EUROPEAN CHEMICALS AGENCY

Helsinki, 1 September 2016

Addressee: [redacted]

Decision number: CCH-D-2114340525-54-01/F
Substance name: tert-butyl 2-ethylperoxyhexanoate
EC number: 221-110-7
CAS number: 3006-82-4
Registration number: [redacted]
Submission number: [redacted]
Submission date: 05.08.2014
Registered tonnage band: 1000 tonnes or more per year

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the 'REACH Regulation'), ECHA requests you to submit information on

1. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3; test method: OECD TG 443) in rats, oral route with the registered substance; specified as follows:**
   - **Ten weeks premating exposure duration for the parental (P0) generation;**
   - **Dose level setting shall aim to induce some toxicity at the highest dose level;**
   - **Cohort 1A (Reproductive toxicity);**
   - **Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation;**

2. **Pre-natal developmental toxicity study (Annex X, Section 8.7.2; test method: EU B.31/OECD TG 414) in rabbits, oral route with the registered substance;**

3. **Exposure assessment and risk characterisation (Annex I, Sections 5. And 6.) for human health: revise exposure estimates;**

4. **Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment: revise the environmental exposure estimation.**

You may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring and conforming to the appropriate rules in the respective Annex, and an adequate and reliable documentation.

You are required to submit the requested information in an updated registration dossier by **9 September 2019. You shall also update the chemical safety report, where relevant.** The timeline has been set to allow for sequential testing.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2. Advice and further observations are provided in Appendix 3.

Appeal

[For the final decision: This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, shall be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under http://echa.europa.eu/web/guest/regulations/appeals.]

Authorised[1] by Claudio Carlon, Head of Unit, Evaluation E2

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix 1: Reasons

1. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)**

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

The basic test design of an extended one-generation reproductive toxicity study (test method B.56./OECD TG 443 with Cohorts 1A and 1B, without extension of Cohort 1B to include a F2 generation, and without Cohorts 2A, 2B and 3) is a standard information requirement as laid down in column 1 of 8.7.3., Annex X. If the conditions described in column 2 of Annex X are met, the study design needs to be expanded to include the extension of Cohort 1B, Cohorts 2A/2B, and/or Cohort 3. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

a) The information requirement

You have not provided any study record of an extended one-generation reproductive toxicity study in the dossier that would meet the information requirement of Annex X, Section 8.7.3.

You have sought to adapt this information requirement by providing information that can be interpreted as an attempt to adapt the information requirement according to Annex XI, Section 1.2. You provided the following information: a screening study (OECD 421; 2008), a prenatal developmetal toxicity study in rats (OECD 414; 2013), and a 90 day study (OECD 408; 2013). In your justification for the adaptation, you refer to findings in a prenatal developmental toxicity study, an oral 90-day repeated dose toxicity study and a reproduction/ developmental toxicity screening test. Based on this information you conclude that "*... the Two-Generation Study could be waived as the available data on fertility are conclusive, an increase of information is not expected from this study also because of animal welfare reasons.*"

However, ECHA notes that your adaptation does not meet the general rules for adaptation of Annex XI, Section 1.2. which requires that there are several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property with respect to the endpoint under consideration while the information of each single source alone is regarded as insufficient to support this notion.

ECHA notes that the data you reported cannot be considered as conclusive. In the reported screening study increase of pre-implantation, post-implantation and post-natal loss, a reduction of live pups, and the mean body weight of pups was reduced at 1000 mg/kg bw/day were observed which need to be followed up in a full study. ECHA also notes that the statistical power of the screening study according to OECD TG 421 is low and the study generates limited information on male and female reproductive performance such as gonadal function, mating behaviour, conception, development of the conceptus and parturition. The OECD TG 408 does not provide information on these functional aspects, and information from OECD TG 414 regarding to sexual function and fertility is limited to the maintenance of the pregnancy from implantation up to close to the parturition. In addition, you did not provide information on hazardous properties to the postnatal development including sexual maturation and histopathological integrity of the reproductive organs at adulthood.

Thus, the information from these studies do not allow to conclude whether the substance has hazardous properties with regard to sexual function and fertility and developmental toxicity. Furthermore, one of the metabolites of the registered substance is 2-ethyl hexanoic acid which is know to be classified as "Repro cat 2".

In the comments in the draft decision you indicated that the findings in the OECD TG 421 screening study at the highest dose tested (1000 mg/kg bw/day) are accompanied by maternal toxicity and that effects at clear maternal toxic doses are considered not relevant for hazard assessment. However, ECHA notes that the observed reproductive effects are not necessarily secondary to those maternal effects and hence, might be relevant for hazard assessment.

In the comment on the draft decision, you indicated that the findings on post-implantation and postnatal loss are followed-up in the provided pre-natal developmental toxicity study in rats. ECHA also notes your comment that the classification of the metabolite 2-ethyl hexanoic acid is due to developmental effects. ECHA acknowledges that the provided prenatal developmental toxicity study covers the concern for post-implantation losses and the concern for pre-natal developmental toxicity stemming from the metabolite 2-ethylhexanoic acid. However, ECHA notes that the pre-natal developmental toxicity study does not address post-natal developmental toxicity and the concern stemming from the increased post-natal loses. Hence, ECHA concludes that the information provided within a weight of evidence adaptation does not address post-natal developmental toxicity to the extent as it is required in an extended one-generation reproductive toxicity study.

In the comment on the draft decision you corroborated that the effects on sexual function and fertility are already adequately addressed and performance of a new study is not expected to enhance the hazard and risk assessment of the substance. ECHA notes your claim that the observed pre-implantation losses are restricted to the developmental toxicity parameters. However, ECHA considers that in general pre-implantation loss may reflect an adverse effect on fertility rather than developmental toxicity. Furthermore, ECHA notes your statement that the mating performance, fertility index, corpora lutea, implantation rate and gestation length were not influenced, based on the results from the OECD TG 421 study. In addition, ECHA notes your statement that the sub-chronic toxicity study (OECD TG 408) includes investigation of the oestrous cycle and sperm parameters which you consider as very sensitive parameters for fertility and hormonal effects. However, due to the lower statistical power of the OECD TG 421 screening study and the sub-chronic toxicity study (OECD TG 408) compared to the extended one-generation reproductive toxicity study, effects on fertility might have been missed in those studies. In addition, ECHA notes that the metabolite of the registered substance, 2-ethylhexanoic acid, is leading to an impairment of fertility (e.g., Pennanen et al., 1993 Fundam Aool Toxicol 21: 204-12) in addition to its developmental toxicity. Therefore, ECHA concludes that the information on sexual function and fertility provided within the weight of evidence adaptation does not provide sufficient confidence to conclude that sexual function and fertility is not affected by the registered substance, especially with regard to the formation of a reproductive toxic metabolite of the substance.

The information requirement of Annex X, 8.7.3. could not be omitted with reference to exposure based arguments since some of the PROCs (process categories) reported in the dossier indicated that the substance is not used exclusively under strictly controlled conditions.

Therefore, your adaptation of the information requirement cannot be accepted.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint. Thus, an extended one-generation reproductive toxicity study according Annex X, Section 8.7.3. is required. The following refers to the specifications of this required study.

b) The specifications for the study design

Premating exposure duration and dose-level setting

To ensure that the study design adequately addresses the fertility endpoint, the duration of the premating exposure period and the selection of the highest dose level are key aspects to be considered. According to ECHA Guidance, the starting point for deciding on the length of premating exposure period should be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

Ten weeks premating exposure duration is required because there is no substance specific information in the dossier supporting shorter premating exposure duration as advised in the ECHA Guidance on information requirements and chemical safety assessment R.7a, chapter R.7.6 (version 4.0, July 2015).

ECHA understands that in the comments on the draft decision you are proposing a shorter premating period because the result from the OECD TG 421 study and sub-chronic toxicity study did not result in effects on fertility. However ECHA considers that the premating exposure duration should cover the full spermatogenesis and folliculogenesis at the time of mating to address adequately fertility. This information is not available from existing studies.

Moreover, you have stated in you comments that if ECHA requests a 10 week premating exposure period then only the male animals should have a 10 week premating exposure period and the females should have a two week premating exposure duration. However, ECHA considers that it is important to expose all the developmental stages of the sperm and follicles before mating in order to be able to evaluate any potential adverse effects on fertility and to have appropriate data for risk assessment and classification purposes. Recital (7) of Commission Regulation (EU) 2015/282 of 20 February 2015. amending Annexes VIII, IX and X to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) regarding the Extended one-generation reproductive toxicity study stated that "*It should be ensured that the reproductive toxicity study carried-out under point 8.7.3 of Annexes IX and X to Regulation (EC) No 1907/2006 will allow adequate assessment of possible effects on fertility. The premating exposure duration and dose selection should be appropriate to meet risk assessment and classification and labelling purposes as required by Regulation (EC) No 1907/2006 and Regulation (EC) No 1272/2008 of the European Parliament and of the Council.*"

Further, you have not provided a substance-specific justification to have a shorter premating exposure duration, as outlined on page 83 of the ECHA Guidance on Information Requirements and Chemical Safety Assessment, Chapter R.7a: Endpoint specific guidance, Version 4.1, October 2015 (http://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf) "*shorter than 10 weeks premating exposure duration may be also used based on substance specific justifications - but not shorter than 2 weeks*". As a consequence, ECHA considers that your proposal to have 14 days premating exposure duration has not been justified.

The highest dose level shall aim to induce some toxicity to allow comparison of effect levels and effects of reproductive toxicity with those of systemic toxicity. The dose level selection should be based upon the fertility effects with the other cohorts being tested at the same dose levels.

In the comments to the draft decision, you have proposed to limit the study design to only Cohort 1A. However, the information requirement of REACH Annex X, Section 8.7.3 requires Cohorts 1A and 1B as part of the basic study design: *"Extended One-Generation Reproductive Toxicity Study (B.56 of the Commission Regulation on test methods as specified in Article 13(3) or OECD 443), basic test design (cohorts 1A and 1B without extension to include a F2 generation), one species, most appropriate route of administration, having regard to the likely route of human exposure, unless already provided as part of Annex IX requirements"*. Hence, your proposal does not fulfil the REACH information requirement and cannot be accepted. It is to be noted that OECD TG 443 foresees that Cohorts 1A and 1B would be conducted in every case.

If there is no existing relevant data to be used for dose level setting, it is recommended that the results from a conducted range-finding study (or range finding studies) are reported with the main study. This will support the justifications of the dose level selections and interpretation of the results.

Species and route selection

According to the test method EU B.56/OECD TG 443, the rat is the preferred species. On the basis of this default assumption, ECHA considers that testing should be performed in rats.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, July 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

c) Outcome

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Extended one-generation reproductive toxicity study (test method EU B.56./OECD TG 443), in rats, oral route, according to the following study-design specifications:

- Ten weekspremating exposure duration for the parental (P0) generation;
- Dose level setting shall aim to induce some toxicity at the highest dose level;
- Cohort 1A (Reproductive toxicity);
- Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation.

Notes for your consideration

The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohorts 2A and 2B and/or Cohort 3 if new information becomes available after this decision is issued to justify such an inclusion.

Inclusion is justified if the new information shows triggers which are described in column 2 of Section 8.7.3., Annex X and further elaborated in ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6 (version 4.0, July 2015). You may also expand the study to address a concern identified during the conduct of the extended one-generation reproduction toxicity study and also due to other scientific reasons in order to avoid a conduct of a new study. The justification for the expansion must be documented. The study design must be justified in the dossier and, thus, the existence/non-existence of the conditions/triggers must be documented.

2. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in a second species

Pursuant to Articles 10(a)(vi) and/or (vii), 12(1)(e) and 13(4) of the REACH Regulation, a technical dossier registered at more than 1000 tonnes per year shall contain as a minimum the information specified in Annexes VII to X of the REACH Regulation.

Pre-natal developmental toxicity studies (test method B.31./OECD TG 414) on two species are part of the standard information requirements for a substance registered for 1000 tonnes or more per year (Annex IX, Section 8.7.2., column 1, Annex X, Section 8.7.2., column 1, and sentence 2 of introductory paragraph 2 of Annex X of the REACH Regulation).

The technical dossier contains information on a pre-natal developmental toxicity study in rats by the oral route using the registered substance as test material.

However, there is no information provided for a pre-natal developmental toxicity study in a second species.

In the comments on the draft decision you confirmed that a pre-natal developmental toxicity study in a second species is a standard information requirement for substances with a tonnage of more than 1000 tonnes per year. However, you did not agree that a new study has to be conducted because a prenatal developmental toxicity study on rabbits performed with the metabolite 2-ethyhexanoic acid is available. ECHA notes that such information and an appropriate justification for a read-across adaptation according to Annex XI, Section 1.5. is currently not included in the registration dossier of the registered substance.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does currently not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

The test in the first species was carried out by using a rodent species (rats). According to the test method EU B.31/OECD 414, the rabbit is the preferred non-rodent species. On the basis of this default assumption, ECHA considers that the test should be performed with rabbits as a second species.

ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 4.0, July 2015) R.7a, chapter R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD TG 414) in a second species (rabbits) by the oral route.

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3. Exposure assessment and risk characterisation (Annex I, Sections 5. And 6.) for human health

Pursuant to Articles 10(b) and 14(1) of the REACH Regulation, the registration shall contain a chemical safety report which shall document the chemical safety assessment conducted in accordance with Article 14(2) to (7) and with Annex I of the REACH Regulation.

In accordance with Article 14(4), the chemical safety report (CSR) must include an exposure assessment and risk characterisation if the substance is assessed to be persistent, bioaccumulative and toxic (PBT) or very peristent and very bioaccumulative (vPvB) or fulfils the criteria for any of the hazard classes or categories set out in Annex I to Regulation (EC) No 1271/2008. ECHA notes that you have classified the substance as Organic peroxide Type C (H242) Skin Sens1 (H317), Aquatic Acute Tox (H400), Aquatic Chronic Tox (H410) and and therefore an exposure assessment and a risk characterisation need to be included in the CSR.

Annex I, Section 5.2.4. requires the Registrant to perform an estimation of the exposure levels for all human populations (workers, consumer and humans liable to exposure via the environment) for which exposure to the substance is known or reasonably foreseeable. Each relevant route of exposure (inhalation, oral, dermal and combined through all relevant routes and sources of exposure) shall be addressed.

Further, Annex I, 5.2.5. states that appropriate models can be used for the estimation of exposure levels. However, special consideration shall be given to representative exposure data where available, when conducting the exposure assessment.

ECHA notes you have used the ECETOC TRA model v3 as the basis for estimating the exposure to the registered substance for workers during manufacture, formulation and industrial use. In the CSR you have generated 59 contributing exposure scenarios based on PROCs using the EasyTRA formatting tool. Some exposure scenarios for human exposure (44 out of 59) have been modified from the initial output from the TRA model taking account of the duration of exposure in a linear way – this is regarded by you as a Tier 2 assessment. For instance, for exposure scenario 42 "industrial use of reactive processing aids" (PROC 10, roller application or brushing) you report a combined RCR of 0.901298. The value of the combined RCR arising from the standard use of the ECETOC TRA model, applying the default values within the model for exposure duration, is approximately 2.5 and would indicate a safe use has not been demonstrated.

The ECETOC TRA model incorporates a banded approach to exposure modification related to duration. Within these bands the model applies a modification factor of 1 (>4 hours – i.e. no reduction) 0.6 (1-4 hours), 0.2 (15 min – 1 hour), 0.1 (<15 mins). In its own guidance, the TRA gives no provision for linear modification of exposure (for both inhalation and dermal exposure). Indeed the model developers state their intention for the model is to retain inherent conservatism. For a 2-hour duration, the default use of the model predicts more than twice the value you report in the CSR.

In your Easy TRA Appendix to the CSR you state "*all of the Tier 2 entry values, including justification for the deviation from Tier 1 defaults, are documented in Appendix 1 (2.1.2 Human Health assessment – Workers – Tier 2 Entry Data)*". It has not been possible to identify or verify the validity of the justification you claim in the context of the values you report. In that context the selection of linear exposure modification factors without justification makes the use of the model inappropriate and erodes any inherent conservatism.

In the comments on the draft decision you indicated that you did not fully agree with the issue but that you will address the ECHA request related to taking account of worker exposure in a linear way in the next update. However, you are reminded that this decision does not take into account any updates submitted after 26 November 2015. All the new information in the later update(s) of the registration dossier will however be assessed for compliance with the REACH requirements in the follow-up evaluation pursuant to Article 42 of the REACH Regulation.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation you are requested to revise the exposure assessment using an appropriate model within its applicability domain and revise the risk characterisation accordingly *or* provide a detailed, suitable and adequate justification for not using default values in the model used for exposure estimation. The chemical safety report shall be amended accordingly.

4. Exposure assessment and risk characterisation (Annex I, Sections 5. and 6.) for environment: revise the environmental exposure estimation

According to Article 14(4) of the REACH Regulation, if the substance fulfils the criteria for any of the hazard classes of Annex I to Regulation (EC) No 1272/2008 listed in Article 14(4) of the REACH Regulation or is assessed to be a PBT or vPvB, the chemical safety assessment shall include an exposure assessment and risk characterisation. The exposure assessment shall be carried out according to section 5 of Annex I and shall include exposure scenarios and exposure estimations for the registered substance. The exposure assessment shall consider all stages of the life-cycle of the substance resulting from the manufacture and identified uses and shall cover any exposures that may relate to the identified hazards. Annex I, section 6 of the REACH Regulation requires you to characterise the risk for each exposure scenario.

In your dossier you present for environmental exposure 7 exposure scenarios (ES):

ES1: Manufacturing of the substance (ERC1)
ES2: Formulation of preparations (ERC2)
ES3: Formulation of preparations (no release to STP) (ERC2)
ES4: Formulation of materials (ERC3)
ES5: Formulation of materials (no release to STP) (ERC3)
ES6: Industrial use of reactive processing aids (ERC6B)
ES7: Industrial use of chemicals for polymer processing (ERC6D)

The environmental exposure assessment and risk characterisation you have provided contain several deficiencies as indicated below.

In the comments on the draft decision you indicated that you did not fully agree with the issues but that you will address the ECHA request related to environmental exposure assessment (dilution factors, use of A and B tables, release times per year and fraction of the main source) in the next dossier update .

a. The dilution factors used in Tier 3 assessment for ES1 and ES2 exceed 1000

Pursuant to Annex I, section 5.2.4. of the REACH Regulation, exposure estimation shall take account of spatial and temporal variations in the exposure pattern.

In particular, the dilution of the substance into the receiving surface water may vary due to the different seasonal conditions. Chapter R.16.6.6.2 of the ECHA's Guidance on information requirements and the chemical safety assessment (ECHA, version: 2.1, October 2012) recommends that the low-flow rate or 10th percentile of the flow rate be used, or, alternatively, when only average flow rate is available, that the flow rate be estimated as one third of this average.

By default, the ECHA Guidance recommends a generic receiving water flow rate of 18000 m^3/d (corresponding to a dilution factor of 10). The flow rate or dilution factor can be changed according to the site specific data. ECHA notes that, according to the above mentioned Guidance, in case of site-specific assessments the dilution factor, which is applied for calculation of the local concentration in surface water, should however not be greater than 1000.

In the Tier 3 assessment for ES1 and ES2, you have used a river flow rate (and consequently dilution rate) which deviate from the default values recommended in ECHA guidance.

For ES1, you have used the river flow rate of 3,948,480 m^3/day (= 45.7 m^3/s) which corresponds to the flow rate of the river Isar at the production site (Munich) (Source: Bayrisches Landesamt für Umwelt, http://www.nid.bayern.de/, query date: September 2012)). Guidance R.16. specifies that "*flow rates of receiving waters are typically highly fluctuating. In this case, the 10th percentile, corresponding to the low flow rate, should always be used. If only time averaged flow rates are available, the flow rate for dilution purposes should be estimated as one third of the average*". The flow rate provided by you appears to correspond to a specific month (September 2012) if not to a specific day during that month. The source website used by you does not provide values for the 10th percentile or average flow rates. Still, the website used by you provides values for the 25th percentile over the period of 1959 to 2012 which are 47 m^3/s (winter), 80.20 m^3/s (summer) and 63.80 m^3/s (whole year). It also indicates that the lowest daily average for all years over that same period of 1959 to 2012 is 8.63 m^3/s. It is not possible to judge whether the value of 45.7 m^3/s provided by you is representative of *reasonable* worst case conditions with regard to the flow rate of the receiving river at the production site.

For ES2, you indicate that a minimum river flow rate of 3,000,000 m^3/day is required for this exposure scenario to apply. By comparison, the default minimum river flow rate recommended in ECHA guidance is 18000 m^3/day. You have not provided any evidence that the formulation sites using the registered substances are all located near a river with a minimum flow rate of 3,000,000 m^3/day. You are required to provide exposure scenarios applicable to all uses of your substance.

The corresponding dilution factors used for the two scenarios are respectively 1975 for ES1 and 1501 for ES2. According to ECHA guidance, dilution factors above 1000 should never be assumed in order not to overlook incomplete mixing in the receiving environment.

In the environment, dilution is in practice not complete near the point of discharge. In the mixing zone, higher concentrations will occur. The distance from the point of discharge where complete mixing may be assumed will vary between different locations. For situations with very high dilution factors, the mixing zones may be very long and the overall area that is impacted by the effluent before it is completely mixed can be substantial.

Therefore, in case of site-specific assessments, ECHA Guidance R.16. (pages 63-64) recommends that the dilution factor that is applied for calculation of the local concentration in surface water should not be greater than 1000.

Using a dilution factor of 1000 would increase the RCRs by a factor of approximately 200 and 150 for respectively ES1 and ES2. The RCRs for the freshwater compartment (water and sediment) for these 2 scenarios are currently 0.3. Furthermore, due to other issues (e.g. for ES2: deviation from default recommendations for release factors, for the number of release times per year, for fraction of the main source) it appears that actual RCRs exceed 1 by two orders of magnitude when using adequate dilution factors and release rates.

Therefore, pursuant to Article 41(1) and 41(3) of the REACH Regulation, you are requested to amend your exposure assessment for the aquatic compartment for exposure scenarios ES1 and ES2 in order to take account of seasonal variations in the river flow rate and of incomplete mixing in the environment.

b. Justification for use of A and B tables

Pursuant to Annex I, section 5.2.1 of the REACH Regulation the exposure estimation entails three elements: emission estimation, assessment of chemical fate and pathways and estimation of exposure levels. Pursuant to Annex I, section 5.1.1 of the REACH Regulation, exposure scenarios (ES) shall include, where relevant, a description of operational conditions (OCs) and of risk management measures (RMMs). As indicated in Annex I, section 5.2.2. of the REACH Regulation, emission estimation shall be performed under the assumption that the risk management measures and operational conditions described in the exposure scenario have been implemented. These RMMs and OCs should be included in the exposure scenarios provided in a CSR.

According to the Guidance on information requirements and chemical safety assessment Chapter R.16: Environmental Exposure Estimation (ECHA, version: 2.1, October 2012), operational conditions "*consist of a set of actions, tools, parameters such as amount of substance, process temperature and pH, duration and frequency of release, type of use (e.g. indoor or outdoor), containment of process (open or closed), continuous or batch process (leading to an intermittent release), capacity of surroundings, etc. having, as a side effect, an impact on the release and the exposure*". Risk management measures "*consist of technologies and procedures aimed at either reducing the releases and/or preventing a release pathway. Examples of risk management measures intended to reduce release are filters, scrubbers, biological or physico-chemical wastewater treatment plants etc.*" Both OCs and RMMs have an impact on the type and amount of release and the resulting exposure.

The release factors associated with Environmental Release Categories (ERCs) cited in ECHA's guidance R.16 can be used for a first tier assessment of the emissions. However, better information may be available that could then be used instead. In particular, release factors can be refined by taking into account RMMs and OCs. In this case, it is important to explicitly link such RMMs and OCs to the release factors and communicate them properly to the downstream users in the exposure scenarios. ECHA's guidance R.16 indicates that A and B tables of the Technical Guidance Document (TGD, 2003) can be considered for refining release factors, as long as specific information on RMMs and on OCs are provided in the exposure scenarios, otherwise they are considered insufficient to meet the REACH requirements.

ECHA notes the release factors you have applied are based on A and B tables of the TGD (2003). No further justification is provided for using these release factors, in particular, the exposure scenario does not specify any RMM. According to ECHA guidance, use of release factors from A and B tables without justification is not acceptable. Specific information on RMM and OC must be provided when using A and B tables of the TGD, otherwise they are considered insufficient to meet the REACH requirements (ECHA guidance R.16.3.5.2.).

Therefore, pursuant to Article 41(1) and 41(3) of the REACH Regulation you are requested to use default release factors and other recommendations of ECHA Guidance R.16 and revise the risk characterisation accordingly *or* provide a detailed justification (e.g. based on RMMs and/or OCs and/or substance properties) for not using the default release factors as recommended in ECHA Guidance R.16 for estimation of environmental exposure. The chemical safety report shall be amended accordingly.

c. The release times per year for ES2, ES4 and ES6 are not in line with ECHA Guidance R16

For ES2, ES4 and ES6, the default number of release days (indicated as "release time per year" in the CSR) deviates from the recommendation of Guidance R16:

- For ES2: the number of release days is set to 300 days/year for an annual tonnage of 1500 tonnes/year (justification: "*Release times per year (IC = 11 (Polymers Industry), formulation Table B.2.3, < 25000 tpa) (EU TGD 2003)*")
- For ES4: the number of release days is set to 300 days/year ffor an annual tonnage of 1500 tonnes/year (justification: "*Release times per year (IC = 11 (Polymers Industry), formulation Table B.2.3, < 25000 tpa, (EU TGD 2003)*")
- For ES6: the number of release days is set to 365 days/year for an annual tonnage of 1500 tonnes/year (justification: "*The substance is used in industrial applications continiously over the whole year (365 days)*")

According to Guidance R16, Chapter R.16.3.2.1., the default number of release days for an annual tonnage of 1500 tonnes/year should be 100 days/year for every industrial use (manufacture, formulation, industrial end uses).

When assuming higher number of release days, you have consequently also assumed a lower daily amount used at each site and may have underestimated the exposure.

The ECHA Guidance indicates that registrants can overwrite the default value for daily use, by using suitable and specific on-site, downstream user, market data, etc. if available. However you have not provided such justification but either refer to default value cited in TGD 2003 (for ES2 and ES4) or simply state that the substance is used "*continuously over the whole year*" (for ES6). The TGD 2003 was used for the previous legislation but does not apply for REACH and cannot be regarded as specific on-site information. For ES6, you claim that the substance is continuously used over the whole year but do not provide any actual evidence for supporting that claim. Therefore, the justifications you have provided for deviating from the default number of release days recommended in Guidance R16 are not sufficient.

Therefore, pursuant to Article 41(1) and 41(3) of the REACH Regulation you are requested either to provide actual evidence for supporting the number of release days you have used for your assessment for ES2, ES4 and ES6, or to use the default number of release days recommended in ECHA Guidance R.16. The chemical safety report shall be amended accordingly.

d. For ES2, ES4 and ES6 the fraction of the main source is lower than 100%

In the Tier 3 assessment for ES2, ES4 and ES6 the you have assumed that less than 100% of the whole registered tonnage (referred to as "fraction of the main source" in the CSR) was used at a site:

- For ES2, the fraction of the main source is set to 12 % (justification: "*Max. local tonnage for biggest formulation site*")
- For ES4, the fraction of the main source is set to 6.667 % (justification: "*Max. local tonnage for biggest formulation site*")
- For ES6, the fraction of the main source is set to 26.667 % (justification: "*Max. local tonnage for biggest industrial use site*")

However, according to ECHA Guidance R16 (Chapter R.16.3.2.1.), by default, 100% of the whole registered tonnage at EU level should be assigned to the region for manufacture, formulation and industrial uses. This default value of 100% is a worst case to cover situations where the total registered tonnage is processed by at a single site. By assuming lower values, you may underestimate the local exposure.

The ECHA Guidance specifies that registrants can overwrite that default value by using suitable and specific on-site, downstream user, market data, etc. if available. You have indicated that the values you used for the fractions of the main source for ES2, ES4 and ES6 were based on the maximum local tonnage for the biggest sites. However you have not provided any more details to substantiate your claims.

Therefore, pursuant to Article 41(1) and 41(3) of the REACH Regulation you are requested to provide actual evidence for justifying the values for the fractions of the main source he has applied for ES2, ES4 and ES6, or to use the default value of 100% recommended in ECHA Guidance R.16. The chemical safety report shall be amended accordingly.

e. Qualitative Exposure assessment for the terrestrial compartment

For the terrestrial compartment, your testing is tailored based on no or negligible exposure. You have ommitted the exposure assessment to the terrestrial environment using the argument that no hazard has been identified. This is a circular argument and cannot be accepted as such.

In the comments on the draft decision you indicated that you did not agree with this issue and made reference to section 6 of IUCLID and section 7.2 of the CSR to claim that exposure to soil is negligible.

ECHA did consider section 6 of IUCLID and section 7.2 of the CSR when evaluating the dossier but judged that they did not suffice to definitively conclude whether exposure to soil is negligible.

In section 6 of IUCLID and in section 7.2 of the CSR you claim that:

1/ "*Due to the unstable nature of organic peroxides, it can be assumed that upon contact with soil and organic matter, the test item undergoes rapid degradation resulting in the formation of respective alcohols and acids*". ECHA considers this claim to be incorrect. Tert-butyl 2-ethylperoxyhexanoate (TBPEH) is not highly reactive (e.g. it can be produced and stored in the absence of diluent). Its hydrolysis half-life is 15.7 d at pH7 and 12 °C. TBPEH is not readily biodegradable. Therefore, the substance is not expected to undergo rapid degradation in soil.

2/ You also claim that direct or indirect exposure of the soil compartment is unlikely throughout the complete life cycle of the substance. However, the CSR does not contain any quantitative exposure assessment for the terrestrial compartment and your claim is based only on qualitative considerations that releases via land spreading of sewage sludge, direct application to soil, deposition via other pathways such as irrigation or contact with contaminated waste, and deposition from the atmosphere / aerial deposition are all inexistent or negligible.

ECHA further notes that in IUCLID section 3.7.2 (Environmental assessment for aggregated sources) the following releases are reported:

- summed releases to water from all life cycle stages: 0.7 tonnes/year
- summed releases to air from all life cycle stages: 16.2 tonnes/year
- summed releases to soil from all life cycle stages: 0.6 tonnes/year

These figures indicate that direct and indirect exposure to soil does occur and can be quantified. The exposure assessment to soil needs to take into account direct releases to soil but also indirect exposure from water and from the air. ECHA notes that there are issues with the exposure assessment for the aquatic and atmospheric compartments also addressed in this draft decision: i.e. with dilution factors, use of A and B tables, release times per year, fraction of the main source. You shall address issues with the exposure assessment for the aquatic and atmospheric compartments also for quantifying indirect exposure to soil.

Therefore, pursuant to Article 41(1) and 41(3) of the REACH Regulation you are required to provide a qualitative exposure assessment clearly demonstrating no or negligible exposure to the terrestrial environmental spere.

Deadline to submit the requested information in this decision

In the draft decision communicated to you the time indicated to provide the requested information was 30 months from the date of adoption of the decision. In your comments on the draft decision, you requested an extension of the timeline to 36 months. You sought to justify this request that a dose-range finding study for the pre-natal developmental toxicity study in rabbits has to be performed in addition and that the capacity of laboratories carrying out such tests is limited already due to the recent requests by ECHA for these types of studies. ECHA has granted the request and set the deadline to 36 months.

ECHA
EUROPEAN CHEMICALS AGENCY

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 28 October 2015.

ECHA notified you of the draft decision and invited you to provide comments.
ECHA took into account your comments and amended the deadline.

ECHA notified the draft decision to the competent authorities of the Member States for proposal(s) for amendment.
ECHA received proposal(s) for amendment and did not modify the draft decision.

ECHA invited you to comment on the proposed amendment(s).

ECHA referred the draft decision to the Member State Committee.

Your comments on the proposed amendment(s) were taken into account by the Member State Committee.

The Member State Committee reached a unanimous agreement on the draft decision during its MSC-48 meeting and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix 3: Further information, observations and technical guidance

1. This compliance check decision does not prevent ECHA from initiating further compliance checks on the present registration at a later stage.

2. Failure to comply with the request(s) in this decision, or to fulfil otherwise the information requirement(s) with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In relation to the information required by the present decision, the sample of substance used for the new test(s) must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance composition manufactured or imported by the joint registrants. It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of substance tested in the new test(s) is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new test(s) must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grade(s) registered to enable the relevance of the test(s) to be assessed.