EUROPEAN CHEMICALS AGENCY

Decision number: TPE-O-0000003202-89-04/F Helsinki, 16 October 2013

**DECISION ON A TESTING PROPOSAL SET OUT IN A REGISTRATION PURSUANT TO ARTICLE 40(3) OF REGULATION (EC) NO 1907/2006**

**For Hydrazine, CAS No 302-01-2 (EC No 206-114-9), registration number:** [redacted]

**Addressee:** [redacted]

The European Chemicals Agency (ECHA) has taken the following decision in accordance with the procedure set out in Articles 50 and 51 of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation).

I. Procedure

Pursuant to Article 40(1) of the REACH Regulation, ECHA has examined the following testing proposal submitted as part of the registration dossier in accordance with Articles 10(a)(ix) and 12(1)(e) thereof for Hydrazine, CAS No 302-01-2 (EC No 206-114-9), by [redacted] (Registrant).

- 28-day repeated dose toxicity study by inhalation (OECD 412) with a four week recovery period.

This decision is based on the the registration dossier as submitted with submission number [redacted] for the tonnage band of 1000 tonnes or more per year. This decision does not take into account any updates after 18 January 2013 the date upon which ECHA notified its draft decision to the Competent Authorities of the Member States pursuant to Article 51(1) of the REACH Regulation.

This decision does not imply that the information provided by the Registrant in his registration dossier is in compliance with the REACH requirements. The decision does not prevent ECHA from initiating a compliance check on the registration at a later stage.

On 7 December 2010, pursuant to Article 40(1) of the REACH Regulation, ECHA initiated the examination of the testing proposal set out by the Registrant in the registration dossier for the substance mentioned above.

ECHA held a third party consultation for the testing proposal from 15 July 2011 until 29 August 2011. ECHA did receive information from third parties (see section III below).

On 18 July 2012 ECHA sent the draft decision to the Registrant and invited him to provide comments within 30 days of the receipt of the draft decision.

On 26 November 2012 the Registrant updated his registration dossier.

ECHA considered the Registrant's comments received. On basis of the comments, only the deadline in Section II was amended. The Statement of Reasons (Section III) was changed accordingly.

On 18 January 2013 ECHA notified the Competent Authorities of the Member States of its draft decision and invited them pursuant to Article 51(1) of the REACH Regulation to submit proposals to amend the draft decision within 30 days of the receipt of the notification.

Subsequently, Competent Authorities of the Member States submitted proposals for amendment to the draft decision.

On 21 February 2013 ECHA notified the Registrant of proposals for amendment to the draft decision and invited him pursuant to Article 51(5) of the REACH Regulation to provide comments on those proposals for amendment within 30 days of the receipt of the notification.

ECHA reviewed the proposals for amendment received and decided not to amend the draft decision.

On 4 March 2013 ECHA referred the draft decision to the Member State Committee.

On 22 March 2013 the Registrant provided comments on the proposed amendments. The Member State Committee took the comments of the Registrant into account.

After discussion in the Member State Committee meeting on 24-25 April 2013, a unanimous agreement of the Member State Committee on the draft decision as modified at the meeting was reached on 25 April 2013. ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Decision on Testing Proposal

The following testing proposal is rejected pursuant to Article 40(3)(d) of the REACH Regulation:

- 28-day repeated dose toxicity study by inhalation (OECD 412) with a four week recovery period.

III. Statement of reasons

The decision of ECHA is based on the examination of the testing proposal submitted by the Registrant for the registered substance and scientific information submitted by third parties.

**Short-term repeated dose toxicity (28-day)**

a) Examination of the testing proposal

Pursuant to Article 40(3)(d) of the REACH Regulation, ECHA may reject a proposed test.

A short-term repeated dose toxicity study (28-day) is a standard information requirement as laid down in Annex VIII, Section 8.6.1. of the REACH Regulation. ECHA notes that the registration dossier for Hydrazine contains an oral 28-day repeated dose toxicity study. The Registrant has therefore complied with Annex VIII, Section 8.6.1. of the REACH Regulation. The Registrant has furthermore complied with Annex IX, Section 8.6.2. of the REACH Regulation by providing long-term toxicity studies by the inhalation and oral route.

The Registrant has however proposed to do a 28-day study by inhalation to "*strengthen the database and to assist the human health risk assessment and the DNEL derivation*".

Pursuant to Annex X, Section 8.6.4 the Registrant shall propose an additional repeated dose toxicity study in case of (a) toxicity of particular concern or (b) indications of an effect for which the available evidence is inadequate for toxicological evaluation and/or risk characterisation, or (c) particular concern regarding exposure.

ECHA recognises that for:

> Point (a) carcinogenicity of the registered substance may be of particular concern. The Registrant did however not sufficiently justify how the proposed 28-day toxicity study would contribute to further clarifying the irritation threshold linked to carcinogenicity of the substance. The lowest effect concentration of 0.066 mg/m$^3$ was derived from the one-year inhalation study with rat showing irritation and pre-neoplastic lesions in the respiratory tract. In a study on the "Oncogenic Potential of Inhaled Hydrazine in the Nose of Rats and Hamsters after 1 or 10 1-hr Exposures" (Latendresse, J. R., Marit, G. B., Vernot, E. H., Haun, C. C., and Flemming, C. D. (1995). *Fundam. Appl. Toxicol.* 27, 33-48) it was concluded that "the duration of exposure is a more significant factor than concentration in $N_2H_4$-induced nasal tumorigenesis. ECHA concludes that the Registrant has not justified why in light of this fact he would expect the 28-day study to further clarify the threshold for local irritation linked to carcinogenicity.
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> Point (b) the Registrant has furthermore not justified why the additional information from the 28-day study would allow a more appropriate toxicological evaluation and/or risk characterisation that would contribute to a refinement of risk management measures for carcinogens.
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> Point (c) the Registrant has not indicated any particular concern regarding exposure. ECHA notes that due to the classification as carcinogen category 1B the Registrant is already facing the obligation to maintain exposure as low as technically possible.

As the Registrant has not sufficiently justified the proposal for a 28-day study in line with Annex X, 8.6.4. ECHA rejects the testing proposal.

ECHA notes that the Registrant agreed to the rejection of the testing proposal when he received according proposals for amendment submitted by Member States Competent Authorities by a.o. referring to a recent proposal for a Binding Limit Value of 0.013 mg/m3 for hydrazine that – if or when implemented – will be "*the corner stone for risk management and it is expected that a more in depth knowledge on the Mode of Action most probably will not influence that Binding Limit Value*".

b) Consideration of the information received during third party consultation

ECHA received third party information concerning the testing proposal during the third party consultation. The third party information included a reference to the Latendresse et al. study referred to above. ECHA considered the scientific validity of the study and concluded that while this study by itself did not provide information on the proposed test, the conclusion related to the importance of exposure duration to hydrazine is highly relevant for the assessment of the need for a 28-day inhalation study.

IV. Information on right to appeal

An appeal may be brought against this decision to the Board of Appeal of ECHA under Article 51(8) of the REACH Regulation. Such appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on the ECHA's internet page at **http://echa.europa.eu/appeals/app_procedure_en.asp**. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

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Jukka Malm
Director of Regulatory Affairs