

Decision number: CCH-D-0000002619-67-04/F

Helsinki, 13 November 2012

**DECISION ON A COMPLIANCE CHECK OF A REGISTRATION PURSUANT TO ARTICLE 41(3) OF REGULATION (EC) NO 1907/2006****For Isoprene, CAS No 78-79-5 (EC No 201-143-3), 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 41(1) of the REACH Regulation ECHA has performed a compliance check of the registration dossier for Isoprene, CAS No 78-79-5 (EC No 201-143-3) submitted by [REDACTED] (Registrant).

This decision is based on 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 6 September 2012, 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 compliance check decision does not prevent ECHA from initiating further compliance checks on the present dossier at a later stage.

The compliance check was initiated on 30 May 2012 and is targeted at the technical dossier information for the standard information requirements of Sections 8.6.2. and 8.7.2. of Annex IX and of Section 8.7.2. of Annex X of the REACH Regulation as well as at human and environmental exposure assessment.

On 15 June 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.

By 16 July 2012 the Registrant did not provide any comments on the draft decision to ECHA.

On 6 September 2012 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 did not propose amendments to the draft decision and ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

## II. Information required

- 1) Pursuant to Articles 41(1)(a) and (b), 41(3), 10(a)(vii), 12(1)(e), 13 and Annexes IX and X of the REACH Regulation the Registrant shall submit the following information generated with the test methods as indicated on the registered substance subject to the present decision:
  - a. Sub-chronic toxicity study (90-day) in mice, inhalation route (Annex IX, 8.6.2., test method EU B.29/OECD 413);
  - b. Pre-natal developmental toxicity study in mice, inhalation route (Annex IX, 8.7.2., test method EU B.31/OECD 414);
  - c. Second pre-natal developmental toxicity study in rats, inhalation route (Annex X, 8.7.2., test method EU B.31/OECD 414);
  
- 2) Pursuant to Articles 41(1)(c), 14 and Annex I of the REACH Regulation the Registrant shall submit in the Chemical Safety Report:
  - a. Human exposure assessment and risk characterisation for the derived exposure scenarios.
  - b. Environmental exposure assessment and risk characterisation for the derived exposure scenarios.

ECHA notes that other registrants of the same substance have already submitted in their registration dossiers information from experimental studies involving vertebrate animals in order to fulfil the relevant information requirements. In accordance with Title III of the REACH Regulation, namely the obligations to request access to available information of studies on vertebrate animals (Articles 27 and 30 of the REACH Regulation), the Registrant shall not perform new testing involving vertebrate animals in order to comply with the present decision where such data is already available and is compelled to request this information from other registrants of the same substance.

More specifically, Article 30(1) of the REACH Regulation imposes on the Registrant to request from other substance information exchange forum (SIEF) participants to share the studies involving tests on vertebrate animals already available. The Registrant and the other SIEF participants shall make every effort to ensure that the costs of sharing the information are determined in a fair, transparent and non discriminatory way.

In addition, the Registrant is reminded of the obligation imposed by Article 11 of the REACH Regulation on all the registrants of the same substance to submit registrations for the same substance jointly.

Pursuant to Article 41(4) of the REACH Regulation the Registrant shall submit the required information in the form of an updated IUCLID dossier to ECHA by **13 February 2013**.

## III. Statement of reasons

Based on the examination of the technical dossier, ECHA concludes that the information therein, submitted by the Registrant for registration of the above mentioned substance for

the purpose of registration within the applicable tonnage band of above 1000 tonnes per year in accordance with Article 6 of the REACH Regulation, does not comply with the requirements of Articles 10, 12 and with Annexes I, IX, X and XI thereof. Consequently, the Registrant is requested to submit the information mentioned above that is needed to bring the registration into compliance with the relevant information requirements.

### **1) Missing information related to endpoints**

#### **a. Sub-chronic toxicity study (90-day)**

A sub-chronic toxicity study (90 day) is a standard information requirement as laid down in Annex IX, section 8.6.2. of the REACH Regulation. The technical dossier did not contain any robust study summaries for this endpoint. The data waiving cites 'other justification', but the information provided in the justification for the data waiving is a brief text stating that the substance is extensively studied and providing some NOAEC/ LOAEC values. This is not a valid adaptation according to column 2 of Annex IX, 8.6.2., or according to Annex XI of the REACH Regulation.

Consequently there is an information gap and it is necessary to provide information for the endpoint of Annex IX, 8.6.2. The Registrant is accordingly requested to submit information for this endpoint generated by the following test on the registered substance: 90-day repeated dose toxicity study in the mouse, by inhalation tests (EU B.29/OECD 413). The requested route of exposure is by inhalation based on the volatility of the substance.

The Registrant is requested to make every effort to obtain from other registrants this information available in joint submissions for the same substance for the update of the technical dossier and the CSR.

#### **b) Pre-natal developmental toxicity study**

A pre-natal developmental toxicity study for a first species is a standard information requirement as laid down in Annex IX, section 8.7.2. of the REACH Regulation.

The technical dossier did not contain any studies, study results or robust study summaries for this endpoint. The Registrant justified the adaptation of the information requirement based on Annexes IX, 8.7.2., Column 2 criteria for adaptations according to which the studies need not be conducted if: the substance is known to be a genotoxic carcinogen or a germ cell mutagen and appropriate risk management measures are implemented.

The Registrant has correctly stated that isoprene is classified for carcinogenicity (Category 2: R45 (Directive 67/548/EEC) and Carcinogenicity, Hazard Category 1B (Regulation (EC) No 1272/2008), and for mutagenicity (Category 3; R68 (Directive 67/548/EEC) and Mutagenicity 2, Germ Cell Mutagenicity, Hazard Category 2 (Regulation (EC) No 1272/2008)). However, the CSR of the Registrant includes no exposure assessment or the description of risk management measures, and it is not possible to verify that the adaptation complies with the rules for the adaptation. Accordingly, the adaptation based on Annexes IX and X, 8.7.2. Column 2 is invalid.

Given that there is no valid adaptation according to Annexes IX and X, 8.7.2. Column 2, it follows that the Registrant has an information gap for the endpoint of Annex IX, 8.7.2. and is therefore obliged to fulfil the information requirement. The Registrant is accordingly requested to submit information for this endpoint generated by the following test on the

registered substance: Prenatal developmental toxicity study in the mouse, by the inhalation route (EU B.31/OECD 414). The requested route of exposure is by inhalation based on the volatility of the substance.

The Registrant is requested to make every effort to obtain from other registrants this information available in joint submissions for the same substance for the update of the technical dossier and the CSR.

c) Second pre-natal developmental toxicity study

A pre-natal developmental toxicity study for a second species is a standard information requirement as laid down in Annex X, section 8.7.2. of the REACH Regulation. The technical dossier did not contain any studies, study results or robust study summaries for this endpoint. The Registrant justified the adaptation of the information requirement based on Annexes IX, 8.7.2., Column 2 criteria for adaptations according to which the studies need not be conducted if: the substance is known to be a genotoxic carcinogen or a germ cell mutagen and appropriate risk management measures are implemented.

The Registrant has correctly stated that isoprene is classified for carcinogenicity (Category 2: R45 (Directive 67/548/EEC) and Carcinogenicity, Hazard Category 1B (Regulation (EC) No 1272/2008), and for mutagenicity (Category 3; R68 (Directive 67/548/EEC) and Mutagenicity 2, Germ Cell Mutagenicity, Hazard Category 2 (Regulation (EC) No 1272/2008)). However, the CSR of the Registrant includes no exposure assessment or the description of risk management measures, and it is not possible to verify that the adaptation complies with the rules for the adaptation. Accordingly, the adaptation based on Annexes IX and X, 8.7.2. Column 2 is invalid.

Consequently there is an information gap and it is necessary to provide information for the endpoint of Annex X, 8.7.2. and the Registrant is therefore obliged to fulfil the information requirement. The Registrant is accordingly requested to submit the information for this endpoint generated by the following test on the registered substance: Prenatal developmental toxicity study in the rat, by the inhalation route (EU B.31/OECD 414). The requested route of exposure is by inhalation based on the volatility of the substance.

The Registrant is requested to make every effort to obtain from other registrants this information available in joint submissions for the same substance for the update of the technical dossier and the CSR.

## 2) Missing information related to the Chemical Safety Report

Annex I sets out the general provisions for assessing substances and preparing chemical safety reports (CSR).

a) Human exposure assessment and risk characterisation for the derived exposure scenarios

According to Article 14(1) and (3) and Annex I, section 0.6 of the REACH Regulation, the Registrant is required to perform a Chemical Safety Assessment (CSA) for the registered substance. The CSA shall cover 1) Human health hazard assessment, 2) Human health hazard assessment of physicochemical properties, 3) Environmental hazard assessment and 4) PBT and vPvB assessment. If as a result from these steps, the substance meets the

criteria for any hazard classes or categories<sup>1</sup> set out in Annex I to Regulation (EC) No 1272/2008 (CLP Regulation), or is assessed to be a PBT or vPvB, the CSA shall also include additional steps: Exposure assessment and Risk characterisation in accordance with Annex I, section 0.6.2. The additional steps of the CSA shall be carried out in accordance with Sections 5 (for Exposure assessment) and 6 (for Risk characterisation) of Annex I of the REACH Regulation.

Further, according to Annex I, section 5.0., the objective of the Exposure assessment is to make quantitative or qualitative estimate of the dose/concentration of the substance to which humans and the environment are or may be exposed. The assessment shall consider all stages of the life-cycle of the substance and shall cover any exposures that may relate to the hazards identified in sections 1) to 4) of section 0.6 of Annex I.

In the technical dossier and in the CSR the Registrant has named three identified uses. The substance has harmonised classification for human health properties (harmful by inhalation, irritant to eyes and skin) and for flammability. However, Section 9 of the CSR includes no exposure assessment (REACH Annex I, section 5). In addition, risk characterisation (Section 10 of the CSR) contains only a very general statement, and it is unclear how risk characterisation has been derived as it is not based on any exposure estimations. The Registrant is accordingly requested to generate exposure estimations and risk characterisation for all identified uses of the substance in and to update the CSR.

b) Environmental exposure assessment and risk characterisation for the derived exposure scenarios

The substance has a harmonised classification for being hazardous to aquatic environment (N; R51/53 Dangerous for the environment; Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (Directive 67/548/EEC) and Aquatic Chronic 3, H412: Harmful to aquatic life with long lasting effects (Regulation (EC) No 1272/2008)). However, the CSR contains no environmental exposure assessment for any of the exposure scenarios (ES) presented in the CSR. The risk characterisation for environment is only a statement: "*Overall conclusion on risks of isoprene to environment is summarized as follows:*

- **conclusion (ii) applies:** *There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already."*

This statement on risk characterisation is not based on any exposure assessment and is therefore invalid.

Therefore, the Registrant is requested to perform an environmental exposure assessment covering all life-cycle stages of the registered substance originating from manufacture and identified uses, and subsequently to perform risk characterisation for each exposure scenario to demonstrate the safe use of the substance, and to update the dossier accordingly.

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<sup>1</sup> • hazard classes 2.1 to 2.4, 2.6 and 2.7, 2.8 types A and B, 2.9, 2.10, 2.12, 2.13 categories 1 and 2, 2.14 categories 1 and 2, 2.15 types A to F.

• hazard classes 3.1 to 3.6, 3.7 adverse effects on sexual function and fertility or on development, 3.8 effects other than narcotic effects, 3.9 and 3.10.

• hazard class 4.1:

• hazard class 5.1;

IV. Timeline for updating the registration dossier

The present decision requires the Registrant to provide information that in accordance with Article 30(1) of the REACH Regulation he is required to obtain by sharing of information. ECHA considers three months to be sufficient time, (1) to request the studies from the respective data owners, (2) to receive the proof of the costs, (3) to make every effort to ensure that the costs of sharing information are determined in a fair, transparent and non discriminatory way, and (4) to pay and be granted permission to refer to the full study reports after receipt of payment by the respective data owner.

V. 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 an appeal shall be lodged within three months of receiving notification of this decision. Further information on the appeal procedure can be found on ECHA's internet page at [http://echa.europa.eu/appeals/app\\_procedure\\_en.asp](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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