ECHA RESPONSE TO THIRD PARTY CONTRIBUTIONS FOR TESTING PROPOSALS INVOLVING VERTEBRATE ANIMALS

The following is an extract of the final ECHA decision of 21 June 2011 on testing proposals for the substance 11-aminoundecanoic acid (EC No. 219-417-6, CAS No 2432-99-7)[1], pursuant to Article 40(3) of the Regulation (EC) No 1907/2006.
All confidential information has been removed.

ECHA has examined the scientific information submitted by third parties during public consultation held from 08 April 2010 to 24 May 2010 for the following testing proposal(s):

- Pre-natal developmental toxicity (OECD 414 guideline) in a second species (rabbit)

Summary of the third party information

Regarding the information provided by the third party suggesting using results from a QSAR model "Nonlinear classification ANN QSAR Model for Combined 28-Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test", ECHA has identified several shortcomings in the data set provided by the third party with regard to the fulfilment of the conditions set under Annex XI, section 1.3 of the REACH Regulation. Therefore, ECHA concludes that predictions obtained from this QSAR model do not constitute reliable additional information on the registered substance.

Regarding the weight of evidence comments and evidence with regard to the need to conduct a second species test for developmental toxicity provided by the third party, ECHA notes the following:

- The conclusions of the OECD HPV assessment cannot directly be extrapolated to dossier evaluation as conducted under the REACH Regulation.
- Evidence of toxicity was observed in studies conducted with the registered substance, therefore the substance cannot be considered as of low toxicological activity as defined in Annexes IX and X, section 8.7, column 2.
- Concerning the rabbit as being the most appropriate species for a second pre-natal developmental toxicity test, there is evidence in the scientific literature (Janer et al., *Regulatory Toxicology and Pharmacology 50 (2008) 206-217*) indicating that pre-natal developmental toxicity tests conducted in the rabbit provide additional useful information in addition to that obtained from pre-natal developmental toxicity tests performed in rats. At the moment, considering the

[1] The substance name is the one used for the call to submit scientifically valid information.

variability related to pre-natal developmental toxicity testing, it remains unwarranted to omit an additional developmental toxicity study in a second species when negative results have been obtained in a pre-natal developmental toxicity study performed in the rat in the absence of additional specific data or evidence constituting robust scientific justifications for not conducting the test in a second species.

- Scientifically validated *in vitro* methods such as the embryonic stem cell text, the limb bud micromas culture and the whole embryo culture may provide additional information which can be assessed together with existing *in vivo* data in a weight of evidence approach. However, ECHA notes that the mentioned *in vitro* tests only cover some of the reproductive toxicity endpoints, modes of action and mechanisms covered by the *in vivo* pre-natal developmental toxicity tests and therefore cannot be used as stand alone replacement tests. Furthermore, these alternative methods are not part of the information requirements laid down in Annex VII to X of REACH and can therefore not be requested by ECHA in the context of a testing proposal examination.

The test for pre-natal developmental toxicity in rabbits proposed by the Registrant is thus necessary to fulfil the information requirement pursuant to section 8.7.2 of Annex X to the REACH Regulation.

Pursuant to Article 40(3)(a) of the REACH Regulation, the Registrant is thus requested to carry out the following test: Pre-natal developmental toxicity study in rabbits, oral route (method B.31 of Regulation (EC) No 440/2008; OECD test guideline 414).