EUROPEAN CHEMICALS AGENCY

Helsinki, 13 November 2019

Addressee: [redacted]

Decision number: CCH-D-2114489560-42-01/F
Substance name: 1,3-bis(isocyanatomethyl)benzene
EC number: 222-852-4
CAS number: 3634-83-1
Registration number: [redacted]
Submission number: [redacted]
Submission date: 10/03/2016
Registered tonnage band: 100-1000

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (the REACH Regulation), ECHA requests you to submit information on:

1. **Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) in a first species (rat or rabbit), oral route with the registered substance ;**

You have to submit the requested information in an updated registration dossier by ***20 November 2020***. You also have to update the chemical safety report, where relevant.

The reasons of this decision are set out in Appendix 1. The procedural history is described in Appendix 2 and advice and further observations are provided in Appendix 3.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

Authorised[1] by Wim De Coen, Head of Unit, Hazard Assessment

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

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Appendix 1: Reasons

1. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) in a first species

In accordance with Articles 10(a) and 12(1) of the REACH Regulation, a technical dossier registered at 100 to 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to IX to the REACH Regulation. The information to be generated for the dossier must fulfil the criteria in Article 13(4) of the same regulation.

A "pre-natal developmental toxicity study" (test method OECD TG 414) for a first species is a standard information requirement as laid down in Annex IX, Section 8.7.2. of the REACH Regulation. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

a) Information provided

You have not provided any study record of a pre-natal developmental toxicity study in the dossier that would meet the information requirement of Annex IX, Section 8.7.2. Instead you have provided the following justification for the adaptation: "*The* [registered] *substance is skin irritant and eye corrosive and severely toxic upon inhalation. In addition, in the sub-chronic inhalation toxicity study in rats no systemic effects but severe local effects were observed causing severe damage to the respiratory tract. Systemic effects appear at a dose at least with a factor >=20 compared to local effects, as no systemic effects occurred in the 90-d study. In addition, the oral systemic effects found in the OECD422 study are limited to effects on bodyweight in the parental animals, while no reproductive/fertility or developmental effects were seen at the highest dose tested (at least a factor 4 higher compared to the effect in parents). In addition, the substance is not mutagenic therefore this does not give an indication for possible effects on the reproduction/development. Overall, considering the severe local effects (inhalation, dermal) at much lower levels compared to systemic effects, the parental body weight effects observed with no reproduction/developmental effects, the local effects are most critical and severe (see the different classification and labeling) and thus the performance of a developmental toxicity study is not considered necessary in accordance with REACH Annex XI, section 1.*"

To support your adaptation you have provided the following sources of information: Combined Repeated Dose Toxicity Study with the Reproduction /Developmental Toxicity Screening Test (OECD TG 422, [redacted] 2009) by the oral route with the registered substance. In a different section of the technical dossier you have provided a sub-chronic repeated dose toxicity study (OECD TG 413, [redacted] 2000) with an analogue substance, Reaction mass of 2,5-bis(isocyanatomethyl)-bicyclo[2.2.1]heptane and 2,6-bis(isocyanatomethyl)-bicyclo[2.2.1]-heptane by the inhalation route.

While you have not explicitly claimed an adaptation, you have provided information that could be interpreted as an attempt to adapt the information requirement according to Annex XI, Section 1.2., weight of evidence. Hence, ECHA has evaluated your adaptation with respect to this provision, only.

b) ECHA's evaluation and conclusion of the information provided

Evaluation approach/criteria

An adaptation pursuant to Annex XI, Section 1.2. requires sufficient weight of evidence from several independent sources of information leading to the assumption/conclusion that a substance has or has not a particular dangerous property with respect to the information requirement in question including an adequate and reliable documentation while the information from each single source alone is regarded insufficient to support this notion.

Your weight of evidence adaptation needs to address the specific dangerous (hazardous) properties of the registered substance with respect to a pre-natal developmental toxicity study (OECD TG 414). Relevant elements are in particular exposure route, duration and levels, sensitivity and depth of investigations to detect pre-natal developmental toxicity (including growth, survival, external, skeletal and visceral alterations) and maternal toxicity.

Evaluation of the provided information

ECHA observes that the provided screening study does not provide the information required by Annex IX, Section 8.7.2. because it does not cover key parameters of a pre-natal developmental toxicity study like examinations of foetuses for skeletal and visceral alterations.

Furthermore, there is a concern from systemic effects as reported in this screening study, which was conducted via the oral route with the registered susbtance. ECHA concludes that the absence of systemic effects in the sub-chronic (90 day) toxicity study via the inhalation route with the analogue substance as stated above may well be due to dose-limiting local effects, as supported by the outcome of local irritation tests. This does not constitute a reliable basis to conclude on an absence of pre-natal developmental effects via the oral route with the registered substance. Similarly, an absence of mutagenic effects does not allow to conclude on an absence of pre-natal developmental effects.

Conclusion

Hence, the sources of information you provided, together with your justification for the adaptation, do not allow to conclude on the dangerous (hazardous) property of the registered substance with respect to the information requirement for Annex IX, Section 8.7.2. Therefore, the general rules for adaptation laid down in Annex XI, Section 1.2. of the REACH Regulation are not met and your adaptation of the information requirement is rejected.

Comments on the draft decision

In your comments on the draft decision you state that "*it is the highest priority of the industry to avoid any contact of workers with the substance at any time. As the handling in the supply chain is already optimized to avoid contact, more detailed information on the hazardous properties (resulting from further animal testing) will not provide the information to improve further worker protection.*" In order to strengthen your adaptation, you intend to perform "*workplace monitoring* [...] *to demonstrate absence of exposure in all scenarios of the manufacture and with all identified uses*", and analytical investigations to determine "*Residual monomer in the product and release of the monomer after polymerization from the product...*". ECHA understands that you attempt to adapt the information requirement according to REACH Annex XI, Section 3, "Substance-tailored exposure-driven testing".

ECHA acknowledges your intention. ECHA observes that biomonitoring methods are established for some diisocyanates, and that personal monitoring specific for a substance is more informative of a worker's exposure than static sampling at the workplace. It is your

responsibility if you wish to undertake additional studies in order to support an adaptation for the current request. ECHA concludes that all conditions under Annex XI Section 3 (a) or (c) must be fulfilled in order to meet the general rules of this adaptation.

In your comments on the draft decision you further state your intention to "*Substantiate read across approach by using data from hydrolysis product, 3-(aminomethyl)phenyl) methanamine ([redacted], CAS 1477-55-0)*" and "*4-Methyl-m-phenylene diisocyanate ([redacted], CAS 584-84-9)*" according to example 2 of the read-across assessment framework.

ECHA acknowledges your intention to submit a read-across adaptation according to REACH Annex XI, Section 1.5. ECHA observes that the studies performed with the analogous (source) substances and read-across justification are not part of your current registration dossier. ECHA concludes that the requirements of Annex XI Section 1.5 must be fulfilled in order to meet the general rules of this adaptation.

In your comments on the draft decision you state your intention to perform this request in case the information requirement cannot be adapted. ECHA acknowledges your intention.

ECHA will evaluate the data submitted to fulfil or adapt the information requirement after the deadline of this decision has passed.

As explained above, the information provided on this endpoint for the registered substance in the technical dossier does currently not meet the information requirement. Consequently there is an information gap and it is necessary to provide information for this endpoint.

According to the test method OECD TG 414, the rat is the preferred rodent species and the rabbit the preferred non-rodent species. On the basis of this default assumption ECHA considers testing should be performed with rats or rabbits as a first species.
ECHA considers that the oral route is the most appropriate route of administration for substances except gases to focus on the detection of hazardous properties on reproduction as indicated in ECHA *Guidance on information requirements and chemical safety assessment* (version 6.0, July 2017) Chapter R.7a, Section R.7.6.2.3.2. Since the substance to be tested is a liquid, ECHA concludes that testing should be performed by the oral route.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, you are requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: OECD TG 414) in a first species (rat or rabbit) by the oral route.

Appendix 2: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of your registration after the date when the draft decision was notified to you under Article 50(1) of the REACH Regulation.

The compliance check was initiated on 07 February 2018.

ECHA notified you of the draft decision and invited you to provide comments within 30 days of the notification.

ECHA took into account your comments and did not amend the request.

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Appendix 3: Further information, observations and technical guidance

1. This compliance check decision does not prevent ECHA from initiating further compliance checks on the present registration at a later stage.

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of your Member State.

3. In relation to the information required by the present decision, the sample of the substance used for the new tests must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is suitable to fulfil the information requirement for the range of substance compositions manufactured or imported by the joint registrants.

   It is the responsibility of all joint registrants who manufacture or import the same substance to agree on the appropriate composition of the test material and to document the necessary information on their substance composition. In addition, it is important to ensure that the particular sample of the substance tested in the new tests is appropriate to assess the properties of the registered substance, taking into account any variation in the composition of the technical grade of the substance as actually manufactured or imported by each registrant.

   If the registration of the substance by any registrant covers different grades, the sample used for the new tests must be suitable to assess these grades. Finally there must be adequate information on substance identity for the sample tested and the grades registered to enable the relevance of the tests to be assessed.