CONSIDERATIONS OF ALTERNATIVE METHODS ON TESTING PROPOSALS IN YOUR REGISTRATION

Please complete this form and provide information for each of the points below.

If you have more than one testing proposal, please copy and paste the three bullet points within the same document and complete the details as appropriate for each testing proposal.

This document will be published on ECHA website along with the third party consultation on the testing proposal(s).

Public substance name: tris[2-[2-(2-methoxyethoxy)ethoxy]ethyl] orthoborate
EC Number (omit if confidential): 250-418-4
CAS Number (omit if confidential): 30989-05-0

Date of considerations: 17 December 2015

- **Hazard endpoint for which vertebrate testing was proposed:**

  Reproductive toxicity (pre-natal developmental toxicity) with the registered substance

- **Considerations that the general adaptation possibilities of Annex XI of the REACH Regulation were not adequate to generate the necessary information):**

  - available GLP studies
    Prenatal developmental toxicity was investigated in a GLP-compliant prenatal developmental toxicity study (OECD 414) in rats dosed at 30, 300 and 1000 mg/kg body weight B-TEGME. A further group of twenty-four time mated females was exposed to the vehicle only (Methyltriglycol or TEGME) to serve as a control. The oral administration of B-TEGME and TEGME by oral gavage in pregnant rats resulted in some delayed ossification effects in foetuses; however, these effects were not considered of toxicological relevance and are most probably secondary to maternal toxicity effects of TEGME that has been used as vehicle in concentrations from ca. 3200 mg/kg bw/d (high dose group) to ca. 4200 mg/kg bw/d (control/vehicle group).

    Taking into account the outcome of the prenatal developmental toxicity in rats and all other relevant available data testing for pre-natal developmental toxicity study on another species is considered necessary to fulfil the standard information requirement according to Annex X, 8.7.2. of the REACH Regulation and to conclusively assess the endpoint developmental toxicity/teratogenicity. Therefore, a pre-natal developmental toxicity study in rabbits is proposed.

  - available non-GLP studies
    No non-GLP-compliant developmental toxicity/teratogenicity studies are available.

  - historical human data
    No historical human data that could address the current data gap are available.

- (Q)SAR
  (Q)SAR tools sufficiently addressing the endpoint developmental toxicity/teratogenicity are currently not available.

- *in vitro* methods
  In vitro methods sufficiently addressing the endpoint developmental toxicity/teratogenicity are currently not available.

- weight of evidence
  Not sufficient data available which could be used in a weight of evidence approach.

- grouping and read-across
  No structurally related compound with data sufficient to address the data gap concerning developmental toxicity/teratogenicity has been identified.

- substance-tailored exposure driven testing [if applicable]
  Not applicable.

- [approaches in addition to above [if applicable]
  Not applicable.

- other reasons [if applicable]
  Not applicable.

- **Considerations that the specific adaptation possibilities of Annexes VI to X (and column 2 thereof) were not applicable** (instruction: free text):

  Column 2 of Annex X states that the **reproductive toxicity** studies do not need to be performed if:
  - *the substance is known to be a genotoxic carcinogen and appropriate risk management measures are implemented, or*
  - *the substance is known to be a germ cell mutagen and appropriate risk management measures are implemented, or*
  - *the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure.*

  None of these conditions are met by the registered substance. The test article is not classified for carcinogenicity or mutagenicity. Therefore, the above listed column 2 adaptions cannot be applied.

  Further column 2 adaptions are:
  - *If a substance is known to have an adverse effect on fertility, meeting the criteria for classification as toxic for reproduction category 1A or 1B: May damage fertility (H360F), and the available data are adequate to support a robust risk assessment, then no further testing for fertility will be necessary. However, testing for developmental toxicity must be considered.*
  - *If a substance is known to cause developmental toxicity, meeting the criteria for classification as toxic for reproduction category 1A or 1B: May damage the*

unborn child (H360D), and the available data are adequate to support a robust risk assessment, then no further testing for developmental toxicity will be necessary. However, testing for effects on fertility must be considered.

The available data on reproductive toxicity revealed no reproductive effect meeting the criteria for classification as toxic for reproduction category 1A or 1B: May damage the unborn child (H360D). Therefore, the above listed adaptions cannot be applied and a pre-natal developmental toxicity study in rabbits is proposed.