EUROPEAN CHEMICALS AGENCY

Helsinki, 12 December 2019

Addressee: [redacted]

Decision number: CCH-D-2114493105-50-01/F
Substance name: tert-butyl peroxypivalate
EC number: 213-147-2
CAS number: 927-07-1
Registration number: [redacted]
Submission number: [redacted]
Submission date: 5 February 2016
Registered tonnage band: 100-1000

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. **In vivo mammalian alkaline comet assay (Annex IX, Section 8.4., column 2; test method: OECD TG 489) in rats, oral route, on the following tissues: liver, glandular stomach and duodenum with the registered substance**

   OR

   Transgenic rodent somatic and germ cell gene mutation assays (Annex IX, Section 8.4., column 2; test method: EU B.58./OECD TG 488) in transgenic mice or rats, oral route on the following tissues: liver and glandular stomach with the registered substance; duodenum must be harvested and stored for up to 5 years. Duodenum must be analysed if the results of the glandular stomach and of the liver are negative or inconclusive.

2. **Extended one-generation reproductive toxicity study (Annex IX, Section 8.7.3.; test method: EU B.56./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.**

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 to the REACH Regulation. 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 adequate and reliable documentation.

You have to submit the requested information in an updated registration dossier by ***19 December 2022***. You also have to update the chemical safety report, where relevant.

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

Appeal

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, has to 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/regulations/appeals.

Authorised[1] by Ofelia Bercaru, Head of Unit, Hazard Assessment

[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. **In vivo mammalian alkaline comet assay (Annex IX, Section 8.4., column 2) OR Transgenic rodent somatic and germ cell gene mutation assays (Annex IX, Section 8.4., column 2)**

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

"Mutagenicity" is an information requirement as laid down in Annex VIII, Section 8.4. of the REACH Regulation. Column 2 of Annex IX, Section 8.4. provides that "If there is a positive result in any of the *in vitro* genotoxicity studies in Annex VII or VIII and there are no results available from an *in vivo* study already, an appropriate *in vivo* somatic cell genotoxicity study shall be proposed by the Registrant."

The technical dossier contains an *in vitro* study "*Salmonella/Escherichia coli mutagenicity assay" ([redacted]; 1996)* performed according to *the OECD test guideline 471* with the registered substance that shows positive results. Positive results have been detected in absence of metabolic activation in the following strains: *S. typhi*. TA 100, TA 1537, TA 102, TA 98, *E. coli* WP2 (pKM 101) and *E. coli* WP2 uvrA (pKM101). Positive results have been detected in presence of metabolic activation in the following strains: *S. typhi.* TA 98, TA 100, TA 1537, TA 102, TA 1535, *E. coli* WP2 (pKM 101) and *E. coli* WP2 uvrA (pKM101). The positive results indicate that the substance is inducing gene mutations under the conditions of the test.

In your dossier you provided the following waiving argument to dismiss the need to conduct a further *in vivo* gene mutation study: "*In accordance with Endpoint Specific Guidance Chapter R.7A, Figure R.7.7-1 "Flow chart of the mutagenicity testing strategy", no further testing (ie. no in vivo testing) need be proposed in the event of a negative mouse lymphoma assay or hprt assay, regardless to whether or not the gene mutation test in bacteria is positive or negative. This therefore implies that when considering whether an in vivo gene mutation request is required for substances requiring Annex IX test proposals due to their volume bands, a negative mouse lymphoma assay or hprt assay is sufficient evidence to waive the need for an in vivo gene mutation test".* ECHA notes that your waiving argument is based on an erroneous interpretation of the Figure R.7.7-1. This flow chart indicates that whenever positive results are obtained in a gene mutation test in bacteria, the information requirements of Annex VIII need to be addressed starting with an *in vitro* cytogenicity test, i.e. either a micronucleus test *in vitro* or a chromosome aberration test *in vitro*. According to the flowchart, independently of the outcome of the *in vitro* cytogenicity test in cases where the gene mutation test in bacteria was positive, the next step is to proceed with Annex IX information requirements for mutagenicity and propose an adequate *in vivo* mutagenicity study. Negative results observed in a mouse lymphoma assay or *hprt* assay are not sufficient to waive *in vivo* testing to follow up on the positive results obtained in the gene mutation test in bacteria.

The technical dossier contains an *in vivo* study "micronucleus cytogenetic assay in mice" ([redacted]; 1995) performed according to the OECD test guideline 474 with the registered substance that shows negative results. ECHA points out that the mammalian erythrocyte micronucleus test as described in the OECD test guideline 474 is

designed to detect cytogenetic damage which results in the formation of micronuclei containing lagging chromosome fragments or whole chromosomes. Hence, ECHA concludes that the test provided was not appropriate to follow-up a concern for gene mutations.

Since the waiver submitted by you is not acceptable as explained above and as an appropriate *in vivo* genotoxicity study to follow up the concern on gene mutations is not available for the registered substance, there is an information gap and it is necessary to provide information for this endpoint.

According to the ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.7.6.3, the transgenic rodent somatic and germ cell gene mutation assays ("TGR assay", OECD TG 488) and the *in vivo* mammalian alkaline comet assay ("comet assay", OECD TG 489) are suitable to follow up a positive *in vitro* result on gene mutation. Hence, ECHA considers that the TGR and the comet assay are suitable tests to follow up the concern on gene mutation for the substance subject to the decision.

In case you decide to perform the TGR assay according to the test method EU B.58/OECD TG 488, the test shall be performed in transgenic mice or rats.

In case you decide to perform the comet assay according to the test method OECD TG 489, the test shall be performed in rats.

According to the information provided in the technical dossier, the registered substance is a liquid of moderate vapour pressure. You indicate in your assessment of the toxicokinetic properties of the registered substance that "*Based on the vapour pressure of approximately 400 Pa TBPPI might become available for inhalation to a certain extend. If the substance would reach the lungs in its vapour or gaseous state, absorption directly across the respiratory tract epithelium by passive diffusion is likely to occur due to its log Pow value and water solubility. An acute inhalation toxicity study performed on rats using TBPPI in its aerosol form revealed a LC50 of 7.8 mg/L. Since specific effects of systemic toxicity were observed these results indicate systemic availability after inhalation*".

In your comments to the draft decision you clarified the conditions of use and reported that whilst PROC 7 was initially listed in the description of the uses, information from the downstream users confirmed that the substance is not used in spray applications. According to the information provided in the comments on the draft decision, the joint registrants have committed to updating the information on the uses in their dossiers in a spontaneous update.

Therefore, having considered the anticipated routes of human exposure and adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.

In case you decide to perform a TGR assay according to the test method EU B.58/OECD TG 488, the test shall be performed by analysing tissues from liver as slowly proliferating tissue and primary site of xenobiotic metabolism, and glandular stomach and duodenum as rapidly proliferating tissue and site of direct contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the registered substance, and probable different local absorption rates of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is

necessary to analyse both tissues to ensure a sufficient evaluation of the potential for mutagenicity at the site of contact in the gastro-intestinal tract. However, duodenum must be stored (at or below −70 ºC) until the analysis of liver and glandular stomach is completed; the duodenum must then be analysed only if the results obtained for the glandular stomach and for the liver are negative or inconclusive.

In case you decide to perform a comet assay according to the test method OECD TG 489, the test shall be performed by analysing tissues from liver as primary site of xenobiotic metabolism, glandular stomach and duodenum as sites of contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the registered substance, and probable different local absorption rates of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract.

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:

In vivo mammalian alkaline comet assay (test method: OECD TG 489) in rats, oral route, on the following tissues: liver, glandular stomach and duodenum;

OR

Transgenic rodent somatic and germ cell gene mutation assays (test method: EU B.58/OECD TG 488) in transgenic mice or rats, oral route on the following tissues: liver and glandular stomach. Duodenum must be harvested and stored for up to 5 years. Duodenum must be analysed if the results of the glandular stomach and of the liver are negative or inconclusive.

In your comments on the draft decision you expressed your agreement to perform the requested study as described above and indicated that your choice would be to conduct a Comet assay according to the OECD TG 489 via the oral route.

Germ cells:

A subsequent germ cell genotoxicity study (TGR/OECD TG 488, or CA on spermatogonia/OECD TG 483) may still be required under Annex IX of REACH, in case 1) an *in vivo* genotoxicity test on somatic cell is positive, and 2) no clear conclusion can be made on germ cell mutagenicity.

Therefore, in case you decide to perform the comet assay, you may consider to collect the male gonadal cells collected from the seminiferous tubules (as described by e.g. O'Brien *et al.*[2]) in addition to the other aforementioned tissues, as it would optimise the use of animals. You can prepare the slides for male gonadal cells and store them for up to 2 months, at room temperature, in dry conditions and protected from light. Following the generation and analysis of data on somatic cells, in accordance to Annex IX, Section 8.4., column 2, you should consider analysing the slides prepared with gonadal cells.

[2] O'Brien, J.M., Beal, M.A., Gingerich, J.D., Soper, L., Douglas, G.R., Yauk, C.L., Marchetti, F. (2014) Transgenic Rodent Assay for Quantifying Male Germ Cell Mutant Frequency. J. Vis. Exp. (90), e51576, doi:10.3791/51576

In case you decide to perform the TGR, you may consider to collect the male germ cells at the same time as the other tissues, in order to limit additional animal testing. According to the OECD 488 the tissues (or tissue homogenates) can be stored under specific conditions and used for DNA isolation for up to 5 years (at or below −70 °C). Following the generation and analysis of data on somatic cells, in accordance to Annex IX, Section 8.4., column 2, you should consider analysing the collected germ cells.

This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

2. Extended one-generation reproductive toxicity study (Annex IX, Section 8.7.3.)

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

The basic test design of an extended one-generation reproductive toxicity study (test method EU 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 IX of the REACH Regulation, if the available repeated dose toxicity studies (e.g. 28-day or 90-day studies, OECD TGs 421 or 422 screening studies) indicate adverse effects on reproductive organs or tissues or reveal other concerns in relation with reproductive toxicity. If the conditions described in column 2 of Annex IX are met, the study design needs to be expanded to include the extension of Cohort 1B, Cohorts 2A/2B, and/or Cohort 3. Further detailed guidance on study design and triggers is provided in in ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017).

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

ECHA considers that concerns in relation with reproductive toxicity are observed. More specifically, reduced fetal body weight and increased post-natal death of pups were observed in the high dose group (310 mg/kg/d), in the reproduction and developmental toxicity screening test conducted with the registered substance ([redacted] 2010). You have considered that the mortality of pups is "*probably related to the maternal toxicity*" observed at this dose in this study. Based on the information provided, ECHA understands that you refer to the reduction in food consumption and in body weight gain of dams during the lactation period. ECHA stresses that these findings on maternal food consumption and body weight gain were detected during the lactation period only and did not reach statistical significance. No such effects were observed during the pre-mating, mating and gestation period. ECHA considers it unlikely that the reduction in food consumption during the latаction period immediately causes offspring mortality. According to the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a/R.7.6: "Reduced body weight of offspring independent of litter size" and "Reduced survival of offspring" constitute a triggers for an extended one-generation reproductive toxicity study at REACH Annex IX level. Therefore, pursuant to Annex IX, Section 8.7.3. an extended one-

generation reproductive toxicity study is thus an information requirement for registrations of the registered substance.

You did not consider the information requirement for reproductive toxicity in Annex IX, Section 8.7.3., column 1, because no adverse effects on reproductive organs or tissues have been observed in the available repeated dose toxicity studies and these studies did not reveal other concerns in relation with reproductive toxicity. You indicated in the technical dossier and in your Chemical Safety Report that "*The available OECD 408 study (Repeated Dose 90-Day Oral Toxicity) in rats with a read-across substance as well as an OECD 422 study (Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test) in rats with the substance itself did not indicate*" adverse effects on the reproductive organs or tissues. You also referred to the results of a pre-natal developmental toxicity study conducted with the registered substance. On that basis you conclude that "*Based on the above presented data no adverse effects on fertility are to be expected. Further testing would therefore most likely not lead to other results and would in conclusion not improve the hazard assessment of the substance.*
The available data are considered reliable and sufficient and therefore further testing (extended onegeneration reproductive toxicity study) is not required and will not be carried out also taking animal welfare reasons into account".
However, ECHA considers that such adverse effects on reproductive organs or tissues or other concerns in relation with reproductive toxicity are observed from these studies. The reduction in fetal body weight and the increased offspring mortality in the screening study constitute a concern in relation with reproductive toxicity. Hence, an extended one-generation reproductive toxicity study is an information requirement.

In your comments to the draft decision you reiterated your views that the reduced fetal body weight and increased post-natal death of pups observed in the mid and high dose groups, in the reproduction and developmental toxicity screening test conducted with the registered substance are secondary to maternal toxicity. You consider that the dams were in poor health state impairing their nursing behaviour and leading in consequence to malnutrition of the pups which explains the reduced body weights and also mortalities observed during lactation period. You concluded that there is no information gap, as there is no concern for reproductive toxicity. Thus, further animal testing, i.e. an EOGRT study, is not required, neither from a scientific nor from a regulatory point of view.

Detailed information on the results obtained in the OECD 422 were included in the comments. However, no substantial new scientific arguments were brought forward in your comments to dismiss the effects observed in these studies. As indicated in the draft decision, according to the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a/R.7.6: "*Reduced body weight of offspring independent of litter size*" and "*Reduced survival of offspring*" constitute triggers for an extended one-generation reproductive toxicity study at REACH Annex IX level.

You have also submitted a category justification document as part of your comments to this draft decision. The category includes four structurally similar peroxyesters for which EOGRT studies have all been requested.

According to you "*the basic structures of all four substances are the same: a carboxylic acid moiety is linked to tert-butyl hydroperoxide forming a peroxyester. Adequate and reliable scientific information indicates that all four compounds have comparable toxicity profiles. Based on identical technical function (radical initiators of polymerisation processes), similar*

chemical structure, assumed similar metabolic pattern and a comparable toxicological profile the category approach is applicable. Results obtained from toxicity studies with one peroxyester may thus be applied to another peroxyester of the category".

For the endpoint reproductive toxicity, you indicated in your category justification document that "*organs of the reproductive system were not affected by any of the compounds. The same applies for all parameters examined regarding fertility. Effects on offspring were only present at doses of pronounced maternal toxicity and as such are attributed to be of secondary nature. Maternal toxicity included reduced food consumption as well as depressed body weight and/or body weight gain, mostly severe at the end of gestation and during lactation period. This is a common finding among all four substances of the category.*"

You specify that an EOGRT study is ongoing on the category member TBPEH (EC 221-110-7 ; CAS 3006-82-4). ECHA understands from the information provided in the comments that you intend to use the information obtained from this study to predict the properties of the registered substance. You asked ECHA to postpone the decision on the need for further studies with the registered substance until results of the EOGRT study with TBPEH are available. The results from this study were due to be provided to ECHA by 9 September 2019.

ECHA has taken into account the information provided in the category justification document attached to the comments on the draft decision. The final results from the EOGRT study conducted with TBPEH have been submitted to ECHA in a dossier update on 9 September 2019. The observation of impairment of the female reproductive performance during the course of the study has led to the modification of the study design and extension of cohort 1B to produce a second generation. Specifically, a reduction in the number of developing follicles and an increase in follicular atresia was noted in high-dose dams of the P generation. Reduced fertility index was noted in the P (high dose) and F1 (high dose and mid dose) generations. Increased incidence of post-natal mortality was detected in the high dose groups of the F1 and F2 generations suggesting inadequate nursing behaviour of dams.
These findings have triggered a self-classification of TBPEH as Repr. 1B - H360F: May damage fertility.

In the category justification document provided alongside the comments to the draft decision, you considered that, on the basis of the data set available at that time, "*organs of the reproductive system were not affected by any of the compounds. The same applies for all parameters examined regarding fertility*". These conclusions are contradicted by the findings of the EOGRT study conducted on TBPEH.

The findings from the EOGRT study on TBPEH and the results from the OECD TG 421 studies raise a concern on the reproductive toxicity of the other members of this category, including the registered substance. In the absence of self-classification of the registered substance as Repr. 1B on the basis of the data obtained on TBPEH, further information on the reproductive toxicity of the registered substance needs to be generated.

Hence, 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 to Annex IX, Section 8.7.3. is required. The following refers to the specifications of this required study.

b) The specifications for the required study

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 the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a, Section R.7.6 (version 6.0, July 2017), the starting point for deciding on the length of the 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* Chapter R.7a, Section R.7.6 (version 6.0, July 2017).

You have contested in your comments the need for a ten-week pre-mating exposure period. You indicate that "*according to the respective OECD guideline (the golden standard) 2 weeks are sufficient. A prolongation to 10 weeks based on the available data is not justified (e.g. testicular toxicity or effects on sperm integrity as mentioned in the respective OECD guideline) for the substance as this would unnecessary prolong the stress to the animals*".

The OECD TG 443 provides generic recommendations on the study protocol for an extended one-generation reproductive toxicity study. As indicated in the ECHA guidance, a two-week pre-mating exposure period is equivalent to the time required for epididymal transit of maturing spermatozoa and should allow the detection of post-testicular effects on sperm (during the final stages of spermiation and epididymal sperm maturation) at mating. According to the OECD TG 443, at the time of termination, when testicular and epididymal histopathology and analysis of sperm parameters are scheduled, the P and F1 males, will have been exposed for at least one entire spermatogenic process.

However, a two-week pre-mating exposure period in the context of an EOGRT study with a basic design does not provide information on the impact of exposure to the substance over the duration of the entire spermatogenic process on the reproductive function. According to the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a/R.7.6 "*Ten weeks cover the full spermatogenesis, sperm maturation and folliculogenesis before the mating allowing a meaningful assessment with the full spectrum of the effects after the same exposure history*". Furthermore, the information generated under REACH need to be adequate for risk assessment and for classification and labelling purposes. According to the ECHA *Guidance on information requirements and chemical safety assessment* Chapter R.7a/R.7.6, in the asbence of substance specific justification, "*a two-week premating period may be too short to produce results appropriate to conclude whether the substance meets the criteria for a category 1B reproductive toxicant, and thus may not be sufficient for classification and labelling purposes*".

Therefore, a ten-week pre-mating exposure period is appropriate in this specific case.
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.

If there is no relevant data to be used for dose level setting, it is recommended that results from a 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 6.0, July 2017) Chapter R.7a, Section 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

Based on the available information, 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 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;

While the specifications for the study design are given above, you shall also submit with the new endpoint study record a scientific justification on each of the following aspects: 1) length of the premating exposure duration and dose level selection, 2) reasons for why or why not Cohort 1B was extended, 3) termination time for F2 generation, and 4) reasons for why or why not Cohorts 2A/2B and/or Cohort 3 were included.

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 relevant information becomes available after this decision is issued to justify such an inclusion. Inclusion is justified if the available information, together with the new information shows triggers which are described in column 2 of Section 8.7.3., Annex IX and further elaborated in ECHA *Guidance on information requirements and chemical safety assessment* R.7a, chapter R.7.6 (version 6.0, July 2017). 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.

Deadline to submit the requested information in this decision

The timeline indicated in the draft decision to provide the information requested is 36 months from the date of adoption of the decision. In your comments on the draft decision you consider that sequential testing is appropriate and that the genotoxic properties of the substance need to be clarified before deciding on the need to conduct the EOGRT study. The timeline set in the decision already allows for conducting the *in vivo* mutagenicity study before starting the EOGRT study. The outcome of the *in vivo* mutagenicity study can then be taken into account when reassessing the need for and the design of the requested EOGRT study.

In the comments on the draft decision, you requested an extension of the timeline to 42 months because 36 months would not allow to conduct the experimental phase of the EOGRT study and the subsequent revisions of the risk assessment and of the technical dossier. You also referred to an ongoing compliance check decision on a structurally similar substance (CAS 13122-18-4) also requesting an EOGRT study, and request that the deadlines to provide both studies allows for conducting these studies in the same testing facilities for consistency reasons.

According to the statement from the testing laboratory attached to your comments, the performance of the preliminary work and of the experimental phase of an EOGRT study requires 14 to 18 months. The timeline of 36 months set in the decision significantly exceeds the duration specified by the testing laboratory and accommodates time to update your risk assessment and technical dossier. It is your responsibility to identify the appropriate test facilities to conduct the studies requested in regulatory decisions and to provide the results within the indicated timeline. In this case, it is your decision to perform both EOGRT studies in a single test laboratory.

ECHA has not extended the timeline to provide the information.

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 19 March 2018.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

ECHA notified you of the draft decision and invited you to provide comments within 30 days of the notification.

ECHA took into account your comments and amended the requests.

ECHA took into account your comments and did not amend the deadline.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

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 requests in this decision, or to otherwise fulfil the information requirements 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 the substance used for the new tests 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 compositions 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 the substance tested in the new tests 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 tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.