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SUBSTANCE EVALUATION REPORT

Public Name: ethylene oxide

EC Number: 200-849-9

CAS Number: 75-21-8

Submitting Member State Competent Authority:

Environment Agency Austria (Spittelauer Lände 5, 1090 Vienna)
on behalf of the Austrian Competent Authority (Austrian Federal Ministry of Agriculture, Forestry, Environment and Water Management, Stubenring 1, 1010 Vienna, Austria)

Year of evaluation: 2012

VERSION NUMBER: 0.2 DATE: November 2013

Conclusions of the most recent evaluation step*	Tick relevant box(es)
Concern not clarified; Need to request further information from the Registrants with the draft decision	
Concern clarified; No need of further risk management measures	
Concern clarified; Need for risk management measures;	X
Other: [*please specify*]	

Executive summary

Ethylene oxide was originally selected for substance evaluation in order to clarify suspected risks about:

- Human health: CMR
- Human exposure: High aggregated tonnage

During the evaluation also other concerns were identified. The additional concerns were:

- Classification and labelling
- Environmental hazard and exposure assessment

Grounds for concern

Ethylene oxide was proposed for substance evaluation based on Article 45(5) of the REACH regulation. The evaluation was targeted to all sections of the chemical safety assessment given in the IUCLID dossiers and chemical safety reports of the registrants. Following main concerns were identified before and during Substance Evaluation by the evaluating Member State. Minor concerns and amendments of the registration dossiers are discussed in the corresponding sections of this report.

- The substance is classified as Carc. 1B and Muta. 1B. Based on the available data it can be assumed that ethylene oxide acts via a non-threshold mode of action. Therefore, a DMEL should be derived for this substance. The registrants have derived a $DMEL_{chronic\ inhalation\ worker}$ of $2mg/m^3$ which corresponds to an additional cancer risk of 4:1000. This DMEL-value is different from the value derived for worker exposure by the German AGS (Ausschuss für Gefahrstoffe) which is $23.6\mu g/m^3$, based on an additional cancer risk of 4.10^{-5}. The DMEL derivations were reassessed by the evaluating Member State, confirming that differences in DMEL values are solely due to the different assumptions for cancer risks.

- High volumes of the substance are manufactured/applied in the EU. The provided exposure assessments of the registration dossiers were based on ECETOC-TRA, a Tier 1-exposure estimation software tool, which is considered to be conservative in principle. This means that derived exposure levels should tend to overestimate probably exposure than to underestimate it. The exposure scenarios were described only by use descriptors and the parameters needed for using ECETOC-TRA. However, as the substance is manufactured/applied by many sites and the ES are not described/discussed in detail, it was uncertain, if the real situations at work place were covered by the ESs given in the registration dossiers. An assessment by the evaluating Member State revealed that initial assumptions (input parameters used for ECETOC-TRA) did not match the real situations. Therefore, more detailed background information and descriptions of the human exposure scenarios were requested during the first year of evaluation. The registrants submitted measured data and a new approach for the human exposure assessment. These data and the new approach were taken into the update of the registration dossiers, which were changed accordingly. Based on these data, the concern was removed.

- The environmental exposure assessment was not performed initially by the registrants based on their justification that there is no need for classification referring to environmental hazards. No data on long-term toxicity to fish and aquatic invertebrates were provided.

These tests were waived based on section 3 paragraph 3.2(b) of Annex XI of the REACH regulation 1907/2006 amended by Commission regulation (EC) No 134/2009. The evaluating Member State considered waiving of a quantitative or qualitative environmental exposure assessment as not acceptable, also because the waived tests might have led to a classification related to environmental hazards. In informal interactions the evaluating Member State invited the registrants to provide further information on environmental exposure. The registrants provided an environmental exposure assessment referring to the release and corresponding risk management measures applied. The evaluating Member State concluded that the concern had been clarified and that no further information on environmental hazard and exposure assessment was needed.

Procedure

The evaluation was done based on the data given in the registration dossiers and in addition on reviews by international bodies (AGS-Ausschuss für Gefahrstoffe, SCOEL, IARC, ATSDR, WHO, National Research Council). Where relevant, the original publications provided by the registrants or publicly available studies were reviewed and evaluated. The evaluation was targeted to all sections of the chemical safety assessment.

This substance evaluation was supported by the registrants. Comments and guidance were submitted to the registrants for the preparation of a revised registration dossier within the first year of substance evaluation for clarifying all concerns, which could be clarified based on the registrant's and Member State's currently available data. If new data had been considered to be necessary, a draft decision would have been prepared for provision of the missing data after the first year. The lead registrant was contacted on the 15th march 2012 (start of substance evaluation: 1st March 2012). The lead registrant agreed to act as contact point and on behalf of the other registrants. The applied studies within the registration dossier were provided to the evaluating Member State by the registrants.

After a detailed review of the registration data and the provided studies by experts of the evaluating Member State, comments and proposals for amendments were sent to the lead registrant. The identified concerns and proposals were discussed between the experts of the evaluating Member State and registrants in phone conferences, if required. The lead registrant provided a revised draft registration dossier for a second review. The update of the registration data (IUCLID file, CSR) was uploaded in December 2012. As the available data and the data provided by the registrants during substance evaluation were considered to be sufficient for drawing conclusions, no new data/tests were considered to be required. The updated dossier is considered to be a key output of this evaluation. As the comments and advices of the evaluating Member State were taken into account for the preparation of the update by the registrants, the identified concerns were targeted, amended accordingly, if necessary and could be clarified.

Conclusions

As available data were considered to be sufficient for chemical safety assessment and covering relevant topics of concern, no new data/tests were considered to be required by the evaluating Member State. Therefore, substance evaluation was finalised after the first year of evaluation and the submission of revised registration dossiers in December 2012 by the registrants. Besides the

identification of missing and relevant data, the DMEL derivation of the registrants was assessed by the evaluating Member State.

Following points taken from the original SEV should be highlighted:

Sensitisation:

Ethylene oxide is covered by index number 603-023-00-X in Annex VI, part 3, Table 3.1 (list of harmonized classification and labelling of hazardous substances) of Reg. (EC) No 1272/2008 (CLP regulation). Referring to this list, the substance is not classified as skin sensitizer.

Nevertheless, human data do not fully exclude a skin-sensitizing potential. There are numerous reports available describing allergenic effects of ethylene oxide after use as clinical sterilant. Ethylene oxide is a direct and potent alkylating agent and reacts with hydroxyl, sulfhydryl, amino and carboxyl groups in human macromolecules. As a hapten it becomes an active allergen after binding to human proteins. Ethylene oxide should thus be classified according to Regulation (EC) No. 1272/2008 as skin sensitizer (Category 1), H317 (May cause an allergic skin reaction).

Carcinogenicity:

So far there is no EU legislation in place setting a Community-wide acceptable risk level for carcinogens. Different risk levels have been set and used in different contexts. REACH Guidance R.8 (ECHA, 2012) gives examples on risk levels used in different countries, organisations and committees. According to the ECHA Guidance, cancer risk levels of 10^{-5} and 10^{-6} could be seen as indicative tolerable risks levels when setting DMELs for workers and the general population, respectively. Kalberlah (2005) discusses the definitions of risk, safety, precaution, acceptable and tolerable risk. This report applies the German traffic light model for exposures to carcinogens at the workplace and compares the results with already used tolerable risk levels by different institutions/countries. For workers this study reports tolerable risk levels between $4*10^{-3}$ – $4*10^{-5}$ referring to a working lifetime of 40 years and continuous exposure at every working day. This study demonstrates the need to find an EU wide consensus on the size of an acceptable and a tolerable risk level.

The additional working lifetime risk of $4 * 10^{-3}$ taken by the registrant could be challenged on the basis of the traffic light model mentioned above which would require urgent measures to reduce the risk. The acceptable risk level according to AGS “Ausschuss für Gefahrstoffe” would be $4 * 10^{-5}$ (with a value of $4 * 10^{-4}$ proposed as an interim level accepted for the introductory phase until 2018).

Application of working lifetime risk values for workers of $4 * 10^{-5}$, as recommended by AGS (2011), would result in the following calculation using same data as the registrants:

BMD_{10} = 19.4ppm (10% response over background)

$hBMD_{10}$ = 29.55ppm (corrected for human exposure situation at workplace: 8h/day, 48weeks, 40 years)

Additional working lifetime risk of $4 * 10^{-5}$ (0.004% over background):

$DMEL_{worker, inhalation, long-term}$ = 11.8ppb = 23.6 µg/m^3

The **DMEL = 23.6µg/m^3** for workplace exposure to ethylene oxide calculated by the evaluating Member State with an additional risk of **4 * 10^{-5}** is by factor of 85 lower than the **DMEL= 2mg/m^3** calculated by the registrants with an additional risk of **4 * 10^{-3}**. The DMEL = 2mg/m^3 is used in the current version of the CSRs and in the registration dossiers. The discrepancy results from rounding and the different lifetime risk used.

Notwithstanding the decision on appropriate risk levels and the resulting DMEL it has to be stated that there is a cancer risk remaining at any DMEL level and it is therefore recommended to minimize the exposure as far as possible.

Conclusion:

This substance evaluation underlines the need for a discussion of acceptable risk levels for workers and the general population. Political agreement is needed at Community level. As a consequence no final conclusion on the appropriate DMEL for ethylene oxide can be drawn. Hence, the level of risk cannot be substantiated at this point of time.

References

AGS (Ausschuss für Gefahrstoffe) (2011) ERB-Begründung zu Ethylenoxid. http://www.baua.de/de/Themen-von-A-Z/Gefahrstoffe/TRGS/pdf/910/910-ethylenoxid.pdf?__blob=publicationFile&v=3

ECHA (2012) Guidance on information requirements and chemical safety assessment Chapter r.8: Characterisation of dose [concentration] response for human health. ECHA-2010-G-19_EN. http://echa.europa.eu/documents/10162/13632/information_requirements_r8_en.pdf

Kalberlah F., Bloser M., Wachholz C. (2005) Toleranz- und Akzeptanzschwelle für Gesundheitsrisiken am Arbeitsplatz. Bundesanstalt für Arbeitsschutz und Arbeitsmedizin. Projektnummer F2010.