Helsinki, 19 May 2014

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

For Chloromethane, CAS No 74-87-3 (EC No 200-817-4)

Addressees: Registrant(s)[1] of Chloromethane (Registrant(s))

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, with the exception of the cases listed in the following paragraph.

Registrant(s) meeting the following criteria are *not* addressees of this decision: i) Registrant(s) who exclusively use the above substance as an on-site isolated intermediate and under strictly controlled conditions and ii) Registrant(s) who cease 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. Pursuant to Article 49 of the REACH Regulation only substances registered as on-site isolated intermediates that are used under strictly controlled conditions fall outside the scope of evaluation activities whereas substances registered as transported isolated intermediates whether or not used under strictly controlled conditions are subject to evaluation.

Based on an evaluation by National Institute of Health on behalf of Ministry of Health as the Competent Authority of Italy (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 the REACH Regulation.

This decision does not take into account any updates of the registrations of the Registrant(s) after 1 December 2012.

This decision does not imply that the information provided by the Registrant(s) in the registrations is in compliance with the REACH requirements. The decision neither prevents ECHA from initiating compliance checks on the dossiers 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 Italy has initiated substance evaluation for Chloromethane, CAS No 74-87-3 (EC No 200-817-4) based on registrations dossiers submitted by the Registrant(s) 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/CMR; Suspected Endocrine Disruptor; Risk

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

characterisation ratio close to 1 (human health), Chloromethane was included in the Community Rolling Action Plan (CoRAP) for substance evaluation pursuant to Article 44(2) of the REACH Regulation to be evaluated in 2012. The CoRAP was published on the ECHA website on 29 February 2012. The Competent Authority of Italy was appointed to carry out the evaluation.

In the course of the evaluation, the evaluating MSCA noted additional concern regarding environmental exposure assessment and risk characterisation with potential human risk via the environment.

The evaluating MSCA considered that further information was required to clarify the abovementioned concerns. Therefore, it 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 28 February 2013.

On 4 April 2013 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.

By 6 May 2013 ECHA received comments from Registrant(s) of which it informed the evaluating MSCA without delay.

The evaluating MSCA considered the Registrants' comments received and did amend Section III of the draft decision.

In accordance with Article 52(1) of the REACH Regulation, on 31 October 2013 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.

Subsequently, two Competent Authorities of the Member States and ECHA submitted proposals for amendment to the draft decision.

On 05 December 2013 ECHA notified the Registrant(s) of the proposal 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 Sections II and III of the draft decision.

On 16 December 2013 ECHA referred the draft decision to the Member State Committee. On 20 December 2013 in accordance to Article 51(5), the Registrant(s) provided comments on the proposal(s) for amendment. The Member State Committee took the comments of the Registrant(s) on the proposal(s) for amendment into account.

After discussion in the Member State Committee meeting on 3-7 February 2014, a unanimous agreement of the Member State Committee on the draft decision as modified at the meeting was reached on 5 February 2014. ECHA took the decision pursuant to Article 51(6) of the REACH Regulation.

II. Information required

Pursuant to Article 46(1) of the REACH Regulation the Registrant(s) shall submit the following information using the indicated test methods/instructions and the registered substance subject to the present decision:

1. Developmental Toxicity: a developmental toxicity study on rabbits via inhalation route (test method: EU B.31/OECD 414) in order to assess the susceptibility related to the species;

2. Risk assessment: Justification for deviating in DMEL derivation for carcinogenic effects and DNEL derivation from the requirements in the REACH Guidance R.8 as specified in Section III.2 below;

3. Missing elements for environmental exposure assessment and the risk characterization as specified in Section III.3 below;

4. Sufficient and consistent information on the specification of personal protective equipment and the duration of use for all scenarios where the use of personal protective equipment is advised: specifying for air-purifying respirators, the proper purifying element (cartridge or canister) and the adequate masks, or self-contained breathing apparatus for the scenarios where the use of respiratory protection is advised.

Pursuant to Article 46(2) of the REACH Regulation, the Registrant(s) shall submit to ECHA by **26 August 2015** an update of the registration dossiers containing the information required by this decision.

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

III. Statement of reasons

Based on the evaluation of all relevant information submitted on Chloromethane and other relevant and available information ECHA concludes that further information is required in order to enable the evaluating MSCA to complete the evaluation of whether the substance constitutes a risk to human health or the environment.

1. Developmental toxicity

Chloromethane has not been classified as a reproductive toxicant in the Harmonized Classification (Annex VI) according to Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures (CLP Regulation).

With the exception of some evidence of delayer ossification observed at 1500 ppm, in presence of maternal toxicity, chloromethane did not cause developmental effects in rats during the critical period of embryo and fetal development (gestation days 7-19). In two developmental toxicity studies on mice, increased incidences of fetal heart defects were observed in absence of maternal toxicity (500 ppm or higher, gestation days 6-18). The no observed adverse effect level (NOAEL) for heart defects was 250 ppm. The teratogenic mode of action is not clear. Developmental toxicity studies are usually required in both a rodent and a non-rodent species.

Regarding the requested route of administration, since chloromethane is a gas at ambient temperature and pressure, the requested study shall be performed by inhalation route.

In the commenting phase, the Registrant(s) challenged the request to perform a new developmental toxicity study in rabbits for the sole purpose of clarifying the classification and due to the fact that the substance was shown not to be a developmental toxicant in rats. However, since mice did show effects for developmental toxicity in two different studies and developmental toxicity studies have usually to be performed also in a non-rodent species, the request has been maintained.

Therefore, pursuant to Article 46(1) of the REACH Regulation, the Registrant(s) are required to carry out the following study using the registered substance subject to this decision: Developmental toxicity study, in rabbits, via inhalation route, (test method: EU B.31/OECD414).

2. Risk assessment

In the risk assessment for human health, the Registrant(s) have adopted a reference value calculated from the occupational exposure limit (OEL) agreed by the German Commission for maximum work place concentrations (MAK Kommission, Maximale Arbeitsplatz-Konzentration, MAK value). This approach has been applied in place of a DNEL (Derived No Effect Level) derivation as defined in the REACH Guidance R.8. Registrant(s) have supported the use of the MAK value by stating that this approach is commonly adopted in the chemical risk assessment at national level.

However, based on the toxicological information available in the dossiers, if the relevant DNEL is established (DNEL is regarded as the appropriate reference value due to the fact that the substance exerts its toxicity *via* a threshold mode of action), the evaluating MSCA has estimated that the exposure levels exceed the DNEL for most of the identified uses and therefore, unacceptable risks can occur. In such cases, proper risk management measures (RMMs) should be put in place for controlling risks. However, no RMMs are currently addressed in the chemical safety report (CSR). With the aim to exclude any reason of concern, the Registrant(s) are requested to provide a full justification as to better substantiate for deviating in DNEL derivation from the requirements in the REACH Guidance R.8.

Additionally, according to REACH Guidance R.8, a national OEL cannot be used in place of a DNEL without an evaluation of the scientific background for setting the national OEL. In the absence of such data, the evaluating MSCA has not been able to carry out a comprehensive evaluation of the scientific ground for setting the MAK value. Besides that, in case a national OEL is adopted, REACH Guidance R.8 advises assessors to carry out a risk assessment considering the alternative approach where the DNEL is derived from animal studies and assessment factors accounting for any uncertainties are applied as well. Then, the two approaches should be compared and any differences should be carefully taken into account.

Moreover, a Member State Competent Authority proposed to require a justification for not providing a DMEL for carcinogenic effects considering the genotoxic potential of the substance for which a threshold for carcinogenic effects cannot be identified. Since a genotoxic mode of action in the induction of kidney tumors in mice cannot be excluded, a justification for not performing a DMEL derivation for carcinogenic effects in accordance with the REACH Guidance R.8 shall be provided.

In the commenting phase of this proposal for amendment the Registrant(s) stated that there is a sufficient evidence for a threshold-based mode of action for carcinogenicity since in an inhalation carcinogenicity study with the substance, kidney tumors were observed only in male mice at high concentrations with the high activity of CYP2E1 specifically expressed in the kidney in male mouse and this enzyme has not been detected in a significant amount in human kidney.

ECHA is of the opinion that these considerations are not sufficient to exclude a role of chloromethane in the induction of kidney carcinogenicity in humans as DNA lesions were detected *in vivo* in the kidney of treated mice. Therefore, the risk characterisation of chloromethane should take into account the possibility that a genotoxic mechanism is involved in the carcinogenicity of the substance.

Hence, based on the potential genotoxicity of chloromethane, a DMEL derivation has been regarded as the most appropriate approach for the risk characterization of non-threshold effects. Besides that, the mode of action of the substance not being sufficiently clear (species-specific effects should be fully demonstrated), a precautionary principle should be applied and therefore, a justification for not performing a DMEL derivation has to be provided.

In addition, the evaluating MSCA is of the opinion that also a DNEL derivation is appropriate in consideration of the finding of the study requested in point 1 while the potential for genotoxicity and carcinogenicity of chloromethane supports the derivation of a DMEL.

In the revised CSR the most conservative approach regarding the use of DMEL/DNEL should be followed.

3. Missing elements for environmental exposure assessment and risk characterization

The data waiving for long-term toxicity studies to aquatic organisms is justified by the Registrant(s) using exposure considerations that are general and related to the negligible amount of industrial release in respect to natural background concentration. However, the Registrant(s) do not report the tonnage of the registered substance manufactured/imported subject to the present decision and the tonnage associated with each use (or group of uses) during the life cycle of the substance for which exposure scenarios need to be developed. Moreover, information about amounts used, frequency, duration of use/exposure, amount lost from process/use, the Operational Conditions (OC) and the Risk Management Measures (RMM) are not described and a valid justification is not provided.

The Registrant(s) reported European measured exposure data, without providing sufficient information about the references, and about the quality and the representativeness of the data. Therefore, the Registrant(s) are requested to describe in detail the exposure scenarios which must be based on OCs/RMMs that reflect clearly the applied good practice for the sector of use related to Chloromethane, according to Annex I, 5.1.1. of the REACH Regulation.

Moreover, the Registrant(s) are requested to provide the amount of use, frequency, duration, amount lost from process/use in accordance with Annex I, 5.2.4. of the REACH Regulation or to give an appropriate justification for the absence of the information.

The Registrant(s) are also requested to provide representative and reliable measured data from monitoring programmes or from literature that should be compiled as tables and annexed to the Chemical Safety Report; the measured data should be presented with

relevant contextual information such as environmental compartment, number of samples, frequency of sampling (see ECHA Guidance Part D and Chapter R.16). Concentrations can be measured in the receiving environment or in the release. If the reported concentration has been measured directly in the release, this should be clearly indicated in the reporting table.

Therefore, taking into account the missing information above requested, and according to the requirements indicated in Annex I, 5.2. of the REACH Regulation, the Registrant(s) are required to refine predicted effect concentration (PEC) values for each compartment and to perform the relative risk characterisation, and to update the CSRs accordingly.

4. Personal protective equipment

To cope with risks from hazardous substances appropriate risk management measures have to be derived in the risk assessment, recommended and applied during use. Within the order of risk management measures, personal protective equipment is considered the last resort, in cases were the measures are not applicable or could not sufficiently reduce the risks (see e.g. Directive 98/24/EC).

Generally, personal protective equipment used must be appropriate for the risk involved, without itself leading to any increased risk (see e.g. Directive 89/656/EEC on the minimum health and safety requirements for the use by workers of personal protective equipment at the workplace). This has to be considered for the derivation of exposure scenarios under REACH as well without prejudice to the Community workplace legislation.

Personal protective equipment (PPE) specification is a requirement of REACH Annex II, 8.2.1. and the efficacy is needed to assess residual exposure occurring to workers when PPE are used. In Annex I, 5.2.4. it is written that "the estimation of the exposure level ... shall take into account (...) implemented and recommended RMM including the degree of containment." The specification of the recommended personal protective equipment is necessary to assure that the equipment does have a protective effect. Without further specification the protection respiratory protection equipment cannot be judged.

Therefore, a specification for air-purifying respirators, the proper purifying element (cartridge or canister) and the adequate masks, or self-contained breathing apparatus for the scenarios where the use of respiratory protection is advised, is requested.

IV. Adequate identification of the composition of the tested material

The substance identity information submitted in the registration dossiers 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 required test, the sample of substance used for the new study shall have a composition that is within the specifications of the substance composition that are given by all Registrants. It is the responsibility of all the Registrants to agree on the tested materials to be subjected to the test subject to this decision and to document the necessary information on composition of the test material. The substance identity information of the registered substance and of the sample tested must enable the evaluating MSCA and ECHA to confirm the relevance of the testing for the substance subject to substance evaluation. Finally, the study must be shared by the Registrant(s).

V. Avoidance of unnecessary testing by data- and cost- sharing

Avoidance of unnecessary testing and the duplication of tests is a general aim of the REACH Regulation (Article 25). The legal text foresees the sharing of information between Registrants. Since several Registrants of the same substance are required to provide the same information, they are obliged to make every effort to reach an agreement for every endpoint as to who is to carry out the test on behalf of the other Registrant(s) and to inform ECHA accordingly within 90 days from the date of this decision under Article 53(1) of the REACH Regulation.

If ECHA is not informed of such agreement within 90 days, it shall designate one of the Registrant(s) to perform the tests on behalf of all of them. If a Registrant(s) performs a test on behalf of other Registrant(s), they shall share the cost of that study equally and the Registrant(s) performing the test shall provide each of the others concerned with copies of the full study reports.

This information should be submitted to ECHA using the following form stating the decision number above at:

https://comments.echa.europa.eu/comments_cms/SEDraftDecisionComments.aspx

Further advice can be found at http://echa.europa.eu/datasharing_en.asp.

VI. General requirements regarding Good Laboratory Practice

ECHA always reminds Registrant(s) 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.

VII. 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.

[redacted]

Jukka Malm
Deputy Executive Director

Annex: List of registration numbers – This annex is confidential and not included in the public version of this decision