Helsinki, 24 November 2015

Decision/annotation number: Please refer to the REACH-IT message which delivered this communication (in format SEV-D-XXXXXXXXX-XX-XX/F)

DECISION ON SUBSTANCE EVALUATION PURSUANT TO ARTICLE 46(1) OF REGULATION (EC) NO 1907/2006

For 3,3'-dimethylbiphenyl-4,4'-diyl diisocyanate, CAS No 91-97-4 (EC No 202-112-7)

Addressees: Registrant(s)[1] of 3,3'-dimethylbiphenyl-4,4'-diyl diisocyanate

This decision is addressed to all Registrants of the above substance with active registrations on the date on which the draft for the decision was first sent for comment, with the exception of the cases listed in the following paragraph. A list of all the relevant registration numbers subject to this decision is provided as an Annex to this decision.

Registrants holding active registrations on the day the draft decision was sent are *not* addressees of this decision if they are: i) Registrant(s) who had on that day registered the above substance exclusively as an on-site isolated intermediate under strictly controlled conditions and ii) Registrant(s) who have ceased manufacture/import of the above substance in accordance with Article 50(3) of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation) before the decision is adopted by ECHA.

Based on an evaluation by the French Agency for Food, Environmental and Occupational Health Safety (ANSES) as the Competent Authority of France (evaluating MSCA), the European Chemicals Agency (ECHA) has taken the following decision in accordance with the procedure set out in Articles 50 and 52 of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH Regulation).

This decision is based on the last updated registration dossier (dated 31 July 2013), as available on 6 May 2014, i.e. the day on which the draft decision was notified to the Registrant(s) pursuant to Article 50(1) of the REACH Regulation.

This decision does not imply that the information provided by the Registrant(s) in the registration(s) is in compliance with the REACH requirements. The decision neither prevents ECHA from initiating compliance checks on the dossier(s) of the Registrant(s) at a later stage, nor does it prevent a new substance evaluation process once the present substance evaluation has been completed.

I. Procedure

Pursuant to Article 45(4) of the REACH Regulation the Competent Authority of France has initiated substance evaluation for **3,3'-dimethylbiphenyl-4,4'-diyl diisocyanate (TODI),** CAS No 91-97-4 (EC No 202-112-7) based on registration(s) submitted by the Registrant(s)

[1] The term Registrant(s) is used throughout the decision, irrespective of the number of registrants addressed by the decision.

and other relevant and available information and prepared the present decision in accordance with Article 46(1) of the REACH Regulation.

On the basis of an opinion of the ECHA Member State Committee and due to initial grounds for concern relating to human health/suspected CMR, suspected sensitiser, environment / suspected PBT, and for a high consumer use, was included in the Community rolling action plan (CoRAP) for substance evaluation to be evaluated in 2013. The updated CoRAP was published on the ECHA website on 20 March 2013. The Competent Authority of France was appointed to carry out the evaluation.

Regarding the initial concern on suspected sensitiser, as the Registrant(s) have classified the substance as a respiratory sensitiser and a skin sensitiser (Resp. Sens. 1; H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled. Skin Sens. 1A; H317: May cause an allergic skin reaction), no additional data are required.

Regarding the initial concern on "high consumer use", the Registrant(s) have advised against consumer uses in the updated dossiers (dated 17 May and 31 July 2013). Therefore, the initial concern is not relevant anymore.

Regarding the initial concern on PBT properties, available information provided by the Registrant(s) according to a Weight of Evidence (WoE) approach revealed that TODI should not be considered as Bioaccumulative (B) nor very Bioaccumulative (vB), and therefore not PBT. As TODI hydrolyses into TODA (orthotolidine; CAS 119-93-7) in aquatic compartment (refer to details below), the bioaccumulation in aquatic compartment should be based on TODA. BCF of TODA is < 100 L/kg, which indicates a low potential of bioaccumulation to aquatic organism, and BCF values below the regulatory threshold for considering TODA as Bioaccumulative (B) or very Bioaccumulative (vB). Based on the above considerations and the additional information requested in the current decision, no additional data are required to clarify the PBT concern at this point. However, during the course of the evaluation, the evaluating MSCA identified an additional concern in relation to the environmental risk assessment.

The evaluating MSCA considered that further information on exposure was required as preliminary conditions to clarify the related concerns for CMR, in particular carcinogenicity and mutagenicity, and environmental risk assessment.

Therefore, ECHA requires additional information on uses and exposure on TODI, the degradation product TODA (CAS 119-93-7; EC 204-358-0; 4,4'-bi-o-toluidine) and/or potential other degradation/reaction substances of concern likely to migrate out of the polymer. In a step-wise approach, depending on the information received in response to requests listed in section II, additional studies or information may be requested.

In particular, TODA is an environmentally and toxicologically relevant degradation product of TODI, because:

1) Scientific evidences show that TODI is rapidly hydrolyzed into TODA,
2) The exposure to TODA by metabolism in the organism (aqueous environment) is expected,
3) TODA has an harmonized classification (Acute Tox. 4; H302; Carc. 1B; H350; Aquatic Chronic 2; H411).

Additionally, it cannot be excluded that potential other degradation/reaction substances of concern may migrate out of the polymer, in particular during the compounding and production of articles. These elements justify ECHA's requests.

Therefore, the evaluating MSCA prepared a draft decision pursuant to Article 46(1) of the REACH Regulation to request further information. It submitted the draft decision to ECHA on 20 March 2014.

On 29 April 2014, ECHA sent the draft decision to the Registrant(s) and invited them pursuant to Article 50(1) of the REACH Regulation to provide comments within 30 days of the receipt of the draft decision.

Registrant(s) commenting phase

By 5 June 2014 ECHA received comments from the Registrant(s) of which it informed the evaluating MSCA without delay. The evaluating MSCA considered the comments received from the Registrant(s). The information contained therein is reflected in the Statement of Reasons (Section III) whereas no amendments to the Information Required (Section II) were made.

Commenting by other MSCAs and ECHA

In accordance with Article 52(1) of the REACH Regulation, on 11 June 2015 the evaluating MSCA notified the Competent Authorities of the other Member States and ECHA of its draft decision and invited them pursuant to Articles 52(2) and 51(2) 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 and ECHA submitted proposals for amendment to the draft decision.

On 17 July 2015, ECHA notified the Registrant(s) of the proposals for amendment to the draft decision and invited them pursuant to Articles 52(2) and 51(5) of the REACH Regulation to provide comments on those proposals for amendment within 30 days of the receipt of the notification.

The evaluating MSCA reviewed the proposals for amendment received and amended Section II: Information required (one point added) and Section III: Statement of Reasons of the draft decision.

Referral to the Member State Committee

On 27 July 2015 ECHA referred the draft decision to the Member State Committee.

By 17 August 2015, in accordance to Article 52(2) and Article 51(5), the Registrant(s) provided comments on the proposals for amendment. The Member State Committee took these comments into account.

After discussion in the Member State Committee meeting on 15–17 September 2015, a unanimous agreement of the Member State Committee on the draft decision as modified at the meeting was reached on 17 September 2015 and ECHA took the decision pursuant to Article 52(2) and 51(6) of the REACH Regulation. Specifically, Section II: information required and, respectively, Section III were amended; Section IV and V were removed as no longer applicable; a new Section IV providing notes for consideration by the Registrant(s) was added.

II. Information required

Pursuant to Article 46(1) of the REACH Regulation the Registrant(s) shall submit the following information:

1. Detailed exposure scenarios for industrial uses (polymerisation, research and development, compounding) by providing:
    - A detailed description of systems and Strictly Controlled Conditions (SCCs) used for the different intended fields of processing [detailed description of phases with potential exposure during the polymerisation step (including sampling); research and development activities, reference documents followed and corresponding up-to-date certificates, and details of the risk management measures applied and recommended to the user];
    - Recent quantitative data on TODI and the transformation product TODA in industrial settings (investigating the dermal and inhalation exposure of workers) and surrounding environment to demonstrate the efficiency of those systems and conditions regarding human and environmental exposure;
    - Exposure scenarios and estimations for workers and the environment for the research and development and compounding steps, and, if not under SCCs, for the polymerisation step;
    - Explanations and justifications of all the parameters used for the calculations of human and environmental exposure based on the guidance documents.

2. Provide the following information:
    - Details on the life cycle (from the chemical use to the service-life of manufactured articles) for each use and/or each type of manufactured articles, including a description of the downstream uses of the granulates and details on the articles;
    - Justify the level of residues of TODI, the transformation product TODA and potential other degradation/reaction substances originating from TODI and likely to migrate out of the polymer. This should be achieved by specifying the range of number of equivalents of TODI used in the polymerisation process and by providing a total extraction study;
    - Propose the corresponding exposure scenario and estimation for each situation of potential emission based on the amounts determined in the total extraction study.

Pursuant to Article 46(2) of the REACH Regulation, the Registrant(s) shall submit to ECHA: by **31 August 2016** an update of the registration(s) containing the information required by this decision, including, where relevant, an update of the Chemical Safety Report.

III. Statement of reasons

Further information on exposure is necessary to assess the risk for human health and the environment and the need to consider further information requests. For human health, there is a concern for mutagenicity and carcinogenicity, as explained in the notes for consideration to the Registrant in Section IV below, which also outlines how to address these concerns. For environment, there is a concern associated to the observed aquatic toxicity, as reflected by the Registrant's self-classification Aquatic Acute 1 and Aquatic Chronic 1.

Regarding the general comments received from the Registrant(s), ECHA would like to recall that according to the *Guidance on information requirements and chemical safety assessment,* Part B: Hazard assessment (v2.1, 2011):
"Degradation products and metabolites should be considered: Further investigation may be required for degradation products and metabolites if considered relevant for the chemical safety assessment, PBT assessment or classification and labelling."

TODI is considered to have a transient existence in the environment, because it is a

diisocyanate which reacts instantaneously with water to form insoluble polyurea and/or TODA, depending on the type of dispersion of TODI in water (in high dispersion conditions, formation of insoluble solid polyureas is expected to be low). As a consequence and as postulated by the Registrant(s) in the environmental part of the dossier, the relevant form of the substance to be considered is not the registered substance itself, but the substances resulting from the reaction of TODI with the water.

The available hydrolysis study qualitatively confirms the transient existence of the TODI and support the Registrant(s)' postulate that TODA is the relevant substance to be considered for the environmental risk assessment. This postulate is considered acceptable by ECHA, as TODA is bioavailable in the environment (soluble in water and not chemically inert), and because the other reaction product (i.e. polyurea) is considered insoluble and inert.

Analogously, the transformation of TODI into TODA should be considered as potentially relevant in relation to the exposure to humans in industrial setting and to articles made of the polymer.

For human health and the environment:

1. Detailed exposure scenarios for industrial uses (polymerisation, research and development, compounding):.

According to the Registrant(s), TODI is processed in closed systems, in strictly controlled conditions, and consequently, the fractions released to waste water and to soil have been estimated to be equal to 0 for the following uses:

- Industrial use of chemicals for polymer processing;
- Industrial use of intermediates.

The Registrant(s) provided descriptions of the closed systems and the strictly controlled conditions and declared that the facility would be converted to a fully closed system by end of 2013. This was confirmed by a declaration from the only downstream user, dated 4 July 2015, provided by the Registrant(s) during the commenting period following to the proposal for amendments.

However, the descriptions of the systems in place are not sufficiently detailed for human health and the environment. In particular, phases with potential exposure should be described with details (for example loading, manual fixation of funnel, manual production of the pre-polymer in a closed bucket, sampling). This requirement includes the polymerisation itself and the research and development activities. In addition, reference documents followed in the industrial facilities such as quality standards, quality management system procedures and other internal procedures, corresponding up-to-date certificates, as well as any patents referred to, should be provided if existing. The details of the risk management measures applied and recommended to the user are requested (this can be done using the template provided in the Guidance on intermediates[2] – Appendix 3).

The efficiency of those systems regarding human exposure and environmental exposure are not supported by quantitative data, in particular regarding the claim of no release to the environment.

Moreover, the Registrant(s) have calculated PEC (predicted environmental concentration) values, which is contradictory with the claim of no release to the environment.

[2] ECHA Guidance on intermediates, version 2, December 2010. ECHA-2010-G-17-EN.

Additionally, all the parameters necessary to calculate the human and environmental exposure values were not clearly indicated in the dossier and it is thus not possible to understand the assumptions considered for the calculations.

Furthermore, according to the Registrant(s), the end-product is a granulate which is then used industrially to produce articles. Workers and the environment may be exposed to TODI, TODA and potential other degradation/reaction substances originating from TODI during the industrial use of the granulate (compounding step). However, this step is not addressed in the dossier. Therefore, the compounding step of the granulate shall be described and exposure scenarios and risk characterisation for workers and the environment shall be provided to demonstrate safe use.

ECHA acknowledges the willingness of the Registrant(s) to provide more information on the use of the registered substance.

Therefore, pursuant to Article 46(1) of the REACH Regulation the concerned Registrant(s) are required to provide exposure scenarios for industrial uses (polymerisation, research and development, compounding) by providing:

- A detailed description of systems and Strictly Controlled Conditions (SCCs) used for the different intended fields of processing [detailed description of phases with potential exposure during the polymerisation step (including sampling); research and development activities, reference documents followed and corresponding up-to-date certificates, and details of the risk management measures applied and recommended to the user];
- Recent quantitative data on TODI and the transformation product TODA in industrial settings (investigating the dermal and inhalation exposure of workers) and surrounding environment to demonstrate the efficiency of those systems and conditions regarding human and environmental exposure;
- Exposure scenarios and estimations for workers and the environment for the research and development and compounding steps, and, if not under SCCs, for the polymerisation step;
- Explanations and justifications of all the parameters used for the calculations of human and environmental exposure based on the guidance documents.

2. Life-cycle of the articles

The emission scenarios presented in the documentation provided by the Registrant(s) are not detailed enough to cover the whole life-cycle of the registered substance (from the chemical use to the service-life of manufactured articles) for each use and/or each type of manufactured articles. The available information on products/articles into which the polymer is included and the use of these products/articles is very limited. In addition, missing scenarios are not properly justified.

In order to clarify the emission pathways, more information on the life-cycle of the registered substance is therefore needed. For each step of the life-cycle, an exposure scenario must be proposed, detailed and justified (in accordance with the relevant guidance documents).

In particular, the following information is needed:

- Description of the downstream uses of the granulates;

- Further details on the products/articles in which the polymer is included and their uses: description of the produced work pieces, where and how they are used, what

for, etc;

- The residual level of TODI in the work pieces (articles) is claimed to be below 1% but this is not supported by quantitative data. A total extraction from the granulate, a quantification of all TODI and TODA and identification and quantification of potential other degradation/reaction substances originating from TODI, shall be performed with a sufficient limit of quantification. This means that this limit has to be low enough in order to detect a low level of TODI/TODA/reaction substances leading to a hazard (carcinogenicity, for example). For this purpose, a Soxhlet extraction, or equivalent technique, with an adequate solvent can be performed. Validation of the performance of the method and analytical performance has to be provided. In addition, exposure estimation for human health and the environment based on these extracted amounts shall be performed. It is important to note that these amounts depend on the number of equivalent of TODI used in the polymerisation process and on the conditions of the compounding step; therefore, a worst-case scenario shall be investigated. For that purpose, information on the range of number of equivalents of TODI used in the polymerisation reaction is requested.

Therefore, pursuant to Article 46(1) of the REACH Regulation and as no additional data is currently provided in the Registrant(s)' dossier, the Registrant(s) are required to provide the following:

- Details on the life cycle (from the chemical use to the service-life of manufactured articles) for each use and/or each type of manufactured articles, including a description of the downstream uses of the granulates and details on the articles;
- Justify the level of residues of TODI, the transformation product TODA and potential other degradation/reaction substances originating from TODI and likely to migrate out of the polymer. This should be achieved by specifying the range of number of equivalents of TODI used in the polymerisation process and by providing a total extraction study;
- Propose the corresponding exposure scenario and estimation for each situation of potential emission based on the amounts determined in the total extraction study.

IV. Notes for consideration by the Registrant

Based on the information currently available in the registration dossier, ECHA considers that there is a concern regarding the mutagenicity and carcinogenicity properties of the registered substance (TODI). In particular, due to the concerns that ECHA has identified with regards to the *in vivo* UDS study for the mutagenicity endpoint, it is not possible at this stage to conclude on the mutagenicity potential. In addition, among the list of classification and labelling notifications present in the ECHA Classification and Labelling Inventory for the registered substance, one notifier has self-classified the substance as Muta 2, thus indicating that classification for this endpoint could not be excluded. In relation to this, ECHA reminds the Registrant(s) of the provisions of article 41 of the Classification, Labelling and Packaging Regulation (CLP, EC No 1272/2008), which states that the notifiers and registrants shall make every effort to come to an agreed entry to be included in the inventory.

Moreover, data found in literature for TODA, which the Registrant(s) confirms to be one of the hydrolysis products of TODI in the registration dossier, are also equivocal (NTP report n°390[3]; Z. You and al., 1993[4]; HSDB data bank[5]; IARC monography on benzidine and

[3] *Toxicology and carcinogenesis studies of 3,3'-dimethylbenzidine dihydrochloride in F344/N rats, NTP n°390.*

[4] Z. You and al., 1993. Ortho-substituent effects on the in vitro and in vivo genotoxicity of benzidine derivatives. Mutation research, 319(1993) 19-30.

[5] http://toxnet.nlm.nih.gov/cgi-bin/sis/search/a?dbs+hsdb:@term+@DOCNO+1640.

derivatives[6]). Therefore, no clear conclusion on genotoxicity can be made.

For carcinogenicity, as no data on carcinogenicity of TODI is available in the registration dossier, ECHA considered it reasonable to assess the carcinogenic effects of TODI based on those of TODA as worst case scenario. Based on the fact that TODA has a harmonised classification as Carc. 1b, that there are data from the literature indicating serious effects for this endpoint, as well as similar classifications for other isocyanates (MDI and MDA), ECHA considered that there is a carcinogenicity potential also for TODI.

Therefore, there is a residual concern on the safe use of the substance. To ensure proportionality and for animal welfare reasons, currently only information on exposure is requested.

Depending on the information provided in response to the present decision, further information on mutagenicity and on other endpoints necessary to clarify the initial grounds of concern may be requested during the follow-up to the substance evaluation. However, ECHA notes that based on the above scientific considerations there may already be sufficient evidence for the Registrant(s) to self-classify the registered substance as Carc. 1b. This would imply that additional risk management measures would have to be put in place. The Registrant(s) are invited to consider the option of self-classification as Carc. 1b, in addition to the existing self-classifications. Depending on the assessment of the data on exposure and/or in the absence of the self-classification proposed above and the information on the related risk management measures submitted in the updated registration dossier by the deadline specified in this decision, the evaluating MSCA will consider the need to request further information on mutagenicity and on other endpoints necessary to clarify the initial grounds of concern during the follow-up to the substance evaluation.

Additionally, the Registrant(s) are reminded of their obligations pursuant to article 22(1) of REACH, to update their registration dossier without undue delay with relevant new information and submitting it to ECHA. For example, this includes the studies on toxicity to aquatic organisms relevant for the registered substance, which the Registrant(s) indicated in his comments on the initial draft decision.

V. Information on right to appeal

An appeal may be brought against this decision to the Board of Appeal of ECHA under Articles 52(2) and 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 the ECHA's internet page at http://echa.europa.eu/regulations/appeals. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

Authorised[7] by Leena Ylä-Mononen, Director of Evaluation

Annex: List of registration numbers for the addressees of this decision. This Annex is confidential and not included in the public version of this decision.

[6] IARC Monographs on the Evaluation of Carcinogenic risks to humans. Volume 99. Some aromatic amines, organic dyes. 2010.

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