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: Amines, polyethylenepoly-, triethylenetetramine fraction
EC Number (omit if confidential): 292-588-2
CAS Number (omit if confidential): 90640-67-8

Date of considerations: 26 July 2017

- **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** (instruction: please address all points below):

- available GLP studies: There are reliable GLP-compliant studies available on developmental toxicity with the registered substance. An OECD 414 in rats via oral route – showing no developmental effects and a study similar to OECD 414 in rabbits via dermal route – showing no developmental effects.

- available non-GLP studies: There are non-GLP studies available on reproductive toxicity with the registered substance but these are all disregarded due to major methodological deficiencies. No conclusions on developmental toxicity can be drawn out of these studies.

- historical human data: There are no appropriate historical human data available addressing the endpoint developmental toxicity.

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

- *in vitro* methods: No validated or regulatory accepted alternative methods are available for replacing animal testing with respect to developmental toxicity.

- weight of evidence: There are reliabel GLP studies available for the registered substance. Therefore, no weight of evidence approach has to be considered.

- grouping and read-across: There are read-across data available on toxicity to devleopment. Studies with the structural analogues N,N'-bis(2-aminoethyl)ethane-1,2-diamine tetrahydrochloride / CAS 4961-40-4 / EC 225-604-3 and N,N'-bis(2-aminoethyl)ethane-1,2-diamine dihydrochloride / CAS 38260-01-4 / EC 253-854-3 suggest that these substances may cause copper depletion at higher dose levels,

which in turn may lead to fetotoxicity at end of pregnancy in rats (Keen, 1983) and reduced body and brain weights at end of pregnancy in mice (Tanaka et al, 1992 and 1993). However, there are considerable uncertainties for read-across to the registered substance with respect to toxicokinetics, dose levels and relevance of route of administration to humans.

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

- A pre-natal developmental toxicity study on a second species is not considered necessary. The available data show the registered substance does not cause teratogenic or early to mid-of-pregnancy developmental defects at a top oral dose level of 750 mg/kg bw. Similarly, no developmental toxicity was seen in a dermal study at a top dose of 125 mg/kg bw. While not yet at the limit dose levels, these dose levels are deemed adequate for this corrosive industrial chemical for which oral exposure is an unlikely route anyway and for which dermal exposure will be avoided as much as possible because of the skin corrosivity. Studies with structural analogues suggest that at end of pregnancy, fetotoxic effects may occur. Such effects, if occuring at all, will be visible in the proposed OECD 443 study for fertility (EOGRTS).