# Comments on the Draft CLH report for tert-butyl hydroperoxide

**Subject:** Proposed harmonized classification and labeling of tert-butyl hydroperoxide (TBHP) as a category 2 mutagen in accordance with Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2

**Substance name:** tert-butyl hydroperoxide
**CAS Number:** 75-91-2
**EC Number:** 200-915-7

In the August 2013 CLH report, on tert-butyl hydroperoxide (TBHP), the TC-C&L concluded that TBHP is a mutagen and that the substance will only be mutagenic at the sites of first contact in somatic cells. Classification with Muta 2:H341 (CLP) was proposed.

We would like to comment on the above document as follows:

**Background**

The TC-C&L in September 2007 agreed to the provisional classification for Muta. Cat. 3; R68 (Muta. 2 H341). As DSD was to be replaced by CLP, this recommendation was not included in an ATP and a new proposal, in accordance with CLP, was therefore required. The Committee for Risk Assessment (RAC) requested a re-evaluation due to the differences between the DSD and CLP criteria. The information used in the current evaluation was based on the RAR of TBHP plus additional information available in the transitional report, mainly a Comet assay in the lung.

**Proposal for a Harmonised Classification and Labelling to be applied to tert butyl-hydroperoxide developed by the Dutch Authorites**

**Comments related to the interpretation of the data set available for TBHP**

We agree with the Dutch evaluation that there is convincing evidence that the substance is mutagenic/ genotoxic *in vitro*. As highlighted by the Dutch authorities, there is limited data available to conclude that the substance will be mutagenic *in vivo* at the sites of first contact in somatic cells as there are contradictory findings for this scenario. Nevertheless, the data (mainly the findings in a dominant lethal test after i.p. administration) are considered by the Dutch authorities sufficient to propose the above given classification, which should be noted represents a severely conservative interpretation of the data.

**Comments related to additional justification based on a read across (harmonization) between d-t-butyl peroxide (DTBP) and TBHP**

We disagree with the read across (harmonization) between TBHP and DTBP as it is done in the dossier by the Dutch authorities, as neither the data set at hand nor the physico-chemical properties of these two peroxides justify such a read across/harmonization taken into account ECHA's guidance/rules for a scientifically sound read across.

The justification by the Dutch Authorities for the harmonization was that, "The substance di-tert-butyl-peroxide (DTBP) was shown to be mutagenic to the bone marrow in an *in vivo* assay. As DTBP forms only radicals also formed by TBHP, it is likely that TBHP is also mutagenic." Neither data from the literature nor effects noted *in vitro* and *in vivo* in both substances support this conclusion. Experiments with DTBP did not result in positive *in vitro* mutagenicity results, whereas TBHP did. *In vivo*, DTBP showed some effects in an

oral micronucleus assay at dose levels above the limit dose. However a micronucleus assay, conducted in conjunction with a 90-day inhalation study was negative. While a micronucleus study following IP administration was positive in bone marrow, the spermatogonial assay was negative, which is contradictory to the results observed with TBHP. In addition, whereas TBHP is water soluble, DTBP is almost insoluble in water.

Taken these data together, we consider the read across/harmonization approach between DTBP and TBHP as not scientifically justified and not in line with ECHAs own guidelines. Therefore we recommend that this read across not be used.