SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

tert-butyl perbenzoate

EC No 210-382-2

CAS No 614-45-9

Evaluating Member State: Italy

Dated: 2 October 2020

Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: 2013

Before concluding the substance evaluation a Decision to request further information was issued on: 14 August 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

Tert-butyl perbenzoate was originally selected for substance evaluation in order to clarify concerns about:

- Skin sensitisation
- Consumer use
- Wide dispersive use

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

- Org. Perox. C
- Acute inhalation toxicity
- Skin irritation
- Genotoxicity
- Pre-natal developmental toxicity
- Human exposure assessment and risk characterisation with potential human risk via the environment

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Testing Proposal final decision (Decision number: TPE-D-0000002332-85-05/F). Information available here:

https://echa.europa.eu/it/information-on-chemicals/dossier-evaluation-status

3. CONCLUSION OF SUBSTANCE EVALUATION

Table 1

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

4. FOLLOW-UP AT EU LEVEL

On the basis of the available information, an harmonised classification of the substance is envisaged by evaluating MSCA (eMSCA), as a follow-up at EU level with the following hazard category: Org. Perox. C H242: Heating may cause a fire, Acute Tox. 4, H332: Harmful if inhaled, Skin Irrit. 2, H315: Causes skin irritation and Skin Sens. 1 H317: May cause an allergic skin reaction.

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

Not applicable.

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

A harmonized classification of the substance is envisaged as a follow-up at EU level for indicated human health.

Table 2

FOLLOW-UP		
Follow-up action	**Date for intention**	**Actor**
Annex XV dossier for Classification	---	---

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

Tert-butyl perbenzoate was originally selected for substance evaluation in order to clarify concerns about:

- Skin sensitisation
- Exposure/Wide dispersive use
- Consumer use

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

- Org. Perox. C
- Acute inhalation toxicity
- Skin irritation
- Genotoxicity
- Pre-natal developmental toxicity
- Human exposure assessment and risk characterisation with potential human risk via the environment

The Substance evaluation started on March 2013.

Table 3

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Acute toxicity inhalation route	The LD50 for the acute inhalation end-point in the evaluated study is 1.01<LD50≤4.9 ml/L. The converted acute toxicity point estimate (ATE) is 1.5 mg/L. A harmonised C&L process for the classification of the substance (being a mist)

	in Cat. 4 for acute inhalation toxicity is warranted.
Skin irritation	On the basis of the skin irritation study evaluated, a harmonised C&L process for the classification of the substance as Skin irritatant Cat 2 is warranted.
Skin Sensitiser	On the basis of the skin sensitisation studies evaluated a harmonised C&L process for the classification of the substance as Skin Sens. Cat 1 in warranted.
Exposure/Wide dispersive use	Exposure for workers has been correctly addressed in the CSR. However, Risk Management Measures should be differentiated according to the risk band selected for each PROC.
Genotoxicity/mutagenicity	During the substance evaluation, eMSCA raised the concern for genotoxicity at the site of contact. In order to clarify the concern, an *in vivo* comet assay was requested to the Registrant(s). The study was provided and inconclusive results were reported in the assay. In order to conclude on the genotoxicity of the test item it would be necessary an *in vivo* comet assay performed at a lower dose range. However the eMSCA considers the request of a new *in vivo* assay unadvisable because such study could be not sufficient to resolve the issue also in view of animal welfare considerations. Therefore, eMSCA concludes that further information for this end point is not needed.
Pre-natal developmental toxicity	During the substance evaluation, eMSCA raised the concern for pre-natal developmental toxicity and requested a new study in a second specie. The study was provided and negative results were reported in the assay. eMSCA concludes that further information for this end point is not needed.
Human exposure assessment and risk characterisation with potential human risk via the environment	Human exposure, via the environment, is unlikely.

7.2. Procedure

The Substance evaluation of the tert-butyl perbenzoate started on March 2013. The initial grounds for concern were relating to: skin sensitisation, exposure/wide dispersive use and consumer use. In the course of the evaluation, the eMSCA noted additional concern regarding acute toxicity (inhalation route), skin irritation, genotoxicity, pre-natal developmental toxicity, human exposure assessment and risk characterisation with potential human risk via the environment.
The eMSCA considered that no further information was required to clarify the concern for skin sensitisation. The eMSCA considered that further information was required to clarify the other abovementioned concerns.
Following an evaluation of the Substance pursuant to Article 45(4), the eMSCA concluded that further information was required in order to assess the concerns identified. The eMSCA prepared a Draft Decision pursuant to Article 46(1) which was submitted to the Agency on 20 March 2014.

On 28 May 2015, the MSC reached unanimous agreement by written procedure on the Draft Decision. ECHA took the decision pursuant to Article 51(3) of the REACH Regulation and sent the decision to the Registrant(s) on 14 August 2015.
On 13 November 2015, the Registrant(s) filed an appeal. However, the Registrant(s)' appeal was dismissed in its entirety. The board of appeal decided that the information requested in the Contested Decision must be submitted to ECHA by 20 March 2019.
Subsequently the Registrant(s) provided the requested information in the updated dossier.

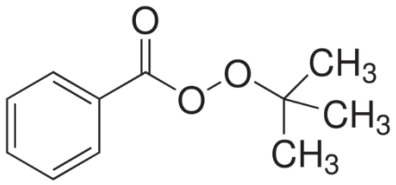
7.3. Identity of the substance

Table 4

SUBSTANCE IDENTITY	
Public name:	tert-butyl perbenzoate
EC number:	210-382-2
CAS number:	614-45-9
Index number in Annex VI of the CLP Regulation:	---
Molecular formula:	C11H14O3
Molecular weight range:	
Synonyms:	Peroxybenzoic acid, tert-butyl ester tert-butyl benzenecarboperoxoate 2-Methyl-2-propanyl benzenecarboperoxoate Benzenecarboperoxoic acid, 1,1-dimethylethyl ester

Type of substance ☒ 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	tert-butyl perbenzoate is a colourless to slightly yellow organic liquid with a mild aromatic odour.
Vapour pressure	0.003 Pa at 20°C
Water solubility	1180mg/L

Partition coefficient n-octanol/water (Log Kow)	log Pow = 3.0 at 25 °C
Flammability	Data waiving: the study does not need to be conducted because the experience in production or handling shows that the substance does not react with water, e.g. the substance is manufactured with water or washed with water.
Explosive properties	Data waiving.
Oxidising properties	Data waiving: the study does not need to be conducted for organic peroxides.
Granulometry	Data waiving: the study does not need to be conducted because the substance is marketed or used in a non-solid or granular form.
Stability in organic solvents and identity of relevant degradation products	Data waiving: the study does not need to be conducted because the stability of the substance is not considered to be critical.
Dissociation constant	Data waiving: the study does not need to be conducted because the substance has no ionic structure.

7.5. Manufacture and uses

7.5.1. Quantities

Table 6

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

This substance is used in formulation or re-packing, at industrial sites and in manufacturing.

Table 7

USES Use(s)	
Uses as intermediate	--
Formulation	This substance is used in polymers. Release to the environment of this substance can occur from industrial use: formulation of mixtures and formulation in materials.
Uses at industrial sites	This substance is used for the manufacture of plastic products and rubber products.

	Release to the environment of this substance can occur from industrial use as processing aid and as processing aid.
Uses by professional workers	--
Consumer Uses	--
Article service life	--

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

The substance is not currently listed on Annex VI of CLP Regulation ((EC) No 1272/2008).

7.6.2. Self-classification

- In the registration(s):

Org. Perox. C	H242: Heating may cause a fire
Acute Tox. 4	H332: Harmful if inhaled
Skin Irrit. 2	H315: Causes skin irritation
Skin Sens. 1	H317: May cause an allergic skin reaction
Aquatic Acute 1	H400: Very toxic to aquatic life
Aquatic Chronic 3	H412: Harmful to aquatic life with long lasting effects

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

Org. Perox. A	H240
Org. Perox. B	H241
Org. Perox. D	H242
Org. Perox. F	H242
Aquatic Chronic 2	H411
Flam. Liq. 1	H224
Ox. Liq. 2	H272
STOT SE 3	H335 Inhalation

7.7. Environmental fate properties

Hydrolysis of tert-butyl perbenzoate occurs rapidly at 25°C at pH 9 but the rate reduces with pH. In a ready biodegradation test 70% biodegradation has been observed in an OECD 301D test within 28d fulfilling the window criterion for the Closed Bottle Test. Based on these results, the substance is considered as readily biodegradable. Concerning bioaccumulation of the substance, the partition coefficient octanol water (log value) of 3 indicates that the substance has low potential to bioaccumulate.

7.7.1. Degradation

Concerning abiotic degradation, hydrolysis of tert-butyl perbenzoate in water, performed according to OECD Guideline 111, occurs rapidly at 25°C at pH 9 (DT50=1.6 days) but the rate reduces with pH. At pH 7 DT50 is 40.5 days and at pH 4 approximately 80 days (Elsner, 2010).
Regarding biotic degradation, four studies are available. In the key study, performed according to OECD 301D Guideline (unpublished study report, 2011), a total

biodegradation of 70% within 28 days was reached (60% of degradation was achieved in a period of 11d). The 10 day window can be increased to 14 days for the Closed Bottle test and this criterion has therefore been fulfilled. Other two closed bottle tests were performed (unpublished study reports, 1989 and 2010) with the following results: 72% within 28 days and 60% of degradation was achieved in a period of 22d, and 70% within 28d (where ca. 60% of degradation was achieved within of 14d). Moreover, it is available a MITI test for which insufficient information was available on the methodology used.
The Registrant(s) concluded that the substance is readily biodegradable and based on the available information, the eMSCA can support this conclusion.
Concerning water, sediment and soil simulation tests the Registrant(s) proposed a data waiving. Based on the available information, the eMSCA does not see any concern for these compartments.

7.7.2. Environmental distribution

No experimental studies investigating the adsorption/desorption behaviour of tert-butyl perbenzoate are available. The Registrant(s) proposed a data waiving with the following justification: *According to Column 2 of REACH Annex VIII, the study does not need to be conducted because the substance is expected to have a low potential for adsorption (Log Kow less than or equal to 3) and both the substance and its degradation products decompose rapidly (readily biodegradable meeting the 10 day window).* However, log Koc values of 2.294 and 2.378 were calculated using KOCWIN Program (v2.00), based on log Kow and on the molecular conductivity index (MCI), respectively. Since the validity of the model for this substance is unknown a reliability of 4 was assigned to this study.
A value of Henry's Law Constant equal to 20.8 Pa m^3/mol at 25 °C was estimated by calculation using the software SRC HENRYWIN (EPISUITE, EPA 2011). Since the validity of the model for this substance is unknown a reliability of 4 was assigned to this study. Based on the available information, the eMSCA can support the Registrant(s) conclusion that no testing on this endpoint is necessary for purpose of this substance evaluation.

7.7.3. Bioaccumulation

No experimental studies with tert-butyl perbenzoate evaluating the bioaccumulation potential of the substance are available. The Registrant(s) proposed a data waiving with the following justification: *According to Column 2 of REACH Annex VIII, the study does not need to be conducted because the substance is expected to have a low potential for adsorption (Log Kow less than or equal to 3) and both the substance and its degradation products decompose rapidly (readily biodegradable).* However, an estimated BCF value of 37.5 L/kg (regression-based method) was reported using BCFBAF Program (v3.01), based on estimated log Kow of 2.89 (reliability 4).
The Registrant(s) concluded that based on the measured log Kow of 3.0 tert-butyl perbenzoate does not bioaccumulate easily. The eMSCA can support this conclusion.

7.8. Environmental hazard assessment

7.8.1. Aquatic compartment (including sediment)

Three acute endpoints for three trophic levels are available. Two chronic endpoints for two trophic levels are available (*Daphnia* and algae). eMSCA noted that the updated information are appropriate to refine the aquatic toxicity.

7.8.1.1. Fish

Concerning short-term toxicity, two experimental studies were provided by the Registrant(s): a key study (Armin Peither 2009a) with reliability 1, semi-static on *Brachydanio rerio* and a supporting study (U.Mark,I.J.B. Meuwsen, 1989) with reliability 3, semi-static on Poecilia reticulata, both according to OECD 203 and EU Method C.1.

No long-term toxicity to fish is provided although foreseen in a testing proposal . Indeed, the Decision number: TPE-D-0000002332-85-05/F allowed to apply the testing Strategy i.e: if, based on the *Daphnia* long-term result and an AF=50, the refined PEC/PNEC is below 1, a long-term fish testing is not necessary.
Therefore, as explained below in the Section: "PNEC derivation and other hazard conclusions" according to eMSCA, the refined $PNEC_{freshwater}$ could be based on the new *Daphnia* long-term result, without the need of vertebrate long-term toxicity studies.

7.8.1.2 Aquatic invertebrates

One experimental study was provided by the Registrant(s): a key study (Dr.Armin Peither, 2009b) with reliability 2, static on *Daphnia magna* performed according to OECD Guideline 202 (*Daphnia* sp. Acute Immobilisation Test) and EU Method C.2 (Acute Toxicity for *Daphnia*).
The Registrant(s) concluded the substance is not acutely toxic to *Daphnia*, and based on the available information, the eMSCA can support this conclusion.
Regarding long-term toxicity, Registrant(s) updated the CSR as foreseen in a testing proposal (Decision number: TPE-D-0000002332-85-05/F), indicating that chronic testing was necessary to verify assumptions made in deriving the aquatic PNEC.
Based on the available information, the eMSCA can support the revised conclusion.

7.8.1.3. Algae and aquatic plants

Two studies on algae are available. One study on *Pseudokirchneriella subcapitata* (previous names: *Raphidocelis subcapitata*, *Selenastrum capricornutum*) performed according to OECD Guideline 201 (Alga, Growth Inhibition Test) [before 23 March 2006]; according to EU Method C.3 (Algal Inhibition test). It was under GLP with measured concentrations of the parent compound (Peither Armin 2009).
The second study is based on nominal concentrations and it is just a supporting study for the conclusion that the ErC50 was higher than that based on measured concentrations.
Based on the available information eMSCA can support the Registrant(s) conclusion that no toxicity testing on this endpoint is necessary for purpose of this substance evaluation.

7.8.1.4. Sediment organisms

For this endpoint, the Registrant(s) provided a data waiving claiming that the toxicity studies on sediment organisms are not needed taking into account that the registered substance easily dissolves in water, has a low log Kow and is readily biodegradable. Therefore, a strong binding to sediment is not expected.
Evidence provided in the registration dossier, including environmental fate properties and exposure pattern of this substance supports that distribution into sediment compartment and exposure to sediment organisms can be considered unlikely.
Based on the outcome of CSA, eMSCA can support the Registrant(s)' conclusion that no toxicity testing on this endpoint is necessary for purpose of this substance evaluation.

7.8.1.5. Other aquatic organisms

Not relevant for this evaluation.

7.8.2. Terrestrial compartment

The Registrant(s) provided a data waiving for toxicity on all three terrestrial taxonomic groups (soil macro-organisms, soil micro-organisms and terrestrial plants) with a justification based on environmental fate properties and exposure considerations, in accordance with Annex IX and X of REACH.

Based on the evidence presented within the registration dossier, exposure to soil compartment is unlikely to occur and therefore no toxicity testing on soil organisms is needed for purpose of this substance evaluation.
Following the assessment of available data provided by the Registrant(s), eMSCA can support the conclusions on this endpoint as well as the EPM-based assessment used for hazard to soil organisms.

Toxicity to soil macro-organisms

The registration dossier does not contain data for this endpoint. In accordance with Annex IX and X of REACH, the Registrant(s) have waived toxicity testing to terrestrial macro-organisms claiming that exposure to soil compartment is unlikely to occur and no toxicity testing on soil macro-organisms is needed.
Following the assessment of available data, eMSCA can support the Registrant(s)' conclusion that no concern for soil macro-organisms can be expected and therefore no toxicity testing on this endpoint is necessary under this substance evaluation.

Toxicity to terrestrial plants

The Registrant(s) provided a data waiving on this endpoint with justification that soil exposure is unlikely and further toxicity data on terrestrial plants are not needed in accordance with Annex IX and X of REACH.
Based on outcome of CSA, eMSCA can conclude that there is no indication of concern for effects to terrestrial plants, supporting the assessment of this endpoint.

Toxicity to soil micro-organisms

The registration dossier does not contain data for this endpoint. In accordance with REACH Annex IX, the Registrant(s) have waived toxicity testing on effects on soil microorganisms, claiming environmental fate properties and exposure considerations.
Available data from registration dossier indicate that exposure to soil compartment is unlikely to occur and therefore no toxicity testing on this endpoint is necessary under this substance evaluation.
Following the assessment of available data, eMSCA can conclude that there is no indication of concern for effects to soil microorganisms.

7.8.3. Microbiological activity in sewage treatment systems

For this endpoint, the Registrant(s) provided an activated sludge respiration inhibition test performed according to the OECD 209 and the EEC Method C.11 Guidelines. The test can be regarded as reliable and GLP compliant with relevant information reported and all validity criteria fulfilled.
The test results, a EC50 of 43 mg/L and a EC10 of 6 mg/L, were used for purpose of CSA.
Therefore, eMSCA considers that the data provided by the Registrant(s) are reliable and suitable for addressing the assessment on this endpoint and no further information is necessary under this substance evaluation.

7.8.4. PNEC derivation and other hazard conclusions

Table 8

PNEC DERIVATION AND OTHER HAZARD CONCLUSIONS		
Hazard assessment conclusion for the environment compartment	**Hazard conclusion**	**Remarks/Justification**
Freshwater	PNEC aqua (freshwater): 8.8 µg/L Intermittent releases: 8µg/L	Assessment factor: 50 Three acute endpoints for three trophic levels are available. Two chronic endpoints for two trophic levels are available (Daphnia and algae). The lowest value of 72h-EC10 =0.44 mg/L for algae with an assessment factor of 50 is used for deriving the PNEC (see eMSCA comments below).
Marine water	PNEC aqua (marine water): 0.88µg/L	Assessment factor: 500 PNEC aqua (marine water) Three acute endpoints for three trophic levels are available. Two chronic endpoints for two trophic levels are available, (*Daphnia* and algae). The lowest value of 72h-EC10 of 0.44 mg/L for algae with an assessment factor of 500 (because two long-term endpoints are available) is used for deriving the PNEC (see below comment).
Sediments (freshwater)	PNEC sediment (freshwater): 0.24mg/kg sediment dry weight	Extrapolation method: equilibrium partitioning method PNEC sediment (freshwater) In the absence of experimental toxicity data on sediment organisms, the PNEC is calculated using the equilibrium partitioning coefficient method with the default values and an estimated Koc value of 239 L/kg. eMSCA can support these hazard assessment conclusions and no remarks are to be reported.
Sediments (marine water)	PNEC sediment (marine water): 0.024mg/kg sediment dry weight	Extrapolation method: equilibrium partitioning method PNEC sediment (marine water)

		In the absence of experimental toxicity data on sediment organisms, the PNEC is calculated using the equilibrium partitioning coefficient method with the default values and an estimated Koc value of 239 L/kg. eMSCA can support these hazard assessment conclusions and no remarks are to be reported.
Sewage treatment plant	PNEC STP: 0.6mg/L	Assessment factor:10 Extrapolation method: assessment factor PNEC STP was derived using the EC10 value from toxicity study on STP aquatic microorganisms, with an AF of 10. eMSCA can support these hazard assessment conclusions and no remarks are to be reported.
Soil	PNEC soil: 0.043mg/kg soil dry weight	Extrapolation method: equilibrium partitioning method PNEC soil In the absence of experimental toxicity data on soil organisms, the PNEC soil is calculated using the equilibrium partitioning coefficient method with the default values and an estimated Koc value of 239 L/kg. eMSCA can support these hazard assessment conclusions and no remarks are to be reported.

eMSCA agrees with Registrant(s) that AF should be 50 for the freshwater compartment. However, according to information available, eMSCA notes that one species is not substantially more sensitive, therefore $PNEC_{freshwater}$ results could be based on the refinement strategy foreseen in Figure R.7.8—4. *Decision scheme for the conclusion on chemical safety assessment (PNEC)* of the ECHA guidance (Guidance on Information Requirements and Chemical Safety Assessment Chapter R.7b: Endpoint specific guidance. Indeed, according to the guidance, in principle a long-term toxicity test on fish should be performed, but, if a value from long-term toxicity testing on *Daphnia sp*. according to OECD 211 are available (as in this updated case), it can be used directly for the refinement of the PNEC value. If, based on the *Daphnia* long-term result and an AF=50, the refined PEC/PNEC is below 1, a long-term fish testing is not necessary.
Therefore, according to eMSCA, the refined $PNEC_{freshwater}$ could be based on the new *Daphnia* long-term result (21-dEC10=0.49 mg/L), instead of to the algae result (72h-EC10

= 0.44 mg/L). The resulting $PNEC_{freshwater}$ could be 9,8 µg/L (slighly lower than that proposed by Registrant(s)).
For the intermittent releases to water, the assessment factor used for is in line with the provisions of ECHA Guidance R10.
Due to the above arguments, eMSCA agrees also on the assessment factor of 500 used for the PNEC marine water.
In conclusion, eMSCA considers that aquatic compartment is not of concern.

7.8.5. Conclusions for classification and labelling

Three acute endpoints for three different trophic levels are available. The lowest ErC50 is found for algae and is 0.8 mg/L. Two chronic endpoints for two trophic levels are available, (*Daphnia* and algae). The lowest value is an ErC10 = 0.44 mg/L. The substance is self-classified as Aquatic Acute 1, H400 as well as Aquatic Chronic 3, H412, based on the acute and chronic algae endpoint, respectively. The substance is readily biodegradable and has a log Kow < 4, therefore eMSCA agrees for classifying the substance as Aquatic Acute 1, H400 M-factors of 1, as well as Aquatic Chronic 3 as reported by the Registrant(s).

7.9. Human Health hazard assessment

7.9.1. Toxicokinetics

The following data from the National Toxicology Program (NTP, 1992) for tert-butyl perbenzoate have been submitted by the Registrant(s) and have been taken into account during the evaluation of toxicokinetic.
In vitro studies conducted by the NTP showed that concentrations of 1.1, 0.11, and 0.011 mg/ml degraded by 0, 31, and 74%, respectively, in 1 hour at 37°C in a suspension of stomach contents. The substance is extremely rapidly degraded in rat and human blood. These experiments resulted in half lives of 4 mg/L to be 10.4 and 4.0 minutes, respectively. When incubated with microsomal or soluble enzyme preparations from rat liver less than 1% of the parent substance remained after 15 minutes. Degradation is extremely rapid also in contact with liver enzymes. Incubation with glutathione showed that tert-butyl perbenzoate solutions of 0.011, 0.11, and 1.1 mg/ml in HEPES buffer, pH 7.4, containing 5 mM glutathione, were degraded by 22, 18, and 10% in 15 minutes, respectively. These results are indicative that the substance, once absorbed in the body, has a short half-life.
Dermal studies determined that approximately 16% of dermal doses of tert-butyl perbenzoate administered to rats was absorbed and rapidly eliminated without tissue accumulation.
Tert-butyl perbenzoate given intravenously was rapidly degraded and eliminated, primarily in urine, with no apparent accumulation in any tissue.
The toxicity of tert-butyl perbenzoate, is limited to the site of contact. This can be seen in the results from oral repeated dose studies where effects on the stomach were observed.
Tert-butyl perbenzoate would not be expected to gain access to the systemic circulation of humans.
Benzoic acid and t-butanol made up 93% of the major degradation and/or metabolic products. As supporting data the OECD ToolBox (4.2) was also run and the results are in line with the in vivo findings. Next to benzoic acid and t-butanol, 7 additional metabolites are predicted.
The degradation products of tert-butyl perbenzoate, which are t-butanol and benzoic acid, are likely to be absorbed into the systemic circulation, but they are relatively nontoxic. Both t-butanol and benzoic acid have been the subjects of other studies and they do not appear to produce other (chronic) toxicity.
Value used for CSA:
Bioaccumulation potential: no bioaccumulation potential
Absorption rate - oral (%): 100
Absorption rate - dermal (%): 20
Absorption rate - inhalation (%): 100
The eMSCA supports this conclusion.

7.9.2. Acute toxicity and Corrosion/Irritation

The following data for tert-butyl perbenzoate have been submitted by the Registrant(s) and have been taken into account during the evaluation of toxicokinetic.

7.9.2.1 Acute toxicity oral

In a test conducted according to OECD guideline 423 on rats the LD50 for tert-butyl perbenzoate after oral exposure via gavage was > 2000 mg/kg bw.
The eMSCA supports this conclusion.

7.9.2.2 Acute toxicity dermal

In a test conducted according to OECD guideline 402 on rats the LD50 for tert-butyl perbenzoate after dermal exposure was >2000 mg/kg bw.
The eMSCA supports this conclusion.

7.9.2.3 Acute toxicity inhalation

In a study conducted on rats according to OECD Guideline 436 two groups of three male and three female albino rats were exposed by nose-only, flow-past inhalation for four hours to the test item at a chemically determined mean concentration of 4.9 and 1.01 mg/L air, group 1 and group 2 respectively. All surviving animals were observed for clinical signs and mortality during the inhalation exposure and the observation period of 14 days. Body weights were recorded prior to exposure on test day 1, and during the observation period on test days 2, 4, 8 and 15 before necropsy.
On day 15 all surviving animals were sacrificed and necropsied. The ranges of aerosol concentration, temperature, relative humidity, oxygen content and airflow rate measured during the exposure were considered to be satisfactory for a study of this type. In addition, the test item was considered to be respirable to rats as mist.
Group 1: One male and one female were found dead on day 2 of the observation period after exposure at 4.9 mg/L air. The remaining two males were found dead on day 3. One female was found dead on day 11. The remaining female was killed for humane reasons on day 15. At 4.9 mg/L air salivation was recorded during up to immediately after exposure in all animals. Decreased activity, ruffled fur and labored breathing were observed in all animals after exposure on day 1 and day 2. These signs persisted partly up to day 6. Decreased activity, hunched posture, ruffled fur and tachypnea were seen from day 13 until necropsy in this female. Marked effects on body weights were recorded in all animals.
Group 2: All animals survived the scheduled observation period at 1.01 mg/L air. Salivation was recorded during and/or immediately after exposure in all animals. Decreased activity was recorded in all males 1 hour after exposure end. Ruffled fur and effects on breathing were recorded in most of the animals on days 1 and 2. There were no clinical signs from day 3 onwards. Effects on body weights were recorded in all animals. There were no macroscopic findings in groups 1 and 2 that were considered to be related to treatment with the test item. In conclusion, the LC50 of tert-butyl perbenzoate obtained in this study was estimated to be between 1.01 and 4.9 mg/L air (chemically determined mean aerosol concentration). There was no indication of relevant sex-related differences in toxicity of the test item. Due to this LC50 range ($1.01 < LD50 \leq 5.0$) the converted acute toxicity point estimate (ATE) is 1.5 mg/L: according to Table 3.1.2 of the CLP Regulation, tert-butyl perbenzoate is to be classified in category 4 for acute toxicity inhalation route (dusts or mists) .
The eMSCA supports this conclusion.

7.9.2.4 Skin irritation

In a study conducted on rats according to OECD Guideline 404 with deviations, six male, young adult New Zealand White albino rabbits, were treated on the intact skin and on the

abraded skin (occlusive application). The abrasions were minor incisions of the stratum corneum, but not sufficiently deep to disturb the derma or to produce bleeding. An amount of 0.5 mL of the undiluted test substance was brought onto the intact and the abraded skin under a surgical patch. The patches were fixed to the application site by means of adhesive tape and the entire trunk of each rabbit was wrapped with an impervious material to maintain the test patches in position and to retard evaporation of the test substance. After an exposure period of 4 hours the patches and the test material applied were removed and the resulting skin reactions were evaluated by the method of Draize et al. Further readings were made after 28, 52 and 76 hours.
The test substance generally caused well-defined or moderate erythema and very slight to slight ischemia (necrosis) in all (six) rabbits. In addition, slight scaliness and very slight incrustation was observed in a limited number of animals. The reactions of the abraded skin were slightly more pronounced than those of the intact skin, but all reactions were considered to be reversible.
On the basis of the study, Registrant(s) stated that the substance is to be classified as Skin irritant Cat 2.
The eMSCA supports this conclusion.

7.9.2.4 Eye irritation

In the three studies submitted by the Registrant(s) no effects of eye irritation was elicitated on the animal tested (albino rabbit). The substance is not to be classified for eye irritation.
The eMSCA supports this conclusion.

7.9.3. Sensitisation

Two studies submitted by the Registrant(s) have been evaluated.
In a first study conducted in 1984 on the registered substance on guinea pig tert-butyl perbenzoate, was evaluated for skin sensitisation in 30 guinea pigs (15 males; 15 females) by the modified technique of Buehler (1965). The results of this study suggest that tert-butyl perbenzoate does not have the potential to be a dermal sensitiser in guinea pigs. Based on the information provided in this study, eMSCA supports the Registrant(s)' conclusion.
In a second study conducted on mice in 2010 according to OECD Guideline 429, tert-butyl perbenzoate dissolved in dimethylformamide was assessed for contact allergenic potential. A local lymph node assay (LLNA) was performed using test item concentrations of 25, 50, and 100%. The animals did not show any signs of systemic toxicity during the course of the study and cases of mortality were not observed. 24 after the first and second application and 1 hour after the second and third application all animal of the mid dose (50%) showed slight redness of the ear skin and all animals of the high dose (100%) showed swollen ears. All animals of the high dose (100%) also showed slight redness of the ear skin 24 hours after the second and 1 hour after the third application. However, these local signs of irritation resolved until the day of preparation (day 6). Animals treated with a concentration of 25% did not show any local signs of irritation during the course of the study. In this study Stimulation Indices (S.I.) of 20.04, 28.16, and 32.77 were determined with the test item at concentrations of 25, 50, and 100%, respectively. The test item tert-butyl perbenzoate was found to be a skin sensitiser.
eMSCA supports this conclusion.
However, the available information does not allow calculation of an EC3 value required to determine the sub-categorisation. Although the substance was clearly positive at a high concentration of 25% (with S.I: of 20.04), it cannot be excluded that also at a concentration of 2% or lower the SI will be 3 (possibly warranting a sub-categorisation as Skin Sens. 1A). Therefore the eMSCA points out that, despite the fact that the substance is of high potency, there is not sufficient data for sub-categorisation and for the substance a classification as Skin Sens. Cat 1 is warranted.

7.9.4. Repeated dose toxicity

Several studies (NTP, 1992) have been submitted by the Registrant(s) on repeated dose toxicity oral route on rats and mice.

Studies on rats

Results of 14-day toxicity study with 5 animals of each sex of F344 rats administered at 0, 70, 140, 278, 556, 1112 mg per kg body weight in corn oil, by gavage were the follows. Toxicity in rats, attributable to tert-butyl perbenzoate, was largely limited to increased stomach weights in males receiving the highest dose.
No deaths occurred among control rats, or among rats that received tert-butyl perbenzoate. Food consumption by dosed males and females was comparable to or slightly higher than that of the control groups. Body-weight gains of all treated male rats, except those in the high dose tert-butyl perbenzoate group, were greater than those of the control group. However, the low weight gain of the control group of male rats may account for these findings. Female rats receiving the highest dose of tert-butyl perbenzoate gained less weight than controls, but the difference was not statistically significant. No treatment related gross lesions were observed in rats at the end of the studies. At study termination, liver weights of female rats receiving 556 and 278 mg/kg tert-butyl perbenzoate were higher by as much as 20%, than those of controls; both these groups, and females in the high dose group (1112 mg/kg), had higher mean liver-to-body-weight ratios. Thymus weights and thymus-to-body-weight ratios of female rats in the highest dose tert-butyl perbenzoate group were about 20% lower than controls. Stomach was considered a possible target tissue for tert-butyl perbenzoate administrated by gavage, but only increases in absolute and relative stomach weight (25%) were seen in male rats receiving the highest dose. Other variations in organ weight observed in male and female rats appeared neither remarkable nor dose related Histopatological examination revealed no lesions that were considered related to administration of tert-butyl perbenzoate.

Results of 13-weeks toxicity study with 10 animals of each sex of F344 rats administered at doses 0, 30, 60, 125, 250, 500 mg t-butyl perbenzoate per kg body weight in deionised water by gavage were as follows.
All treated and control male rats survived to the end of the study. One female in the 250 mg/kg group died during week 5; a control in the female study was removed because it was missexed. Food consumption was similar in all groups of the treated and control animals except in high dose female rats, whose food consumption was about 7% less than controls. Body-weight gains of male and female rats in the highest dose groups were depressed after about week 7.
A variety of clinical observations were noted in both male and female rats during the course of the study, but none were attributed to administration of tert-butyl perbenzoate. Similarly, at necropsy, no apparent chemical-related gross lesions were observed in either sex of rats. Forestomach weights were increased in male rats receiving the 250 and 500 mg/kg doses and in female rats receiving 60 mg/kg and higher doses. Weights of the glandular stomachs also were increased in both males and females, but the increases were largely restricted to high dose animals and the percent increase was smaller than observed in the forestomach. Other changes in organ weights included slightly decreased spleen weights in males and females receiving the high dose, and increased kidney weights in female rats receiving 250 mg/kg.
Epithelial hyperplasia and inflammation were observed in the forestomach of dosed rats. Dose-related increases in the incidence and severity of squamous epithelial hyperplasia were seen in male and female rats. Within the hyperplastic epithelium there was increased mitotic activity of the basal cell layer, rete peg-like downgrowths of hyperplastic cells, and variable hyperkeratosis, which appeared to increase in severity with the degree of hyperplasia present. Inflammatory cell infiltration also was evident in the forestomach of rats in the higher dose groups. These inflammatory changes included leukocytic exocytosis with neutrophil aggregates within the hyperkeratotic layer, as well as within intraepithelial clefts and vesicles; congestion of subepithelial capillaries, perivascular edema, and microhemorrhages were components of inflammation in some rats.

Due to the changes in organ weights included slightly decreased spleen weights in males and females receiving the high dose, and increased kidney weights in female rats receiving 250 mg/kg, the NOAEL in this study is identificated by eMSCA is 125 mg/kg bw/day since the effects on foresthomach at 60 mg/kg bw/day and higher doses in females are not considered relevant for human.

Studies on mice

Results of 14-day toxicity study on tert-butyl perbenzoate with 5 animals of each sex administrated at 0, 70, 140, 278, 556, 1112 mg per kg body weight in corn oil, by gavage. As these studies were carried out in a manner to also evaluate the effect of equimolar doses of the normal degradation products of tert-butyl perbenzoate in biological media, separate groups of animals were also dosed as follows: 30, 60, 120, 242, 484 mg t-butanol; or 40, 80, 160, 321, 642 mg benzoic acid per kg body weight in corn oil, by gavage.

No male mice receiving tert-butyl peroxybenzoate died during the study. One female mouse receiving the highest dose was killed in moribund condition on study day 3. Weight gains of groups of treated male and female mice were generally similar to those of controls. Mice showed no clinical signs considered to be related to administration of the chemical. The only lesion observed at necropsy that was considered possibly treatment-related was a single pigmented focus in the stomach of a female mouse receiving the highest dose. Similarly, little or no effect of administration of was observed on most absolute or relative organ weights. However, stomach weights were increased by as much as 2-fold, in a dose-dependent manner, in the 3 highest dose groups of male mice and in the 2 highest dose groups of female mice. Lesions considered related to administration of tert-butyl peroxybenzoate were observed only in the forestomach. These lesions included hyperplasia, ulceration, and acute inflammation of the forestomach mucosa. Hyperplasia was the most common lesion and was characterized by increased cellularity and basophillia of the epithelium, with variable degrees of hyperkeratosis. Hyperplasia was observed in the forestomachs of all mice that received the 2 highest doses and which survived the 14-day study, and in 3 of 5 females receiving the third highest dose, 278 mg/kg. A shallow ulcer was observed in the forestomach of 1 female mouse receiving the highest dose, corresponding to the gross lesion mentioned above.

Comparative results with t-Butanol and Benzoic acid: no male mice receiving t-butanol died during the study. However, 3 males receiving the highest dos e of benzoic acid died during week 1. Another female, receiving the highest dose of t-butanol, died on day 4; and a female receiving the highest dose of benzoic acid was killed in moribund condition midway through the study. Food consumption was somewhat lower in groups of mice of both sexes receiving t-butanol and benzoic acid, but differences were not significant in either sex compared to controls. Mice dosed with t-butanol showed no clinical signs considered to be related to administration of the chemical. However, male and female mice receiving the 642 mg/kg dose of benzoic acid exhibited rough hair coats, labored breathing, hunched posture, salivation, and enlarged abdomen. As indicated, 3 of 5 male mice in this benzoic acid dose group died during week 1. Increases in stomach weights were observed in mice receiving t-butanol, but these were not dose-related; no increases in stomach weights were observed in mice receiving benzoic acid.

Results of 13-weeks toxicity study with 10 animals of each sex of B6C3F1 mice administered at doses 0, 30, 60, 125, 250, 500 mg tert-butyl peroxybenzoate per kg body weight in deionized water by gavage were the follows.

Two mice died during the study. One control male died on day 4 of apparent gavage error, and a female in the 250 mg/kg dose group died on day 3. Mean diet consumption and body-weight gains by all dosed groups of mice were similar to those of the respective control groups. Clinical observations during the course of the study and gross observations at necropsy revealed few signs of toxicity or macroscopic lesions related to tert-butyl peroxybenzoate administration. Evidence of toxicity in mice was limited to increased stomach weights and lesions in the stomachs of dosed animals. Forestomach weights of both sexes receiving 250 and 500 mg/kg were increased by 50% or more. Additionally, glandular stomach weights of female mice in the 500 mg/kg group, and the glandular stomach-to-body-weight ratios of female mice in the 250 mg/kg group were significantly

increased compared to controls. Other changes in organ weights and organ-to-body-weight ratios were not considered related to chemical toxicity. Histopathological examination of the forestomachs revealed compound-related hyperplasia of the stratified squamous epithelium in male and female mice. In males, all dose groups were affected, although hyperplasia in a single animal in the 30 mg/kg group was minimal and not clearly compound-related. In females, the lesion was seen in the 60 mg/kg and higher dose groups. This lesion increased in both frequency and severity as the dose increased. Hyperplasia was characterised by increased cellularity and basophilia of the squamous epithelium, with hyperkeratosis that also appeared to increase with dose.

In these studies, as well as in the other repeated studies presented in the dossier, toxicological effects in organs are not considered to fulfil the CLP criteria for classification as target organ toxicity, repeated exposure, as forestomach effects are considered not relevant for humans and based on slight spleen and kidney weight changes in the higher dose groups in the 13 week study on F344 rats, 125 mg/kg/day was selected as the NOAEL for DNEL derivation.

eMSCA supports this conclusions.

7.9.5. Mutagenicity

In vitro data

Tert-butyl perbenzoate causes both chromosome aberrations and gene mutations *in vitro*.
The substance yielded a positive result in the *in vitro* mammalian chromosome aberration test (NTP, Matthews, H.B. 1992) with and without metabolic activation (Klimisch score 2, reliable with restrictions) according to the Registrant(s).
The substance also yielded positive results in the AMES test (NTP, Matthews, H.B. 1992) in Salmonella typhimurium strains TA100, TA1537, and TA98, with and without metabolic activation, as well as in the Mouse Lymphoma Forward Mutation Assay (Pence, D.H.; 1984) with and without metabolic activation. Both studies are Klimisch score 2 (reliable with restrictions) according to the Registrant(s). This indicates that the substance causes gene mutations *in vitro*.

In vivo data

The substance was tested in mice a micronucleus assay on peripheral lymphocytes after oral exposure (NTP, Matthews, H.B., 1992). The negative results reported in this assay was considered by eMSCA not sufficient to rule out *in vivo* mutagenicity because no evidence of target cell exposure (local cytotoxicity, i.e. alteration of PCE/NCE ratio) was reported. Moreover, toxicokinetic studies (NTP, Matthews, H.B.; 1992) demonstrated that tert-butyl perbenzoate is rapidly degraded in the stomach and consequently no systemic exposure is observed after oral administration.
On the other hand, while systemic genotoxicity is unlikely, a genotoxic effect at the site of contact cannot be excluded in consideration of the positive results reported in the *in vitro* studies also in the absence of metabolic activation and of the chemical nature of the compound. In fact, there is empirical evidence that highly reactive substances such as acrylates, peroxides and epoxides are generally negative in bone marrow studies (chromosome aberration test and micronucleus test), while often showing genotoxicity in the liver or in the sites of initial contact (stomach after oral exposure; lung/nasal tissues after inhalation exposure).
Therefore, eMSCA requested an *in vivo* alkaline single-cell gel electrophoresis assay for DNA strand breaks (Comet assay, OECD 489) in rats, oral route, with examination of liver and either glandular stomach or duodenum/jejunum.
In the *in vivo* comet assay, male rats (seven per group) were treated orally with 0, 400, 800 and 1600 mg/kg bw/day and killed at 28 hours (4 hours after the second dose administration).

In addition, two further groups of male rats were included in the study; one group (seven rats) were dosed via the oral route with the vehicle alone (corn oil) at 0 and 24 hours, and a second group (three male rats) were dosed orally with N-Nitroso-N-methylurea (MNU) at 0 and 24 hours to act as the positive control.
The glandular stomach and liver were processed for comet slides. Samples of glandular stomach and liver were preserved in formalin for possible histopathological analysis in the event of a positive response. The results showed that there was no evidence of an increase in the liver percentage tail intensity or median percentage tail intensity in the test item animals compared to the concurrent vehicle control group.
Statistically significant increases in the glandular stomach percentage tail intensities and median percentage tail intensities of the test item groups were demonstrated when compared to the concurrent vehicle control group, without a clear dose-response relationship. Histopathological analysis was performed on the preserved stomach samples to verify the possible evidence of cytotoxicity. Inflammatory cell infiltrate was observed in 6/7, 7/7, 5/7 animals that received respectively MTD, MTD/2 and MTD/4. The histopathological analysis (Haematoxlin/Eosin staining) demonstrated evidence of inflammatory and degenerative changes in the glandular stomach in all treated groups. An evidence of DNA damage was reported only in the presence of evident cytotoxicity. Therefore no firm conclusion can be derived because the apparent genotoxic effect observed could be the secondary effect of the local toxicity. In order to conclude on the genotoxicity of the test item it would be necessary an *in vivo* comet assay performed at a lower dose range. However the eMSCA consideres the request of a new *in vivo* assay unadvisable because such study could be not sufficient to resolve the issue also in view of animal welfare considerations. In fact the *in vivo* experiment could be considered conclusive only if DNA damage is detected in the absence of histopathological findings at least in one dose level. In all the other cases the study should be considered inconclusive.
In conclusion, the substance was considered to be unable to induce DNA strand breakage to the liver (distal site) while no conclusion can be drawn for the glandular stomach (site of contact) *in vivo*, under the conditions of the test.

Conclusion

Tert-butyl perbenzoate is part of class of perbenzoate, the organic peroxide that are strong oxidizing agents able to induce the formation of free radicals. The genotoxicity observed in the *in vitro* assays is compatible with its nature of organic peroxide able to produce oxidative DNA damage at the site of contact. On the other hand, the negative results reported in the MN *in vivo* can be explained by the high reactivity of the substance that strongly limits its capability to reach distal targets (bone marrow). The results obtained in the *in vivo* comet assay confirm the inability of the substance to reach the distal site (liver), while at the site of contact (glandular stomach) DNA breakage was reported in all treated groups and in concomitance of inflammatory effects.
On the basis of the available studies a final conclusion about the *in vivo* genotoxicity of tert-butyl perbenzoate cannot be drawn.
eMSCA considered the available data set for the classification for mutagenicity inconclusive.

7.9.6. Carcinogenicity

No relevant information is available for tert-butyl perbenzoate in relation to carcinogenicity. The inconclusive results reported in the *in vivo* genotoxicity assays together with the absence of pre-neoplastic leasions in the 90 day (Matthews, H.B., 1992) study are not sufficient to support the request of a carcinogenesis study.

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

An OECD TG 421 reproductive and developmental toxicity screening study has been performed on rats: four groups of 10 males and 10 females were treated by gavage once

daily at 0, 100, 300, 750 (males) and 1000 mg/kg (females) and no signs of reproductive toxicity or impaired fertility have been recorded up to the highest concentration used in both sexes.
Tert-butyl perbenzoate did not cause any change on reproductive and endocrine tissues in repeated dose toxicity on rodents.
In OECD TG 414 studies on rats, developmental delays in the presence of reduced maternal weight gain and food consumption were the only effects reported (at 300 mg/kg bw/day) and led to set up a NOAEL at the nominal dose of 100 mg/kg bw/day.
Studies on developmental toxicity have been implemented as required. The study on the second, non-rodent species has been performed according to the OECD TG 414 (New Zealand White rabbit, oral route by gavage) at the 3 nominal doses of 25, 80 and 250 mg/kg bw/day plus a control group with vehicle (Aqueous 1% methylcellulose). Exposure of females to the chemical occurred daily (once at approximately the same time each day) from Day 6 to Day 28 (included) after mating. No adverse effects were observed up to the highest dose tested (250 mg/kg bw/day) were observed in the F1; however, at 250 mg/kg bw/day a transient effect on F0 has been observed, namely a reduction in maternal weight gain and food consumption ence a NOAEL of 80 mg/kg bw/day should be taken into account.
Moreover, in the OECD ToolBox no alerts for reproductive toxicity have been picked up (DART: "Not known precedent reproductive and developmental toxic potential") and no adverse effects on reproductive organs has been reported in 90d-studies.
Overall, eMSCA concludes that no reproductive and endocrine-like adverse effects have been shown, whereas due to the transient effects on F0, the NOAEL for developmental toxicity in rats (100 mg/kg bw/day) and rabbits (80 mg/kg bw/day) should be taken into account.

7.9.8. Hazard assessment of physico-chemical properties

Not evaluated.

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

The following DNELs were derived by eMSCA.

Table 9

CRITICAL DNELS/DMELS					
Endpoint of concern	**Type of effect**	**Critical study(ies)**	**Corrected dose descriptor(s) (e.g. NOAEL, NOAEC)**	**DNEL/ DMEL**	**Justification/ Remarks**
Inhalation Workers repeated dose toxicity	Systemic effects - Long-term		Human$NOAEC_{inhalation}$=110mg/m^3	4 mg/m^3	AF for dose response relationship: 1 AF for difference in duration of exposure: 2 AF for interspecies differences (allometric scaling): 1 AF for other interspecies differences: 2.5

					AF for intraspecies differences: 5 AF for the quality of the whole database: 1 AF for remaining uncertainties: 1 Overall Assessment Factor: 25
Dermal Workers	Systemic effects - Long-term		$NOAEL_{oral}$= 80 mg/kgbw/day	1.33 mg/kg bw/day	AF for dose response relationship: 1 AF for difference in duration of exposure: 2 AF for interspecies differences (allometric scaling): 2.4 AF for other interspecies differences: 2.5 AF for intraspecies differences: 5 AF for the quality of the whole database: 1 AF for remaining uncertainties: 1 Overall Assessment Factor: 60

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

On the basis of the available information, an harmonised classification of the substance is envisaged by eMSCA, as a follow-up at EU level with the following hazard category: Org. Perox. C H242: Heating may cause a fire, Acute Tox. 4,H332: Harmful if inhaled, Skin Irrit. 2, H315: Causes skin irritation and 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

Not evaluated.

7.12. Exposure assessment

7.12.1. Human health

7.12.1.1. Worker

In general, eMSCA agrees with the approach taken by the Registrant(s) in performing the exposure and risk assessment for human health. Based on the toxicological profile of the substance, both a systemic and a local risk assessment have been conducted.
The overall systemic health risks have been characterized by means of the long-term DNELs derived for the dermal and inhalation routes.
Additionally, being *tert-butyl peroxybenzoate* classified as skin sensitizer Cat. 1 (H317: *May cause an allergic skin reaction*), the Control Banding Approach has been applied for characterizing local effects (Appendix 1).
In this regards, the following comments and remarks should be taken into account:

- According to the classification as Skin Sens. 1 – H317, the substance has been correctly allocated to the high Hazard Band (REACH Guidance Part E; Appendix 1; section 1);
- The likelihood of exposure seems to be set out based on the value of the vapour pressure (Appendix 1; section 2). However, being the substance classified for the local effects (sensitization) on the skin, the likelihood of exposure should instead be ranked based on the levels reported in the "*predicted EASE dermal exposure*" column (in ECETOC TRA 3). Therefore, each PROC should be ranked as "high", "moderate" or "low" exposure on the basis of the numeric value and the description of the process. An exposure matrix should be built on, accordingly.
- Following to that, in the risk matrix, the risk bands should be revised taking into account that different PROC might results in different likelihood of exposure as well as potential risk (Appendix 1; section 3).
- In conclusion, Risk Management Measures should be differentiated according to the risk band selected for each PROC (Appendix 1; section 4).

7.12.1.2. Consumer

Not applicable. There are no consumer or professional uses of this substance.

7.12.2. Environment

The life cycle of the substance is limited to the stage of industrial uses as process regulator and no consumer/professional uses (indoor/outdoor), i.e. wide dispersive uses, are identified. Therefore, the exposure estimation and risk characterization are limited to release to the environment related to manufacturing/formulation and industrial uses of the substance.

7.12.2.1. Aquatic compartment (incl. sediment)

The aquatic compartment is the most relevant issue concerning the environmental exposure assessment. For all exposure scenarios, the risk characterisation ratios are below 1, however, for manufacture, the values are close to 1 for the fresh water compartment (included sediment).

7.12.2.2. Terrestrial compartment

Relevant exposure of the soil compartment may only occur via application of sludge from an STP to agricultural soil. At the estimated exposure concentrations, the risks are controlled for all scenarios.

7.12.2.3. Atmospheric compartment

No relevant releases into the atmosphere are expected; therefore, a risk characterization for this compartment is not necessary.

7.12.3. Combined exposure assessment

eMSCA agrees with the approach taken by the Registrant(s) on human health and the environment. For the environment, total releases from all the exposure scenarios covered have been considered. At the estimated regional exposure concentrations, the risks for the environment are controlled.

7.13. Risk characterisation

For the human health, the overall risk characterization is acceptable and the risks can be considered under control. As mentioned under chaper 7.12.1.1, where relevant, RMMs should be revised considering the appropriate risk band for each PROC.

For the environment, the overall risk characterization is acceptable and the risks can be considered under control.

7.14. References

Registration dossier for tert-butyl perbenzoate, European Chemicals Agency. http://echa.europa.eu/

Matthews, H.B. 1992: NTP Technical Report on Toxicity Studies of t-Butyl Perbenzoate (CAS NUMBER: 614-45-9) Administered by Gavage to F344/N Rats and B6C3F1 Mice (study report), Report no: NIH Publication No. 92-3134. Report date: Jul 1, 1992.

Unpublished study report, Mouse Lymphoma Forward Mutation Assay t-Butyl Peroxybenzoate, 1984

7.15. Abbreviations

AF Assessment factor
BW Body weight
CAS Chemical abstracts service
C&L Classification and labelling
CLP Classification, labelling and packaging (Regulation (EC) No 1272/2008)
CSR Chemical Safety Report
DART Developmental & Reproductive Toxicity
DMEL Derived Minimal Effect Level
DNEL Derived no effect level
eMSCA Evaluating Member State Competent Authority
MTD Maximum Tolerated Dose
NOAEC No Observed Adverse Effect Concentration
NOAEL No Observed Adverse Effect Level
NOEC No Observed Effect Concentration
OECD Organisation for Economic Co-operation and Development
PBT Persistent, Bioaccumulative, Toxic
PEC Predicted Environmental Concentration
PNEC Predicted No Effect Concentration
RCR Risk characterization ratio
vPvB Very Persistent and very Bioaccumulative