: Article Category

BCF: Bioconcentration Factor

BE CA: Belgian Competent Authority

ChV: Chronic Value

CSA: Chemical Safety Assessment

CSR: Chemical Safety Report

EC: Effect Concentration

ERC: Environmental Release Category

LD: Lethal Dose

NOAEL: No Observed Adverse Effect Level

NOEC: No Observed Adverse Effect Concentration

PBT: Persistent, Bioaccumulative and Toxic

PROC: Process Category

QSAR: Quantitative Structure-Activity Relationship

REACH: Registration, Evaluation, Authorisation and Restriction of Chemicals

UVCB substances: Substances of Unknown or Variable Composition, Complex reaction products or Biological materials)

VP: Vapour pressure

WAF: Water Accommodated Fraction