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Decision number: CCH-D-0000001600-87-10/F Helsinki, 2 July 2012

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

For m-phenylenebis(methylamine), CAS 1477-55-0 (EC NUMBER 216-032-5), 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 the ECHA has performed a compliance check of the registration dossier for m-phenylenebis(methylamine), CAS 1477-55-0 (EC number 216-032-5), Registration Number: [redacted] submitted by [redacted] (Registrant), latest submission number [redacted], for 1000 tonnes or more per year.

The compliance check was initiated on 16 June 2011.

On 15 November 2011 ECHA notified the Registrant of its draft decision and invited him pursuant to Article 50(1) of the REACH Regulation to provide comments within 30 days of the receipt of the draft decision.

On 15 December 2011 the Registrant provided to ECHA comments on the draft decision.

ECHA considered the Registrant's comment received concerning the prolongation of the commenting period and did not amend the draft decision.

On 2 March 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 submitted proposals for amendment to the draft decision.

On 4 April ECHA notified the Registrant of the 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 has reviewed the proposals for amendment received and decided to amend the draft decision.

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On 16 April 2012 ECHA referred the draft decision to the Member State Committee.

On 2 May 2012 the Registrant provided comments on the proposed amendment. The Member State Committee took the comments of the Registrant into account.

After discussion in the Member State Committee meeting on 6-8 June 2012, a unanimous agreement of the Member State Committee on the draft decision as referred to MSC and modified at the meeting was reached on 7 June 2012.

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

II. Information required

1) Pursuant to Articles 41(1)(a) and (b), 41(3), 12(1)(e) and Annexes IX-X of the REACH Regulation the Registrant shall submit the information using the test method as indicated below:

   a. Sub chronic toxicity (90 days), via the inhalation route in the rat (Annex IX, 8.6.2; OECD TG 413));
   b. Pre-natal developmental toxicity via the oral route in the rat (Annex IX, 8.7.2.; OECD TG 414; EU Test Method B.31);

   Data from a second pre-natal developmental toxicity study on another species is a standard information requirement according to Annex X, 8.7.2. of the REACH Regulation. The Registrant should firstly take into account the outcome of the pre-natal developmental toxicity on a first species and all other relevant available data to determine if the conditions are met for adaptations according to Annex X, 8.7. column 2, or according to Annex XI. If the Registrant considers that testing is necessary to fulfil this information requirement, he should include in the update of his dossier a testing proposal for a pre-natal developmental toxicity study on a second species.

   The Registrant shall determine the appropriate order of the studies taking into account the possible outcomes and considering the possibilities for adaptations of the standard information requirements according to column 1 or 2 provisions of the relevant Annexes of the REACH Regulation.

2) Pursuant to Articles 41(1)(c), 41(3), 10(a)(iii) and (b), 14, Annex I and Annex II of the REACH Regulation the Registrant shall submit in the chemical safety report:

   a. Derived No-Effect Levels (DNEL) derivation, exposure assessment and risk characterisation for short term and long term worker exposure (Annex I, sections 1.4., 5 and 6);
   b. A description of the operational conditions (OCs) and risk management measures (RMMs) employed for exposure scenarios 2 and 3 to ensure that the releases to the environment and exposure to workers are negligible (Annex I, Section 5.1.1);
   c. Consumer exposure assessment and risk characterisation and subsequently a demonstration that the risk to humans can be considered to be adequately controlled. Moreover, the CSR shall address all the identified uses of a substance (Annex I, sections 0.3, 5 and 6);

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d. Details of the personal protective equipment employed and recommended for handling the substance as specified below in section III, 2)(d) (Annex I, 0.3, 0.5 and 5.1.1; Annex VI, 5.6.; Annex II, Section 8.2.2.2 (b)(i)).

Pursuant to Article 41(4) of the REACH Regulation the Registrant shall submit the information in the form of an updated IUCLID dossier to ECHA by **2 January 2014**.

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 more than 1000 tonnes per year in accordance with Article 6 of the REACH Regulation, does not comply with the requirements of Articles 10, 12 and 13 and with Annexes I, II, 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

Pursuant to Articles 10(a)(vi), 12(1)(e) of the REACH Regulation, a registration for a substance produced in quantities of 1000 tonnes or more per year shall contain as a minimum the information specified in Annexes VII and VIII and testing proposals for the provision of information specified in Annexes IX and X of the REACH Regulation.

(a) - (b) The technical dossier contains adaptations to the standard information requirements for the endpoints:

- Sub chronic toxicity (90 days) (Annex IX, 8.6.2.);
- Pre-natal developmental toxicity (Annex IX, 8.7.2);

Sub chronic toxicity (90 days) is a standard information requirement for registrations in the 100 tonnes or more range pursuant to Annex IX, Section 8.6.2. Pre-natal developmental toxicity is a standard information requirement for registrations in the 100 tonnes or more range pursuant to Annex IX, Section 8.7.2.

The Registrant has omitted the studies in question with a reference to exposure based waiving. The following statements are included in the dossier under repeated dose toxicity:

> For the oral route "*Regulation (EC) 1907/2006 states that a subchronic (90 day) toxicity study should be conducted using the most appropriate route of administration. However, the chemical safety assessment shows the substance is used only by workers in industrial or professional settings where correct training and strict application of risk management measures are expected. Hence the potential for oral exposure is minimal and further animal studies via the oral route are considered unnecessary on the grounds of rodent welfare*" and "*Currently available data on frequency and duration of human exposure does not indicate the need for a long-term oral repeated dose toxicity study (12 months or longer)*".

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For the inhalation route "*Further animal studies via the inhalation route are contraindicated by the corrosive nature of the substance and strict application of risk management measures to prevent exposure of industrial or professional workers.*"

For the dermal route "*Further animal studies via the dermal route are contraindicated by the corrosive nature of the substance and strict application of risk management measures to prevent exposure of industrial or professional workers.*"

The following statement is included in the dossier under developmental toxicity:

"*Regulation (EC) 1907/2006 states that a pre-natal developmental toxicity study should be conducted using the most appropriate route of administration. However, the chemical safety assessment shows the substance is used only by workers in industrial or professional settings where correct training and strict application of risk management measures are expected. Hence the potential of the substance to influence prenatal development in humans is minimal and further animal studies are considered unnecessary on the grounds of rodent welfare.*"

According to Article 13(1) and Section 3 of Annex XI of the REACH Regulation, testing in accordance with Annex IX may be omitted based on a thorough and rigorous exposure assessment, provided that any one of the three criteria of Section 3 of Annex XI are met and that adequate justification and documentation are provided.

The first criterion 3.2(a) requires "*absence of or no significant exposure in all scenarios of the manufacture and all identified uses*". Moreover, relevant PNECs or DNELs are to be derived and exposure results are to be well below the derived PNECs or DNELs.

The second criterion 3.2(b) requires the Registrant to demonstrate "*throughout the life cycle strictly controlled conditions as set out in Article 18(4)(a) to (f)*".

The third criterion 3.2(c) sets out conditions which have to be fulfilled for a substance incorporated in an article particularly that the substance is not released during its life cycle, that the likelihood of exposure of workers and general public under normal and foreseeable circumstances is negligible and that the substance is handled under the conditions set out in Article 18(4)(a) to (f) during all manufacturing and production stages including waste management.

The Registrant has not indicated which of these criteria he is using to adapt the information requirements for the tests referred to in this decision under points (a)-(b) of section 1) above. ECHA has analysed the exposure scenarios and risk characterisation contained in the registration dossier and makes the following observations:

The qualitative exposure assessment provided indicates that exposure levels are beyond insignificant, therefore the criterion set out in 3.2.(a)(i) is not satisfied. Given the uses listed in the registration dossier and the details presented in the CSR under exposure scenario 3 worker exposure would seem likely. In particular, given the fact that curing of the two part epoxy resin takes place *in situ* upon mixing of the components with curing times of approximately 72 hours and considering the Registrant's exposure estimation which includes the statement "*A large number of construction workers are expected to be exposed to products containing the test substance during periods of 1-2 hours throughout the working day*", exposure seems likely. Furthermore, the Registrant has stated that exposure

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of consumers is not expected because the substance is not available for release from cured epoxy resins. However, the product categories PC1 (adhesives, sealants) and PC9 (coating and paints, thinners, paint removers) are listed under consumer uses of the substance. While it is accepted that cured products limit opportunity for exposure, it is nevertheless unclear whether two-part epoxy resins may be sold to consumers thereby increasing the potential for exposure to the registered substance as a result of the *in situ* mixing of the two part components and subsequent curing period. If the registered substance is available in two-part epoxy resins sold to consumers, then exposure to consumers cannot be ruled out and the criterion set out in 3.2.(a)(i) is not satisfied from the perspective of consumer exposure.

Criterion 3.2(a)(ii) requires that a DNEL has to be derived from the results of available tests taking into account the increased uncertainty resulting from the omission of the information requirement and criterion 3.2(a)(iii) requires that a comparison of the derived DNEL with the results of the exposure assessment shows that exposures are well below the derived DNEL. As no DNELs have been derived for the sub chronic toxicity (90 day) and pre-natal developmental toxicity endpoints and only a qualitative exposure assessment has been performed none of the conditions of criterion 3.2 (a) for exposure-based adaptation are satisfied.

Strictly controlled conditions as set out in Article 18(4)(a) to (f) are not demonstrated and therefore criterion 3.2(b) for exposure-based adaptation is not satisfied. In particular, condition (a) as set out in Article 18(4) does not appear to be fulfilled because it has not been demonstrated that the substance is rigorously contained by technical means during its whole lifecycle.

The third criterion 3.2(c) concerns the substance incorporated in an article. Since the substance is not incorporated in an article within the meaning of Article 3(3), this criterion does not apply to this case.

For these reasons, ECHA concludes that the justifications provided by the Registrant for waiving the concerned tests do not fulfil the criteria set out in Annex XI, Section 3. Consequently there is an information gap for Annex IX, 8.6.2.

To decide on the most appropriate route for testing the following considerations were taken into account. The registered substance is classified as skin corrosive 1B, H 314 (causes severe skin burns and eye damage), and local effects in the respiratory tract are likely as acknowledged by the registrant with the allocation of EUH071 (corrosive to the respiratory tract). According to the CSR the registered substance is used in adhesives, coatings and composites in the construction industry. PROC 10 (roller application or brushing), PROC 11 (non industrial; spraying) and PROC 19 (hand-mixing with intimate contact and only PPE available) are mentioned in the CSR. PROC 10 and 11 indicate relevant aerosol exposure. However, currently no information is available to quantitatively assess the concentration causing such effects upon repeated inhalation exposure to aerosols. Since it is not possible to derive a long term DNEL for local effects in the respiratory tract by extrapolation from oral information, results from an inhalation study with repeated exposure are needed to obtain a sound scientific basis for such a DNEL.

In comparison with the need to obtain information via the inhalation route to clarify the local effects in the respiratory tract, the further clarification of systemic effects via the oral route appears less critical for worker protection at this point in time. In particular, the available 28-day study via oral administration revealed adverse effects in line with local

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corrosivity/irritation in the gastrointestinal tract, but no systemic effects were evident. The NOEL was determined as 150 mg/kg BW/day.

The Registrant provided comments on proposals for amendment from the German and Danish Competent Authorities with regard to the selection of the appropriate route of administration for the sub chronic toxicity (90 days) study wherein he acknowledged the possibility for exposure via the inhalation route for workers.

The Registrant is accordingly required to provide information on sub chronic toxicity (90 days) via the inhalation route in the rat (OECD TG 413).

Furthermore, the Registrant is required to provide information on pre-natal developmental toxicity via the oral route in the rat (EU Test Method B.31; OECD TG 414). According to the test method the substance is usually administered orally by intubation. The test method also specifies: "*if another route of administration is used, the tester should provide justification and reasoning for its selection, and appropriate modifications may be necessary*". The information provided in the dossier does not indicate that the oral route should not be used.

When considering the need for a testing proposal for a prenatal developmental toxicity study in a second species, the Registrant should take into account the outcome of the pre-natal developmental toxicity study on the first species and all available data to determine if the conditions are met for adaptations according to Annex X, 8.7. column 2, or according to Annex XI; for example if the substance meets the criteria for classification as toxic for reproduction Category 1B: May damage the unborn child (H360D), and the available data are adequate to support a robust risk assessment, or alternatively, if Weight of Evidence assessment of all relevant available data provides scientific justification that the study in a second species is not needed.

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) DNEL derivation, exposure assessment and risk characterisation for long term worker exposure (Annex I, sections 1.4, 5 and 6)

Pursuant to Annex I, 1.4 of the REACH Regulation, Derived No-Effect Levels (DNELs) shall be established for the substance, reflecting the likely route(s), duration and frequency of exposure. In addition, Annex I, 5.2.4 of the REACH Regulation requires that exposure estimation shall be carried out for all human populations for which exposure is known or reasonably foreseeable, taking particular account of:
"*— duration and frequency of exposure according to the operational conditions,*
— the activities of workers related to the processes and the duration and frequency of their exposure to the substance".

Pursuant to Annex I, 6.3 and 6.4 of the REACH Regulation the risk characterisation for human health consists of a comparison of the exposure of each human population known to be or likely to be exposed with an appropriate DNEL. Pursuant to Annex I, 6.4 of the REACH Regulation the risk to humans and the environment can be considered to be adequately controlled if the exposure levels estimated in Section 6.2 do not exceed the DNELs.

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The CSR does not contain any DNEL(s). According to Annex I, section 1.4.2., if it is not possible to identify a DNEL, then this shall be clearly stated and fully justified. The Registrant has provided justifications for not providing DNEL(s) based on the corrosivity of the substance. For systemic effects, both short term and long term, the Registrant has indicated that toxic effects are attributed to the corrosive nature of the substance rather than true systemic effects. Even though irritant and corrosive effects are the most immediately apparent it is important to consider the long term consequences that will arise through either dermal contact or by inadvertent ingestion. Exposure is inevitable given the use scenarios, especially PROC 19 (Hand-mixing with intimate contact and only PPE available), where contact with the substance is intimate. Protective gloves will not completely prevent exposure. There is even evidence to show inadvertent ingestion is higher when users wear protective gloves.

For local effects in the respiratory tract, both short term and long term, the Registrant has indicated that DNEL(s) cannot be determined as irritation or corrosion data showing a dose response correlation are not available. However, it is concluded that a repeated dose inhalation study as explained under section III.1 will provide the relevant information to allow derivation of DNEL for local effects.

The long term exposure estimation for workers in the dossier contains the following statements under exposure scenarios 1-3 respectively:

"No long-term exposure to the neat substance is anticipated due to the limited duration of activities connected to transfer of the material from stainless-steel drums to the storage tank, plus routine use of appropriate PPE. Similarly, long-term exposure to reduced concentrations of the test substance is prevented by correct laboratory practice and use of recommended PPE during sampling and quality control activities".

"No long-term exposure to the neat test substance is anticipated due to the limited duration of activities connected to transfer of the material from stainless-steel drums to that storage tank, plus routine use of appropriate PPE".

"No long-term exposure to the neat substance is anticipated due to routine use of PPE plus the limited duration of activities connected to mixing and dispensing of the two component epoxy resin."

ECHA considers the above qualitative statements insufficient to demonstrate the absence of long term exposure of workers to the registered substance. In particular for exposure scenario 3, long term exposure to workers can be considered reasonably foreseeable given the use scenarios, especially PROC 19 (Hand-mixing with intimate contact and only PPE available), PROC 10 (Roller application or brushing) and PROC 11 (Non industrial spraying) where contact with the substance is expected.

Annex I, section 6.5 states that for those human effects and environmental spheres for which it was not possible to determine a DNEL or a PNEC, a qualitative assessment of the likelihood that effects are avoided when implementing the exposure scenario shall be carried out.

The Registrant is accordingly required to derive and provide DNELs for the inhalation, oral and dermal routes of worker exposure or failing this adequate justification of the impossibility to derive such DNEL(s). The Registrant is also required to provide an exposure assessment

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and risk characterisation for long term worker exposure to assure that the risks are adequately controlled during long term exposures and to update the CSR accordingly.

(b) A description of the operational conditions (OCs) and risk management measures (RMMs) employed for exposure scenarios 2 and 3 to ensure that the releases to the environment and exposure to workers are negligible.

According to Article 3(37) of the REACH Regulation, exposure scenario is defined as "*the set of conditions, including operational conditions and risk management measures, that describe how the substance is manufactured or used during its life-cycle and how the manufacturer or importer controls, or recommends downstream users to control, exposures of humans and the environment*".

Pursuant to Articles 10(b) and 14(4) as well as Annex I, Section 5.1.1 of the REACH Regulation, generated exposure scenarios shall cover a description of the operational conditions and risk management measures applied to reduce or avoid direct and indirect exposure to humans and the different environmental compartments to the substance.

The risk characterisation for exposure scenario 2 "*Industrial Polymer Production*" provided by the Registrant states that "*all waste water containing the test substance is treated on-site before release to the municipal sewage treatment system. The concentration of test material in waste water released from the site is below the limit of detection and is therefore considered to be below the calculated PNEC of 0.0094 mg/L*". However, the risk management measures used to achieve this are not adequately described in exposure scenario 2.

Therefore, the Registrant is required to describe the on-site techniques including the efficiency of such techniques employed to achieve negligible emission to water, and to update the CSR accordingly.

Concerning exposure scenario 3, the CSR provided by the Registrant states under operational conditions that formulated products containing the test material are expected to be dispensed via manual, battery operated or pneumatic devices. Two components of epoxy resin are mixed and setting (curing) takes place over a period of approximately 72 hours. ECHA notes that the full extent of the operating conditions is not evident from this description as the operational conditions for all of process categories listed are not adequately described. Neither are the risk management measures and waste management methods sufficiently detailed as to allow a meaningful conclusion to be drawn regarding the reliability of the qualitative exposure assessment and risk characterisation employed by the Registrant for both workers and the environment.

Therefore, the Registrant is required to describe the operational conditions and risk management measures employed to ensure negligible exposure of the registered substance to workers and the environment, and to update the CSR accordingly.

(c) Consumer exposure assessment and risk characterisation and subsequently a demonstration that the risk to humans can be considered to be adequately controlled.

According to Annex I, Section 5.2.4 and Section 6.2 of the REACH regulation an estimation of the exposure levels and risk characterisation shall be carried out for all human populations for which exposure is known or reasonably foreseeable. Moreover, according to Annex I, Section 0.3, the CSR shall address all the identified uses of a substance.

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The Registrant has not provided any exposure assessment or risk characterisation for consumer uses. Furthermore, there are no exposure scenarios covering consumer uses. The following statement is quoted in the dossier "*Due to the chemical binding processes that occur during curing, finished products do not contain the chemical and consumer exposure is not of concern.*" As mentioned under point 1) above ECHA notes that the product categories PC1 (adhesives, sealants) and PC9 (coating and paints, thinners, paint removers) are listed under consumer uses. While it is accepted that cured products limit opportunity for exposure, it is nevertheless unclear whether two-part epoxy resins may be sold to consumers thereby increasing the potential for exposure to the registered substance as a result of the *in situ* mixing of the two part components and subsequent curing period.

Furthermore, ECHA notes that the Registrant does not advise against the use of the substance in formulations for use by consumers as also required by Annex VI, section 3.7 of the REACH Regulation.

The Registrant is accordingly required to clarify all identified uses by consumers providing detailed evidence of the negligible exposure to consumers. If there is potential for exposure to consumers, relevant exposure scenarios shall be developed in accordance with Annex 1, section 5 and subsequent exposure estimation and risk characterisation shall robustly demonstrate that the risk to humans can be considered to be adequately controlled in accordance with Annex I, section 6.

(d) Details of the personal protective equipment employed and recommended for handling the substance.

Pursuant to Annex VI, section 5 of the REACH Regulation the information provided in the registration dossier shall be consistent with that in the Safety Data Sheet (SDS). According to Annex I, 0.3, 0.5 and 5.1.1 applied Risk Management Measures (RMM) have to be indicated in the CSR. Annex II, section 8.2.2.2 (b)(i), requires the Registrant to describe the relevant RMM in detail in order to minimise the exposure for workers handling the registered substance. In particular, the following requirements for hand protection in order to avoid dermal exposure need to be provided consistently in the SDS and CSR:

— the type of material and its thickness,
— the typical or minimum breakthrough times of the glove material.

The Registrant has provided instructions in all exposure scenarios to use impervious nitrile rubber gloves to protect against exposure.
Although the Registrant has provided instructions to use impervious nitrile rubber gloves in case of a potential skin contact, the specific information regarding thickness and typical or minimum breakthrough time of the gloves has not been provided. Therefore, the information requirements for exposure control have not been fulfilled.

The Registrant is accordingly required to provide information on the thickness and typical or minimum breakthrough time of the glove material with regard to the amount and duration of dermal exposure for all exposure scenarios.

Furthermore, the Registrant should consider providing advice on an appropriate maximum duration for the use of the gloves.

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

ECHA always 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). National authorities monitoring GLP maintain lists of test facilities indicating the relevant areas of expertise of each facility.

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.

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. 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