Decision number: CCH-D-2114308160-68-01/F Helsinki, 10 September 2015

DECISION ON A COMPLIANCE CHECK OF A REGISTRATION PURSUANT TO ARTICLE 41(3) OF REGULATION (EC) NO 1907/2006

For 4,4'-methylenebis(cyclohexylamine), CAS No 1761-71-3 (EC No 217-168-8), 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 4,4'-methylenebis(cyclohexylamine), CAS No 1761-71-3 (EC No 217-168-8) submitted by [redacted] (Registrant).

This decision is based on the registration dossier as submitted with submission number [redacted], for the tonnage band of 100 to 1000 tonnes or more per year. This decision does not take into account any updates submitted after 23 July 2015, 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.

The scope of this compliance check is limited to the standard information requirement of Annex VI, Section 2 and Annex VII to IX, Section 8 of the REACH Regulation.

This compliance check decision does not prevent ECHA to initiate further compliance checks on the present dossier at a later stage.

The compliance check was initiated on 13 September 2012.

On 21 November 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. That draft decision was based on submission number [redacted].

On 26 December 2012 ECHA received comments from the Registrant.

On 26 February 2015 the Registrant updated his registration dossier (submission number Nr [redacted]).

Concerning the information requirements of Annex IX, Sections 8.7.3., the compliance check requirement to submit information of a two-generation reproductive toxicity study (EU B.35, OECD TG 416) or an extended one-generation reproductive toxicity study (EU B.56, OECD TG 443) has been removed from this draft decision due to the legislative amendments to the REACH Regulation regarding Annex IX, Section 8.7.3. In light of this,

ECHA Secretariat did not consider further the Registrant's comments or update(s) concerning the information requirement of Annex IX, Section 8.7.3. However, ECHA

Secretariat did consider further the Registrant's comments and update(s) concerning the information requirements of Annex VI, Section 2., Annex IX, Section 8.6.2. and Annex IX, Section 8.7.2. On the basis of this information, Section II was amended. The Statement of Reasons (Section III) was changed accordingly. In particular, the requirement for the sub-chronic toxicity study has been removed from this draft decision, for the reasons explained in the 'Note to the Registrant' in section III.

On 23 July 2015 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 for amendment of the draft decision within 30 days of the receipt of the notification.

As no proposal for amendment was submitted, ECHA took the decision pursuant to Article 51(3) of the REACH Regulation.

The present decision relates solely to a compliance check requesting information on substance identity and a Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.). The other information requirement for a Two-generation reproductive toxicity study or an Extended one-generation reproductive toxicity study (Annex IX, Section 8.7.3.) is addressed in a separate decision although all endpoints were initially addressed together in the same draft decision.

II. Information required

A. Information in the technical dossier related to the identity of the substance

Pursuant to Articles 41(1)(a), 41(3) and 10(a)(ii) as well as Annex VI , section 2 of the REACH Regulation the Registrant shall submit for the registered substance:

1. The composition of each substance (Annex VI, 2.3.);
2. Chromatogram (Annex VI, 2.3.6.);
3. The description of the analytical methods or the appropriate bibliographical references for the identification of the substance (Annex VI, 2.3.7.); and

B. Information in the technical dossier derived from the application of Annexes VII to XI

Pursuant to Articles 41(1)(a) and (b), 41(3), 10(a)(vii), 12(1)(d), 13 and Annex IX of the REACH Regulation the Registrant shall submit the following information using the substance subject to this decision 4,4'-methylenebis(cyclohexylamine), CAS No 1761-71-3 (EC No 217-168-8) and the test method as indicated:

4. Pre-natal developmental toxicity study in rats or rabbits, oral route (Annex IX, 8.7.2.; test method: EU B.31/OECD 414).

Note for consideration by the Registrant:

The Registrant may adapt the testing requested above according to the specific rules outlined in Annexes VI to X and/or according to the general rules contained in Annex XI of the REACH Regulation. In order to ensure compliance with the respective information requirement, any such adaptation will need to have a scientific justification, referring to and conforming with the appropriate rules in the respective Annex, and an adequate and reliable documentation.

Failure to comply with the request(s) in this decision, or to fulfil otherwise the information

requirement(s) with a valid and documented adaptation, will result in a notification to the Enforcement Authorities of the Member States.

C. Deadline for submitting the required information

Pursuant to Articles 41(4) and 22(2) of the REACH Regulation the Registrant shall submit to ECHA by **19 September 2016** an update of the registration dossier containing the information required by this decision, including, where relevant, an update of the Chemical Safety Report.

At any time, the Registrant shall take into account that there may be an obligation to make every effort to agree on sharing of information and costs with other registrants.

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 100-1000 per year in accordance with Article 6 and 11(2) of the REACH Regulation, does not comply with the requirements of Articles 10, 12 and 13 and/or with Annexes VI-IX 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.

A. Information in the technical dossier related to the identity of the substance

Pursuant to Article 10(a)(ii) and Annex VI, section 2 of the REACH Regulation, the technical dossier of the registration shall include information on the identity of the substance. Annex VI, section 2 lists information requirements that shall be sufficient to identify the registered substance.

1. Composition of the substance (Annex VI, 2.3.):

The substance composition corresponds to the chemical representation of what the substance consists of and is therefore an essential part of substance identification and the corner stone of all the REACH obligations.

ECHA notes that the registration does not contain sufficient information for establishing the composition of the registered substance and therefore its identity, as required under Annex VI, section 2.3. of the REACH Regulation.

ECHA notes that the Registrant identified the registered substance as a mono-constituent substance. In line with the Guidance for identification and naming of substances under REACH (Version: 1.2, March 2012) mono-constituent substances are well-defined substances in which one constituent is present at a concentration ≥ 80% (w/w) (referred to thereinafter as "main constituent"). ECHA notes that the Registrant identified the substance as the well-defined substance: 4,4'-methylenebis(cyclohexylamine). Such substance corresponds to a multi-constituent substance including all three (cis/trans) isomers of 4,4'-methylenebis(cyclohexylamine). In addition the Registrant provided a gas chromatography report giving information that the three isomers are present in the substance and specifying for each of them the different concentration values. Based on the name and on the analytical data provided, ECHA concludes that the substance is a multi-constituent substance.

Furthermore, the Registrant did not include information on the typical concentration of the different isomers present in the substance in section 1.2 of the IUCLID dossier. Such information is necessary for ECHA to have a precise chemical representation of what the specific multi-constituent substance, which is the subject of this registration, consists of.

The Registrant is accordingly requested to provide the concentration ratio of the stereoisomers present in the substance. If such ratio is subject to variation, information on the concentration of each stereoisomer shall be given as a range.

As for the reporting of the ratio of (stereo)isomers in the registration dossier, the information should be included in the Remarks field under the reference substance assigned in IUCLID section 1.2 of the registration dossier.

In addition the Registrant is requested to modify the type of substance selecting "Multi constituent" from the dropdown list of the composition field under the "Type of substance" header in section 1.1.

In his comments to the draft decision the Registrant stated: "*The test substance identification will be described as a multiconstituent substance. We agree with ECHA that the substance was erroneously submitted as a monoconstituent substance.*" In the updated dossier, however, no new information has been provided. Consequently, ECHA has not amended the draft decision.

2. Chromatogram (Annex VI, 2.3.6.)

ECHA notes that the copy of a gas chromatogram has been attached to the dossier. However, ECHA observes that the provided chromatogram as such is not legible, in so far as a clear distinction between the different peaks detected can not be visually made.

Therefore the Registrant is requested to provide a legible print-out of the chromatogram as well as the report from the chromatographic analysis.

As for the reporting in the registration dossier, the information should be included in IUCLID section 1.4.

In his comments to the draft decision the Registrant agreed to provide a chromatogram. In the updated dossier, however, no new information has been provided. Consequently, ECHA has not amended the draft decision.

3. Description of the analytical methods (Annex VI section 2.3.7.)

ECHA observes that the Registrant provided the result of a gas chromatographic analysis, however, a detailed description of the method used to record the chromatogram, which is requested according to Annex VI section 2.3.7, was not included in the analytical report. The Registrant states in the gas chromatogram report that such information is confidential. ECHA regards this information as necessary for supporting the composition information. More specifically a description of the method used to analyze the substance enables understanding how the identification and quantification of the constituents present in the registered substance was carried out.

Accordingly, the Registrant is requested to provide a description of the analytical method used for the chromatographic analysis, including the experimental set-up. The information shall be sufficient for the method to be reproduced in line with the requirements of Annex VI section 2.3.7.

As for the reporting of the chromatographic data in the dossier, the information should be attached in IUCLID section 1.4.

In his comments to the draft decision the Registrant stated that he "did not provided details of the GC method as it is covered by the non-disclosure agreement with the method owner. Registrant will find the legal way how to enable method disclosure and then will update the dossier accordingly without undue delay." In the updated dossier, however, no new information has been provided. Consequently, ECHA has not amended the draft decision.

B. Information in the technical dossier derived from the application of Annexes VII to XI

Pursuant to Articles 10(a)(vii), 12(1)(d) of the REACH Regulation, a registration for a substance produced in quantities of 100-1000 tonnes per year shall contain as a minimum the information specified in Annex VII-IX of the REACH Regulation.

In the updated registration, the Registrant has adapted the standard information requirements for repeated dose toxicity (90-days; Annex IX, Section 8.6.2) and Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) by applying a read-across adaptation following REACH Annex XI, Section 1.5. With respect to the repeated dose toxicity endpoint and adaptation provided, further information is included at the end of Section III. For the pre-natal developmental toxicity study it is evaluated in the following section whether the provisions of Annex XI 1.5 are met.

a. Grouping of substances and read-across approach

Article 13(1) of the REACH Regulation provides that information on intrinsic properties of substances may be generated by means other than tests. Such other means include the use of information from structurally related substances (grouping of substances and read-across), "*provided that the conditions set out in Annex XI are met*".

Annex XI, 1.5. has the following provision: "*Substances whose physicochemical, toxicological and ecotoxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity may be considered as a group or 'category' of substances. Application of the group concepts requires that physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s) with this group by interpolation to other substances in the group (read-across approach).*"

b. Grouping approach and read-across hypothesis proposed by the Registrant

The Registrant has provided the following read-across hypothesis (analogue approach):
"The target 4,4'-methylenebis(cyclohexanamine) (PACM, CAS no. 1761-71-3) and its analogue chemical 2,2'-dimethyl-4,4'-methylenebis(cyclohexylamine) (DM-PACM; CAS no. 6864-37-5) are cycloaliphatic amines which share a common molecule skeleton. The functional groups of 4,4'-methylenebis(cyclohexanamine) (PACM, CAS no. 1761-71-3) are also present in the analogue, namely: primary aliphatic amino and cyclohexane groups. The target and analogue differ only in one functional group: one ortho-substituted methyl group is attached on each cyclohexane of the source chemical, while no methyl groups are attached to the cyclohexane groups of the target chemical.
It is suggested that read across can be performed for fate as well as ecotoxicity endpoints based on the close structural similarity between 4,4'-methylenebis(cyclohexanamine) (PACM, CAS no. 1761-71-3) and its analogue 2,2'-dimethyl-4,4'-

methylenebis(cyclohexylamine) (DM-PACM; CAS no. 6864-37-5). As the functional groups of the target chemical are also present in the analogue except for the additional methyl groups attached to the analogue chemical, similar behavior in the environment, biota, and mammalian organisms can be expected.
A common mode of action of 4,4'-methylenebis(cyclohexanamine) (PACM, CAS no. 1761-71-3) and its analogue can be hypothesized for ecotoxicity as well as mammalian toxicity endpoints based on the primary amine functionality of the chemicals."

c. Information submitted by the Registrant to support the grouping approach and read-across hypothesis

The Registrant has provided the following studies to support the read-across approach:

i. Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD 422; 2010) conducted in rats via the oral route with the registered substance 4,4'-methylenebis(cyclohexanamine), CAS no. 1761-71-3). The following doses were used: 0, 15, 50, 100 mg/kg/day. The following effects were observed (i) Systemic toxicity: at 50 mg/kg/day '*Treatment related and toxicologically relevant microscopic findings were noted for various organs, including the stomach (vaculolation of the stomach musculature; both sexes), liver (centrilobular vacuolation; both sexes), skeletal muscle (vacuolar myofiber degeneration and myofiber degeneration; both sexes), and the eyes (vacuolation of the cuboidal epithelium of the iris; both sexes).*'; and at 100 mg/kg/day a reduced body weight gain, and microscopic findings in the '*brain (vacuolation of the choroid plexus; both sexes)*' were noted in addition to the findings listed above. (ii) Reproductive/developmental toxicity: '*Reproduction toxicity was observed at 50 and 100 mg/kg characterized by a reduction in implantation site number. Developmental toxicity included a lower gestation and viability indices and increased postnatal loss for females at 50 mg/kg, and a reduced number of living pups at first litter check at 100 mg/kg.*';
ii. Sub-chronic toxicity study (OECD 408, 1990) conducted in rats via the oral route with the analogue substance 2,2'-dimethyl-4,4'-methylenebis(cyclohexylamine), CAS no. 6864-37-5. The following doses were used: 0, 2.5, 12, and 60 mg/kg/day (5 days/week). The following effects on systemic toxicity were observed: (i) at 12 mg/kg/day: '*The pathological examinations exhibited hepato and nephrotoxic and myocardially toxic findings.*', accompanied by reduced body weight gain and; (ii) and at 60 mg/kg/day observed effects included reduced retarded body weight gain, changes in white and red blood cell counts, and pathological findings were considered '*hepato and nephrotoxic, myocardially toxic and adrenotoxic (progressive transformation)*';
iii. Sub-chronic toxicity study (OECD 413, 1992) conducted in rats via the inhalation route (nose/head only; 6 hours/day, 5 days/week) with the analogue substance 2,2'-dimethyl-4,4'-methylenebis(cyclohexylamine), CAS no. 6864-37-5. The following doses were used: 0, 2, 12, and 48 mg/m^3. The following local effects and systemic toxicity were observed: '*Toxicity was observed in the high dose group (local irritative effects, decreased body weight gain, increased relative weights of liver, lung and kidney without pathology. In high dose males only, there was increased relative weights of adrenals and testes, without pathology or histopathology. Selected liver enzymes were increased in serum, and red blood cells were increased with decreased hemoglobin but increased hemosiderin deposits in the spleen. The only effect noticed in the mid-dose group was a single clinical chemistry parameter whose value was statistically significantly different from control values, but in the absence of liver histopathology and evidence of toxicity in other enzyme levels, this was considered not biologically significant.*'; and
iv. Pre-natal developmental toxicity study (OECD 414, 2001) conducted in rats via the

oral route with the analogue substance 2,2′-dimethyl-4,4′-methylenebis(cyclohexylamine), CAS no. 6864-37-5. The following doses were used: 0, 5, 15, 45 mg/kg/day. The following effects were observed (i) Maternal toxicity: *'At the mid-dose level (15 mg/kg bw/day), maternal toxicity was slight, substantiated only by reduced absolute (8%) and corrected (23%) body weight gain'; and 'The high dose of 45 mg/kg bw/d elicited some maternal toxicity: reduced food consumption (7% below controls), lower mean terminal body weights, impairment in absolute (13%) and corrected (44%) body weight gain. Minor macroscopic changes in the liver were observed: paleness, accentuated lobular pattern and/or whitish areas.'* (ii) Teratogenicity: *'There were no substance-induced, dose-related influences on the gestational parameters and no signs of prenatal developmental toxicity, especially no substance-induced indications of teratogenicity, up to and including the high dose-level (45 mg/kg/day).'*

d. ECHA evaluation of the grouping approach and read-across hypothesis in light of the provisions of Annex XI, 1.5.

ECHA understands that the proposed prediction is based on the hypothesis that two different substances, 4,4′-methylenebis(cyclohexanamine), CAS no. 1761-71-3 (target substance) and 2,2′-dimethyl-4,4′-methylenebis(cyclohexylamine), CAS no. 6864-37-5 (source substance) are assumed to cause the same effects due to identified structural similarities. Furthermore, ECHA notes that the Registrant has clearly identified the structural (dis)similarities between the source and the target substance; that there are certain physicochemical properties that appear to be similar; and that the data matrix provided allows a side-by-side comparison of the available information for the source and targets substance. Moreover, ECHA notes that the Registrant assumes this read-across hypothesis apply to all toxicological properties.

ECHA however observes that no explanation has been provided on how and why, as a result of the identified structural similarity, pre-natal developmental toxicity of the registered substance can be predicted from the available information. Furthermore, ECHA notes that the provided evidence contradicts the proposed prediction for the following reasons:

There are qualitative differences in the toxicological profiles (i.e. different effects observed) between the source and the target substances with regard to systemic toxicity:

i. The OECD 422 conducted on registered (target) substance study shows histopathological effects in stomach; liver, brain, skeletal muscle and eyes; in contrast
ii. the OECD 408 study conducted on the proposed analogue (source) substance shows histopathological effects in liver, kidney, heart, and adrenal glands.

Also for pre-natal developmental toxicity there are differences in the toxicological profiles between the source and the target substance:

iii. The OECD 422 study conducted on the registered (target) substance shows reproductive and developmental toxicity; in contrast
iv. the OECD 414 conducted on the proposed analogue (source) substance study observed no signs of pre-natal developmental toxicity.

e. Conclusion on the read-across approach

ECHA concludes that the proposed analogue substance (the source) and the registered (the target) substance are structurally similar. ECHA considers that structural similarity alone is not sufficient for predicting toxicological properties. It has to be justified why such prediction is possible in view of the identified structural differences and the provided evidence has to support such explanation. ECHA notes that with regard to repeated dose

toxicity different target organs/tissues for toxicity have been identified (as reflected in the histopathological findings) when the OECD 422 study conducted with the target substance is compared with the OECD 408 study conducted with the source substance. This suggests that the toxicity source substance differs from that of the target substance. Furthermore, with regard to developmental toxicity the OECD 422 study conducted with the target substance indicates a concern for developmental toxicity. In contrast, the OECD 414 study conducted with the source substance does not show effects with regard to developmental toxicity. Therefore, there are clear differences observed in the toxicity profiles of the source and target substances, and ECHA considers that this finding invalidates the hypothesis that the two different substances, 4,4'-methylenebis(cyclohexanamine), CAS No. 1761-71-3 (target substance) and 2,2'-dimethyl-4,4'-methylenebis(cyclohexylamine), CAS No. 6864-37-5 (source substance) cause the same effects, and ECHA considers it is not possible to predict the properties of the registered substance by postulating that the source and read-across substance have the same properties.
Besides the reference to the structural similarity there is no mechanistic explanation provided by the Registrant why the repeated dose (90-day) toxicity or the pre-natal developmental toxicity may be predicted using the results from the source substance. In view of the above reasoning, ECHA considers that human health effects of the registered substance cannot be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach). ECHA concludes that the Registrant has failed to meet the requirement of Annex XI, Section 1.5. that human health effects may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach).

Pursuant to Article 41(1) of the REACH Regulation, ECHA concludes that the adaptation of the Pre-natal developmental toxicity study (Annex IX, Section 8.7.2) in the technical dossier based on the proposed read-across approach to the analogue substance 2,2'-dimethyl-4,4'-methylenebis(cyclohexylamine), CAS no. 6864-37-5, does not comply with the general rules of adaptation as set out in Annex XI, 1.5., and cannot be accepted by ECHA

4. Pre-natal developmental toxicity study (Annex IX, 8.7.2.)

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. Adequate information on this endpoint needs to be present in the technical dossier for the registered substance to meet this information requirement.

The Registrant has conducted with the registered substance a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD 422). However, this study, which is only meant to fulfil the requirements of Annex VIII, 8.7.1., cannot be regarded as the equivalent of a pre-natal developmental toxicity (test method: EU B.31/OECD 414) and therefore cannot fulfil the requirements of Annex IX, 8.7.2. of the REACH Regulation. *Inter alia*, the OECD 422 study does not have a sufficient statistical power, and does not ensure analysis of all of the foetuses, while this is achieved in a pre-natal developmental toxicity study.

In the updated dossier, the Registrant has adapted the standard information requirements for Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.) by applying a read-across adaptation following REACH Annex XI, Section 1.5. This adaptation of the standard information requirements has been rejected as explained in Section III.B. points a-e above.

As explained above, the information available on this endpoint for the registered substance in the technical dossier does 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 EU B.31/OECD 414, the rat is the preferred rodent species, the rabbit the preferred non-rodent species and the test substance is usually administered orally.

Therefore, pursuant to Article 41(1) and (3) of the REACH Regulation, the Registrant is requested to submit the following information derived with the registered substance subject to the present decision: Pre-natal developmental toxicity study (test method: EU B.31./OECD 414) in rats or rabbits by the oral route.

C. Deadline for submitting the required information

In the draft decision communicated to the Registrant the time indicated to provide the requested information was 36 months from the date of adoption of the decision. This period of time took into account the fact that the draft decision also contained the requests for a sub-chronic toxicity study (OECD 413); and two-generation reproductive toxicity study (EU B.35, OECD TG 416) or an extended one-generation reproductive toxicity study (EU B.56, OECD TG 443) (Annex IX, Section 8.7.3.). As these studies are no longer addressed in the present decision, ECHA Secretariat considers that a reasonable time period for providing the required information in the form of an updated IUCLID5 dossier is 12 months from the date of the adoption of the decision. The decision was therefore modified accordingly.

Note for consideration by the Registrant:

Sub-chronic toxicity study (90-days)

In the draft decision communicated to the Registrant there was a request for a sub-chronic toxicity study (90-days). The information provided by the Registrant in his updated dossier led ECHA to conclude that sub-chronic toxicity study (90-days) is no longer needed and therefore the initial request is removed from the amended draft decision. However, it is important, as explained below, to communicate the reasons for such conclusion.

As already explained above (see section III.B. points a-e) the proposed adaptation based on a grouping of substances and read-across approach has been rejected by ECHA. However, ECHA notes that the in the updated dossier the Registrant has provided a Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD 422) conducted with the registered substance. Based on the identified LOAEL of 50 mg/kg/day and an assessment factor of 3 (sub-acute to sub-chronic) the Registrant has extrapolated to the 90-day LOAEL (17 mg/kg/day); and concluded that the registered substance meets the classification criteria for STOT Rep. Exp. 2 - H373; Target organs Liver, muscles. Subsequently, the Registrant has in the up-dated dossier self-classified the substance accordingly.

ECHA notes that according to Column 2, Annex IX, section 8.6.2 The sub-chronic toxicity study does not need to be conducted if: ' – *a reliable short-term study (28 days) is available showing severe toxicity effects as R48, for which the observed NOAEL-28 days, with the application of an appropriate uncertainty factor, allows the extrapolation towards the NOAEL-90 days for the same route of exposure'*.

Based on the above mentioned information provided in the updated dossier ECHA concludes that the conditions of Column 2 of Annex IX, section 8.6.2 are met in this case. Therefore

there is no need to conduct a sub-chronic toxicity study (90-days) for the registered substance subject to the present decision. ECHA has therefore removed the request from the amended draft decision.

However, ECHA notes that the Registrant is currently in his dossier using the sub-chronic studies conducted using the analogue substance 2,2'-dimethyl-4,4'-methylenebis(cyclohexylamine); CAS no. 6864-37-5 as a starting point for the DNEL derivation. As explained above (see section III.B. points a-e) the read-across approach has been rejected. Consequently, data on the analogue substance is no longer a valid starting point for the DNEL derivation as it is not adequate for the purpose of classification and labelling and/or risk assessment. The Registrant is advised to: re-derive all affected DNELs by applying the assessment factors as recommended by ECHA (see Guidance on information requirements and chemical safety assessment Volume 8, Chapter R.8) to the most appropriate starting point identified in study conducted with the registered substance; and update the technical dossier accordingly.

The results of the study requested under section II.B. shall be taken into account when revising the DNELs.

IV. Adequate identification of the composition of the tested material

ECHA stresses that the information submitted by other joint registrants for identifying the substance has not been checked for compliance with the substance identity requirements set out in Section 2 of Annex VI of the REACH Regulation.

In relation to the information required by the present decision, the sample of substance used for the new studies must be suitable for use by all the joint registrants. Hence, the sample should have a composition that is within the specifications of the substance composition that are given 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 substance tested in the new studies 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 by each registrant. If the registration of the substance by any registrant covers different grades, the sample used for the new studies must be suitable to assess these grades.

Finally there must be adequate information on substance identity for the sample tested and the grade registered to enable the relevance of the studies to be assessed.

V. General requirements for the generation of information and Good Laboratory Practice

ECHA reminds registrants of the requirements of Article 13(4) of the REACH Regulation that ecotoxicological and toxicological tests and analyses shall be carried out in compliance with the principles of good laboratory practice (GLP).

According to Article 13(3) of the REACH Regulation, tests that are required to generate information on intrinsic properties of substances shall be conducted in accordance with the test methods laid down in a Commission Regulation or in accordance with other international test methods recognised by the Commission or the European Chemicals

Agency as being appropriate. Thus, the Registrant shall refer to Commission Regulation (EC) No 440/2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 as adapted to technical progress or to other international test methods recognised as being appropriate and use the applicable test methods to generate the information on the endpoints indicated above.

VI. 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. The notice of appeal will be deemed to be filed only when the appeal fee has been paid.

Authorised[1] by Guilhem de Seze, Head of Unit, Evaluation

[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.