Public name/IUPAC name: *tert*-butyl 2-ethylhexaneperoxoate (TBPEH)
CAS number: 3006-82-4
EC number: 221-110-7
Registration number: 01-2119498310-40-0000

Lead Registrant on behalf of the Organic Peroxides Consortium:
United Initiators GmbH & CoKG, Dr. Gustav-Adolph-Str. 3, Pullach, D-82049, Germany

CLH proposal from December 2021

Proposals for amendments/changes under Article 50(1) of the REACH Regulation

General remarks:

The following response to ECHAs CLH proposal addresses different aspects at a level possible within the given time frame. Please note that no reply to individual points raised by ECHA does not mean that the registrant agrees with ECHAs conclusion or accepts the argument.

ECHA proposal	Registrant response
Identified uses	The organic peroxides consortium only defends industrial uses for the substance TBPEH. In fact, the industrial uses are considered to be intermediate uses by the lead registrant and many member registrants. The lead registrant and consortium members do not support any professional and consumer uses for this substance. Members still having these widespread uses in their dossier were contacted to remove them from their registration dossiers. There were no objections from non-consortium members to the removal of all consumer and professional uses. In conclusion, it is important to note that the use of the substance only occurs under well-controlled industrial settings and widespread uses can be excluded.
Classification as Skin Sens. 1B (H317) proposed	Agreement with classification as Skin Sens. 1B (H317).
Classification as Repr. 1B for fertility (H360f) proposed	Agreement with classification as Repr. 1B for fertility (H360f).

Classification as Repr. 1B for prenatal development (H360d) proposed	The current relevant human health classification as proposed by the registrant for TBPEH is Repr. 1B (H360f) for fertility. TBPEH has been proposed by ECHA to be also classified as Repr. 1B (H360d) for prenatal development based on the following studies. This commenting document evaluates the toxicologically-relevant effects of TBPEH in order to determine whether the dataset for TBPEH supports the above proposal for the classification of this substance for deleterious effects on prenatal development. Five studies evaluating the prenatal developmental and reproductive toxicity of TBPEH are currently available and listed here as follows: • OECD 421 Dose Range Finding Reproduction/developmental toxicity screening test, Wistar rat, males and females, n=10, animals/sex/dose, 2006. • OECD 421 Reproduction/developmental toxicity screening test, Wistar rat, males and females, n=10, animals/sex/dose, 2008. • OECD 414 Prenatal Developmental Toxicity Study, Pregnant female Hsd. Brl. Han: WISTAR rats, 24/dose group, GLP, 2013. • OECD 414 Prenatal Developmental Toxicity Study, inseminated New Zealand White rabbits (26-27 animals/dose group), GLP, 2018. • OECD 443, EOGRTS including cohorts 1A and 1B, Han:WIST rats, P0: n=24/sex/group, 4 groups, 2020. <u>OECD 421 Reproduction/developmental toxicity screening test (2008)</u> It is initially noted that the CLH proposal is utilising the data acquired from this OECD 421 reproduction/developmental toxicity screening test to justify the proposal for Repr. 1B for prenatal development (H360d). In the performed reproduction/developmental toxicity screening test (OECD 421), an increase in post-implantation loss and reduction in the number of live pups was found at 1000 mg/kg bw/d. In the F1 offspring, there was a reduction in mean body weights of pups and an increase in post-natal loss at 1000 mg/kg/day. It is important to note that the OECD 421 study is a protocol study that exclusively designed to “generate limited information concerning the effects of a test chemical on male and female reproductive performance such as gonadal function, mating behaviour, conception, development of the conceptus and parturition”.

Increase in post-implantation loss and reduction in the number of live pups was found at the highest dose of 1000 mg/kg per day.

A NOAEL was determined from the OECD 421 study as 300 mg/kg bw/day for parental and prenatal developmental toxicity. Evaluating the raw data, the following tables presents the post-implantation loss (%/litter) across the dose groups.

Table 1 Parenteral generation – all dams with living pups on Day 4 post-partum

Endpoint	**0 mg/kg bw/day**	**100 mg/kg bw/day**	**300 mg/kg bw/day**	**1000 mg/kg bw/day**
Total mean post-implantation loss (%/litter)	1.5	1.3	1.0	4.9
Early resorptions (%/litter)	0.3	0.0	0.2	4.0
Late resorptions (%/litter)	0.3	1.2	0.0	2.3
Dead foetuses	0.3	0.0	0.2	4.0
Viable foetuses (%/litter)	13.2	10.9	11.5	7.2

It is the view of the CLH proposal that it was the effect of the treatment at the highest dose of 1000 mg/kg that was linked to an increase of post-implantation loss that justifies the classification for Repr. 1B (H360d) for prenatal development. As mentioned above, this screening study was not designed to determine adverse effects on prenatal development, and moreover, for the doses of 0, 100, 300 and 1000 mg/kg bw/day, the values for the mean post-implantation loss were reported as 1.5, 1.3, 1.0 and 4.9% per litter, respectively. This means that there was more post-implantation loss in the concurrent control group than in the low-dose and mid-dose groups. It was only the high-dose group that produced the value of 4.9% per

	litter, however, it was produced in the absence of an appropriate dose-response relationship at lower doses, and it was an effect only occurred at the top dose and presented in a statistically-limited OECD 421 study (of only 10 animals per sex). It is thus that the statistical analysis is rather limited in the OECD 421 study, due the fact that only 10 animals of each sex are included in this protocol of this study. In the DRF study for the OECD 421 study it was also seen that for the doses of 0, 100, 300 and 1000 mg/kg bw/day, the values for the mean post-implantation loss were reported as 1.3, 1.3, 0.3 and 1.0% per litter, respectively, and thus, post-implantation loss was not influenced by treatment with the test item. Therefore, the results are inconsistent between the final study report and the dose range-finding study. There was marked variability in the study data from the OECD 421 study, and it is noted that increased post-implantation loss in a test substance-treated group is typically only considered an adverse effect when it reaches a level that is at least double that observed in the concurrent controls. According the DRF OECD 421 study this did not occur. In final OECD 421 study, the post-implantation loss reached a level that was at least double that seen in the concurrent control, however, the average post-implantation loss (relevant to prenatal developmental toxicity and natural delivery studies is 6.0 and 8.8%, respectively (MARTA and MTA, 1996). It should be noted also that post-implantation loss occurs in untreated as well as treated rodents and contributes to the normal variation in litter size. Moreover, more confidence can be placed in that the post-implantation loss was not adverse when considering that a dose-response relationship was present (together with an absence of malformations) and the concurrent control mean is within the historical control range, and it was also found to be below the historical control.

Table 2 Study and historically observed mean ranges for post-implantation parameters by species and strain

Endpoint	**OECD 421 Rat [at 1000 mg/kg/d]**	**OECD 414 Rat [at 1000 mg/kg/d]**	**HCD [Hsd. Brl. Han: WISTAR Rat]**	**OECD 414 Rabbit [at 300 mg/kg/d]**	**HCD [NZW Rabbit] (Ema et al., 2012)**
Total post-implantation loss (%/litter)	4.9	9.2	10.6 [5.8-14.1]	Occurrence of abortion: n = 8	Abortion rate: up to 9.0%
Early resorptions (%/litter)	4.0	6.4	8.2 [5.8-11.3]	30.7	N/A
Late resorptions (%/litter)	2.3	2.4	1.1 [0.0-1.4]	0.5	N/A
Dead foetuses	4.0	0.4	1.3 [0.0-4.8]	2.3	4.9-8.2
Viable foetuses (%/litter)	7.2	10.1	10.2 [9.2-12.0]	6.5	7.3-8.2

In both rodents and rabbits, the dead conceptus undergoes gradual degradation, followed by maternal reabsorption, and is referred to as a resorption; in rabbits, it is usually aborted instead of being reabsorbed. As indicated in the table above, an inverse relationship exists between the average litter proportions of total post-implantation loss and viable and successful foetuses. Moreover, the OECD 421 studies indicate that there were not significant differences in the numbers of successful implantations between the historical controls and treatment groups.

	In relation to the shortcomings of the study, this OECD 421 study was not performed in accordance with GLP. Also, in the OECD 421 study, it was stated that treatment at 1000 mg/kg was associated with an increase of post-implantation loss (of 4.9% per litter) and the post-natal loss was stated to statistically increase with 5/10 of the dams affected with a reduction of live pups (43 dead and 20 pups missing until day 4 post-partum). In order to calculate the post-implantation loss, an accurate number of full-term pups is needed and it has been stated that 20 pups were missing until day 4 post-partum. These 20 pups that were missing were not missing for reasons related to treatment and this means that if these 20 missing pups have been used to evaluate the post-implantation loss, it is likely that the estimation of the post-implantation loss has been overestimated. Also there were no other signals exist as there was a complete absence of malformations. Taken together with the post-implantation loss that is within the HCD range, shows that these findings do not indicate an exquisite effect on morphogenesis and suggest that the maternal homeostasis and nutritional status may have resulted in this subsequent insult to the products of conception. The registrant is of the view that this finding cannot therefore be utilised to derive classification for the proposed deleterious and direct effects on prenatal development. Based on the data acquired from this OECD 421 study, ANSES has then made the interpretation that "regarding the increase of post-implantation loss, this is rather considered as a developmental effect but it cannot be excluded that it is secondary to fertility alteration." Therefore, it is even the opinion of the evaluator that the observed post-implantation loss is likely to be secondary to a fertility alteration rather than a direct prenatal developmental effect. It is therefore the registrants intention to evaluate the data from this OECD 421 study together with more specific studies that hold relevance to prenatal development, to determine the real effects on prenatal development and not the apparent effects from an insufficient study whereby the evaluators have already determined the post-implantation loss to be secondary to a fertility alteration. <u>F1 offspring: Reduction in mean body weights of pups and increase in post-natal loss at the top dose of 1000 mg/kg/day</u> The CLH proposal notes that there was a reduction in mean pup body weights at the top dose of 1000 mg/kg bw/day and the inference has been made that this occurred without maternal toxicity. However, an analysis of mean pup bodyweight revealed no significant difference in any of the treatment groups. Furthermore, the difference in pup body weight in the top dose of 1000 mg/kg/day was slight (ca.

12% lower than controls), and there was a lack of an exhibited dose-response relationship, and the values were within the historical control range for the breed (Wistar rats) (CRL, Edinburgh). As no other signals of prenatal developmental toxicity exist, and the low foetal weight is within the historical control range for the breed (Wistar rats), this effect on foetal body weight is considerednot an adverse effect. It indicates that the foetuses weighing 5.7 grams at birth are able to survive and thrive and that the weight reduction was likely to be temporary.

Table 3 Mean pup weight in each litter for OECD 421 reproduction/developmental toxicity screening test

Parameter	**Dose groups (mg/kg bw/day)**			
	0.0	100	300	1000
Mean pup weight at birth	5.7	5.9	5.8	5.0

Therefore, the proposal for classification for Repr.1B H361d on the basis of this data is not justified, as the increased number of smaller pups only occurred at the highest dose tested of 1000 mg/kg bw/day, and there were no statistical significant difference in any treatment group. It is also noted that when considering percentage of dams none had greater than 10 pups in their litters, and this parameter was apparent in the top dose group suggesting this could be the cause of the apparent increase in ‘small’ pups at the top dose. Treatment at 1000 mg/kg was also associated with decreased food consumption in male (mean of 19.5 at days 1-8) and female (13.2 at GD 1-8) animals during the first week of the pre-pairing period and during lactation, indicating that there may have a fertility alteration but that direct prenatal developmental toxicity has not taken place. Clinical signs of salivation were seen in the top dose females at 1000 mg/kg bw/day. There was also a lack of similar effects on post-implantation loss in the range-finding study at the higher dose level (1000 mg/kg bw/day). This indicates maternal homeostasis has been disrupted and that the mother’s nutritional status was altered at 1000 mg/kg bw/day revealed by decreased food consumption in male and female animals during the first week of the pre-pairing and lactation periods. It is this subsequent insult to the products of conception that has led to the slight post-implantation loss secondary to altered fertility during this exact period. This is further substantiated by the fact that there were no malformations found and

	therefore this data does not signal an exquisite effect on morphogenesis and that the embryo or foetus is not more sensitive to treatment. The presence of significant maternal toxicity signals that the healthy mother has been affected during the pre-pairing and lactation periods and this can be evidenced by the clinical signs present as well as decreased food consumption that has led to slight post-implantation loss so that the affected mother could protect the foetuses secondary to an alteration of her physiological balance and therefore fertility (see effects on p53-stress response gene related to systemic toxicity). A NOAEL of 300 mg/kg bw/day was proposed based on parental and prenatal developmental toxicity, however, no numerical values were provided as to the exact post-implantation loss and slight reduction in pup bodyweight seen only at the highest dose. These values were not based on statistically significant reductions in post-implantation loss and pup body weight. In addition to its lack of statistical significance, it is thus likely that this effect has occurred in the presence of slight parental toxicity. Further to the OECD 421 study, there were two prenatal developmental toxicity studies performed on TBPEH, one in rats and one in the rabbit as follows. <u>OECD 414 Prenatal Developmental Toxicity Study in Han Wistar rats (2013)</u> This study tested Han Wistar rats from GD 5 to 19 with TBPEH by oral (gavage) administration at the dose levels of 200, 400 and 1000 mg/kg bw/day. There were no lesions that indicated direct prenatal developmental toxicity from TBPEH. TBPEH did not increase significantly the incidence of external and visceral variations and caused no skeletal malformations. As per the prior reproductive study, clinical signs of salivation was seen in the animals at 400 and 1000 mg/kg bw/day, indicating the presence of maternal toxicity. TBPEH did not reveal any adverse effect on the pregnancy and the intrauterine mortality of the conceptuses, the number of viable foetuses and their sex distribution, but it did show statistically significantly ($p<0.01$) reduced maternal body weight gain on the first three days of treatment and the statistically significantly ($p<0.01$) reduced maternal food consumption in the first week of treatment in the 1000 mg/kg bw/day dose. This decrease in maternal net body weight is an indicator of maternal systemic toxicity. <u>Increased incidence of foetuses with delayed ossification of skeletons in the 1000 mg/kg bw/day group</u> Furthermore, decreased maternal body weight gain during the late gestational period is linked with reduced skeletal mineralisation, and thus, the lower mean body

	weight (19 grams on GD 5-11) and the increased incidence of foetuses with delayed ossification of skeletons (7-13%) in the 1000 mg/kg bw/day group might be attributed to the statistically significantly reduced body weight gain and the affected food intake between GD 5 and 11 of the dams at this dose level. This slight delay in ossification at this highest dose level of 1000 mg/kg bw/day is not considered adverse; when the underlying cartilaginous structures are present and properly articulated; and considered a background finding and these values were within expected historical control findings (up to 16% for incomplete ossification) (CRL, Horsham; Mylchreest et al., 2005). These findings imply a less targeted, more generalised response. Based on these findings, a NOAEL was established for maternal toxicity and prenatal developmental toxicity at the highest dose of 1000 mg/kg bw/day. The registrant thus concludes that these findings do not justify classification as Repr. 1B for prenatal development. <u>OECD 414 Prenatal Developmental Toxicity Study in NZ White rabbits (2018)</u> A second prenatal developmental toxicity study (Anonymous, 2018) was performed in rabbits according to OECD 414. TBPEH was examined for its possible prenatal developmental toxicity. More significant groups of 26 (low and mid dose) and 27 (high dose) inseminated New Zealand White rabbits were treated with TBPEH by oral (gavage) administration daily at three dose levels of 30, 100 and 300 mg/kg bw/day respectively from GD 6 up to GD 27. There were no lesions that indicated direct prenatal developmental toxicity from TBPEH. The visceral development of the foetuses was not affected. There was only slightly lower foetal weight (mean of 29.71 grams) is within the HCD range of 40.5 (33.6–44.6) for NZ White rabbits. The CLH proposal has stated that 'early embryonic death (15% versus 6% in control) and post-implantation loss (17% versus 8% in control) (data compared to number of implantations) were increased at 300 mg/kg bw/day. These effects are statistically significant if the number and percent of resorptions are evaluated, but more importantly these findings are found to be not statistically significant if the mean number and SD are calculated. We can see that the mean number of viable foetuses were decreased (sum: 91 viable foetuses in treated group versus 191 in controls; not statistically significant) in the 300 mg/kg bw/day dose group. However, abortion and post-implantation loss, reduced foetal weight observed in the 300 mg/kg bw/day group as well as abortion of two does at 100 mg/kg bw/day can be considered as secondary to the markedly reduced food consumption (means of 43.1 at GD 6-9, 52.2 at GD 9-12, 43.3 at GD12-15 and 32.5 at GD 18-21).

	Significantly reduced food consumption was observed from start of the treatment up to GD 21 in the 300 mg/kg bw/day dose group ($p<0.01$ from GD 6 to 18 and $p<0.05$ from GD 18 to 21). The majority of the animals which had total post-implantation loss at 300 mg/kg bw/day had minimal or zero food consumption during the in-life phase and the post-implantation loss observed can be attributed to low food consumption seen and based on individual data. The study shows that there has been subtle body weight changes of up to 6% decrement in final body weight of females at 300 mg/kg/day and this is linked to the resulted slight increase on post-implantation loss. This indicates that the marginal increase of early embryonic death (15% versus 6%) and post-implantation loss (17% versus 8%) were linked to body weight changes and reduced food consumption, rather than a direct prenatal developmental effect. There is thus a meaningful biological relationship between this body weight decline and this is a marginal effect on post-implantation loss. As no other signals of direct prenatal developmental toxicity exist in the studies, disruption of maternal homoestasis and nutritional status (and thus systemic toxicity to the mother) is seen here and this is the most likely cause of the post-implantation loss observed. Moreover, as the body weight change was <6%, and this reveals an indirect effect or rather an effect secondary to the occurrence of markedly reduced food consumption and maternal toxicity and non-prenatal developmental toxicity seen at the highest dose of 300 mg/kg bw/day. These findings substantiate the findings from the OECD 421 and OECD 414 studies. <u>Crown-rump length observed in the highest dose of 300 mg/kg bw/day dose group</u> Crown-rump length observed in the highest dose of 300 mg/kg bw/day dose group as well as increasing skeletal variations mainly due to delayed ossification. However, this was considered to be linked to the lower body weights and as likely to be secondary to the severe maternal toxicity seen, and thus indicated that direct prenatal developmental toxicity did not take place. It can be evidenced that a maternal dimension is relevant as maternal body weight (means of -238.8 grams at GD 6-9, -85.8 grams at GD 9-12 and -101.3 grams at GD 15-18), food consumption (means of 43.1 at GD 6-9, 52.2 at GD 9-12, 43.3 at GD12-15 and 32.5 at GD 18-21) were affected and clinical findings (GI tract findings, vaginal bleeding, lying down, weakness, reduced activity and sneezing) occurred in parallel at 300 mg/kg bw/day. These are severe clinical signs of maternal systemic toxicity and do

	not indicate an exquisite effect on morphogenesis to the offspring and suggest that the mother is more sensitive at this high dose. Based on these findings, a NOAEL was established for maternal toxicity at lower dose of 30 mg/kg bw/day and prenatal developmental toxicity at the mid-dose of 100 mg/kg bw/day; based on effects being on present at the top dose of 300 mg/kg bw/day. In conclusion the slight effects on development were in most cases not statistically significant and only seen at marked maternal toxicity, which does not justify a classification as Repr. 1B (development). <u>OECD 443, EOGRTS including cohorts 1A and 1B in Han Wistar rats (2020)</u> In the EOGRTS, a lower body weight was also reported in pups at 300 mg/kg bw/day. However, the mean number of post-implantation loss, the mean number of total births, mean number of viable pups and live born and the live birth index (live pups/total birth) were comparable in all groups. Delivery data of dams was not adversely affected at 100, 300 or 1000 mg/kg bw/day dose level (P0 and Cohort 1B). The number of F1 offspring with reduced body weight on PND 0 (-6.5%) and body weight gain was suppressed between PND 0-21 (-8.6%). The lower foetal weight is within the laboratory's historical control range for the breed (10.77 grams), and therefore, this effect on foetal body weight is considerednot an adverse effect. It indicates that the foetuses weighing 10.77 grams at birth are able to survive and thrive and that the weight reduction was likely to be temporary. <u>Anogenital distance at 1000 mg/kg bw/day</u> The anogenital distance of each pup was determined on post-natal day 4. The anogenital distance was normalized to the cube root of the body weight. (The individual body weight of pups was determined with an accuracy of 0.01 g on post-natal day 4). The anogenital distances were not adversely affected by the TBPEH in male or female offspring at 100, 300 and 1000 mg/kg bw/day. Statistical significance was only detected at the shorter absolute anogenital distance of male and female pups at the highest dose of 1000 mg/kg bw/day. That said, once this data was normalised, the anogenital distances were found to be comparable with the control both in male and female offspring at 1000 mg/kg bw/day. <u>Eye opening at 100 mg/kg bw/day</u>

	Eye opening usually occurs within PND 11 to 18 in rats, with the average acquisition around PND 13 to 14. The number of F1 offspring with a negative response for eye opening at the control, 100, 300 and 1000 mg/kg bw/day was found to be 42, 31, 32 and 69%, respectively. However, a negative response for eye opening was only shown to be statistically significant (69%) on PND 14 at the highest dose of 1000 mg/kg bw/day (compared with 42% in the concurrent control group). This finding imply a less targeted, more generalised response, and is not indicative of direct prenatal developmental toxicity. Thus, the effects noted in the high dose group are sufficiently covered by a classification with Repr. 1B (fertility) and an additional classification for development is not required.
	<u>Overall Conclusion</u> This response to ECHAs CLH proposal evaluates the toxicologically-relevant effects of TBPEH in order to determine whether or not, it is considered that the dataset for TBPEH supports the above proposal for the classification of this substance. Based on the existing evidence, and following evaluation, it is thus considered that that Repr. 1B – H360d can be refuted and the effects upon which this proposed classification represent indicate effects which are secondary to a fertility alteration. Since no effects have provided sufficient evidence of direct prenatal developmental toxicity and that the potential capacity for an alteration of fertility were observed in the presence of parental toxicity, it is therefore appropriate to propose no classification for prenatal developmental effects. Regarding prenatal developmental toxicity, no classification is proposed since the effects observed were not sufficiently severe and occurred at doses in presence of maternal toxicity. Overall, based on the dataset for TBPEH, it is concluded that the proposed classification of Repr. 1B for prenatal development (H360d) is not supported and as the indicated alteration to fertility is covered by the Repr. 1B for fertility (H360f), no classification is proposed for prenatal development.

References:

[1] CRL. Reproductive Toxicology. Historical Control Data in Rats. Charles River Laboratories. Edinburgh. URL: https://www.criver.com/sites/default/files/noindex/historical-control-data/hcd-edi-rats.pdf
[2] CRL. Reproductive Toxicology. Historical Control Data in Rats. Charles River Laboratories. Horsham, PA. URL: https://www.criver.com/sites/default/files/resources/ReproductiveToxicologyHistoricalControlDatainRats.pdf

[3] CLH report Proposal for Harmonised Classification and Labelling Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2 International Chemical Identification: tert-butyl 2-ethylhexaneperoxoate (TBPEH) EC Number: 221-110-7 CAS Number: 3006-82-4. ANSES (on behalf of the French MSCA) 14 rue Pierre Marie Curie F-94701 Maisons-Alfort Cedex. Version number: V2. December 2021.
[4] Ema M, Aoyama H, Arima A, Asano Y, Chihara K, Endoh K, Fujii S, Hara H, Higuchi H, Hishikawa A, Hojo H, Horimoto M, Hoshino N, Hosokawa Y, Inada H, Inoue A, Itoh K, Izumi H, Maeda M, Matsumoto K, Matsuo S, Matsuura I, Mineshima H, Miwa Y, Miyata H, Mizoguchi Y, Nakano N, Naya M, Nishizawa H, Noritake K, Noyori H, Ohta T, Oku H, Shimizu T, Shimomura K, Shiozawa K, Takakura I, Tanaka R, Uesugi T, Yabe K, Yamauchi T, Yokoi R. Historical control data on prenatal developmental toxicity studies in rabbits. Congenit Anom (Kyoto). 2012 Sep;52(3):155-61. doi: 10.1111/j.1741-4520.2012.00365.x. PMID: 22925216.
[5] Mylchreest, E., Munley, S.M., and Kennedy Jr., G.L. (2005) Evaluation of the Developmental Toxicity of 8-2 Telomer B Alcohol. Drug and Chemical Toxicology, 28:315-328.
[6] OECD. SIDS INITIAL ASSESSMENT PROFILE (SIAP), CoCAM 6, September 30 - October 3, 2014, by NL ICCA.
[7] OECD 421 Dose Range Finding Reproduction/developmental toxicity screening test, Wistar rat, males and females, 2006. Non-GLP Dose Range-Finding Study for an OECD 421 Reproduction/Developmental Screening Study of TBPEH (CAS # 3006-82-4), in the Wistar Rat. TBPEH. RCC Study Number: A42355. Dr. A. Pössnecker, Dr. D. Flade., 2006.
[8] OECD 421 Reproduction/developmental toxicity screening test, Wistar rat, GLP OECD 421 Reproduction/Developmental Toxicity Screening Study of TBPEH (CAS # 3006-82-4) in the Wistar Rat. TBPEH. RCC Study Number: A42366. Report (Part I of II). Dr. A. Pössnecker, Dr. D. Flade, 2008.
[9] OECD 414 Prenatal Developmental Toxicity Study, Pregnant female Hsd. Brl. Han: WISTAR rats. Prenatal Developmental Toxicity Study With TBPEH in the Rat. Final Report. Study Number: 552.410.3876. TOXI-COOP ZRT. Sponsor: United Initiators GmbH, Dr.-Gustav-Adolph-Str. 3, D-82049 Pullach, Germany. Date: 11 July 2013.
[10] OECD 414 Prenatal Developmental Toxicity Study in New Zealand White rabbits. Prenatal Developmental Toxicity Study with TBPEH in the Rabbit by Oral (Gavage) Administration. Final Report. Study No: 552-414-2327. Date of Final Report: 8 May 2018. TOXI-COOP ZRT. Sponsor: United Initiators GmbH, Dr.-Gustav-Adolph-Str. 3, D-82049 Pullach, Germany, 2018.
[11] OECD 443, EOGRTS including cohorts 1A and 1B, Han:WIST rats, Extended One-Generation Reproduction Toxicity Study with TBPEH in the Rat. Final Report. Volumes 1 to 5. Study No. 552-443-3843. Date of Final Report: March 12, 2020. TOXI-COOP ZRT. Sponsor: United Initiators GmbH, Dr.-Gustav-Adolph-Str. 3, D-82049 Pullach, Germany, 2020.