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: Fatty acids, C18-unsatd., dimers, reaction products with polyethylenepolyamines
EC Number (omit if confidential): 614-452-7
CAS Number (omit if confidential): 68410-23-1

Date of considerations: 22 February 2018

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

  Sub-chronic toxicity (90-day): oral with the substance Fatty acids, C18-unsatd., dimers, reaction products with polyethylenepolyamines

  Reproductive toxicity (pre-natal developmental toxicity) with the substance Fatty acids, C18-unsatd., dimers, reaction products with polyethylenepolyamines

- **Considerations that the general adaptation possibilities of Annex XI of the REACH Regulation were not adequate to generate the necessary information** (instruction: please address all points below):

  - available GLP studies

    An OECD 422 Repeated oral dose study was conducted with Fatty acids, C18-unsatd, dimers, oligomeric reaction products with tall-oil fatty acids and triethylenetetramine was *submitted within the registration for use in read-across. The no-observed-adverse-effect-level (NOAEL) for general and systemic toxicity after approximately 6 weeks of dosing in males and 7 weeks of dosing in females was considered to be 1000 mg/kg bw/day (i.e. the highest dose tested).*

  - available non-GLP studies
    Literature search conducted no public available data found on the specific substance.

  - historical human data
    Literature search conducted no public available data found on specific substance.

  - (Q)SAR
    As noted in the EU JRC (2010) Review of QSAR Models and Software Tools for predicting Repeated dose and Reproductive Toxicity (EUR 24522 EN - 2010), there are relatively few QSAR models for 90-day repeated dose and reproductive toxicity endpoints, and those that are available have limited

applicability domains. This is due to the lack of high quality data suitable for QSAR model development as well as the biological complexity of reproductive toxicity, which covers many incompletely understood mechanisms of action. The Danish EPA developed a QSAR database (http://qsar.food.dtu.dk/), which they use as for screening substances undergoing REACH evaluation. Although developmental toxicity is an endpoint in the Danish database, fertility and reproduction is not. In view of these limitations, PC considers that QSARs do not currently provide a viable means to assess the potential reproductive toxicity of **Fatty acids, C18-unsatd., dimers, reaction products with polyethylenepolyamines.** *Furthermore, even if validated QSAR models for male/female fertility effects were available, in our view, such data would be unlikely to be considered by ECHA (or Member States) as sufficient for the registration of the substance* Fatty acids, C18-unsatd., dimers, reaction products with polyethylenepolyamines.

- *in vitro* methods
  Suitable in-vitro methods are not available for the two endpoints in question

- weight of evidence
  Insufficient chronic data available

- grouping and read-across
  The substance C18-unsatd., dimers, oligomeric reaction products with tail-oil fatty acids and triethylenetriamine (EC Number 500-191-5) was selected as a main (source) substance for grouping/readacross this substance represents the highest tonnage band and also because it is a fatty acid TETA adduct. Due to the presence of free TETA further testing with C18-unsatd., dimers, oligomeric reaction products with tail-oil fatty acids and triethylenetriamine is considered to represent a toxicologically conservative approach for risk characterisation of all substances within the cluster.

  The data requirements for the following polyamidoamine substances are addressed by read-across to the polyamidoamine source substance; Fatty acids, C18-unsatd., dimers, oligomeric reaction products with tail-oil fatty acids and triethylenetriamine (EC No. 500-191-5, Cas No. 68082-29-1) [TOFA DimerFA TETA PAA]:

  Fatty acids, C18-unsatd., dimers, oligomeric reaction products with fatty acids, 16-18 and C-18 unsatd., branched and linear, tetraethylenepentamine and triethylenetetramine (EC No. 500-382-3, Cas No. 157707-73-8) [MonoFA DimerFA TETA TEPA PAA]

  Fatty acids, C18-unsatd., dimers, polymers with oleic acid and triethylenetetramine (EC No. 614-339-2, Cas No. 68154-62-1) [Oleic DimerFA TETA PAA]

  Fatty acids, C18-unsatd., dimers, oligomeric reaction products with tall oil fatty acids and tetraethylenepentamine (EC No. 500-289-8; Cas No. 103758-98-1) [TOFA DimerFA TEPA PAA]

  Target: Fatty acids, C18-unsatd., dimers, reaction products with polethylenepolyamines (EC No. 614-452-7, Cas No. 68410-23-1) [DimerFA PEPA PAA]

The justification for read-across is given below

The polyamidoamine substances: TOFA DimerFA TETA PAA, MonoFA DimerFA TETA TEPA PAA, Oleic DimerFA TETA PAA, TOFA DimerFA TEPA PAA and DimerFA PEPA PAA are formed as a result of the chemical reaction between the following components:

1. A monocarboxylic acid: Tall oil fatty acid (TOFA), monomeric fatty acid (MonoFA) or oleic acid; and/or
2. A polycarboxylic acid: dimerised fatty acid (DimerFA); and
3. An amine: triethylenetetramine (TETA; n = 2), tetraethylenepentamine (TEPA; n=3) and polethylenepolyamines; n= 2 to 7)

Taking into account the starting reaction materials, the manufacturing process and the composition of the reaction products, the polyamidoamine substances are considered comparable in terms of chemical characteristics.

- 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):

  There is insufficient substance specific data currently available to adapt the testing proposal for repeated dose toxicity or reproductive toxicity.