SUBSTANCE EVALUATION

CONCLUSION DOCUMENT

as required by REACH Article 48

for

Butanone oxime

EC No 202-496-6

CAS No 96-29-7

Evaluating Member State(s): Germany

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Evaluating Member State Competent Authority

BAuA
Federal Institute for Occupational Safety and Health
Federal Office for Chemicals
Friedrich-Henkel-Weg 1-25
D-44149 Dortmund, Germany

Web: www.baua.de
Mail: chemg@baua.bund.de

Year of evaluation in CoRAP: 2013

Member State concluded the evaluation without the need to ask further information from the registrants under Article 46(1) decision.

Please find (search for) further information on registered substances here:

http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

DISCLAIMER

The Conclusion document has been prepared by the evaluating Member State as a part of the substance evaluation process under the REACH Regulation (EC) No 1907/2006. The information and views set out in this document are those of the author and do not necessarily reflect the position or opinion of the European Chemicals Agency or other Member States. The Agency does not guarantee the accuracy of the information included in the document. Neither the Agency nor the evaluating Member State nor any person acting on either of their behalves may be held liable for the use which may be made of the information contained therein. Statements made or information contained in the document are without prejudice to any further regulatory work that the Agency or Member States may initiate at a later stage.

Foreword

Substance evaluation is an evaluation process under REACH Regulation (EC) No. 1907/2006. Under this process the Member States perform the evaluation and ECHA secretariat coordinates the work.

In order to ensure a harmonised approach, ECHA in cooperation with the Member States developed risk-based criteria for prioritising substances for substance evaluation. The list of substances subject to evaluation, the Community rolling action plan (CoRAP), is updated and published annually on the ECHA web site[1].

Substance evaluation is a concern driven process, which aims to clarify whether a substance constitutes a risk to human health or the environment. Member States evaluate assigned substances in the CoRAP with the objective to clarify the potential concern and, if necessary, to request further information from the registrant(s) concerning the substance. If the evaluating Member State concludes that no further information needs to be requested, the substance evaluation is completed. If additional information is required, this is sought by the evaluating Member State. The evaluating Member State then draws conclusions on how to use the existing and obtained information for the safe use of the substance.

This Conclusion document, as required by the Article 48 of the REACH Regulation, provides the final outcome of the Substance Evaluation carried out by the evaluating Member State. In this conclusion document, the evaluating Member State shall consider how the information on the substance can be used for the purposes of identification of substances of very high concern (SVHC), restriction and/or classification and labelling. With this Conclusion document the substance evaluation process is finished and the Commission, the registrants of the substance and the competent authorities of the other Member States are informed of the considerations of the evaluating Member State. In case the evaluating Member State proposes further regulatory risk management measures, this document shall not be considered initiating those other measures or processes.

[1] http://echa.europa.eu/regulations/reach/evaluation/substance-evaluation/community-rolling-action-plan

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1. CONCERN(S) SUBJECT TO EVALUATION

Butanone oxime was originally selected for substance evaluation in order to clarify suspected risks about:

- carcinogenic properties of butanone oxime and
- actual working and workplace conditions especially for professional uses and to decide if further risk management measures are needed.

During the evaluation also another additional concern was identified:

- concern on human health risks for the general population resulting from consumer use of butanone oxime.

2. CONCLUSION OF SUBSTANCE EVALUATION

The available information on the substance and the evaluation conducted has led the evaluating Member State to the following conclusions, as summarised in the table below.

Conclusions	**Tick box**
Need for follow up regulatory action at EU level	X
Need for Harmonised classification and labelling	X
Need for Identification as SVHC (authorisation)	
Need for Restrictions	
Need for other Community-wide measures	
No need for regulatory follow-up action	

3. JUSTIFICATION FOR THE CONCLUSION ON THE NEED OF REGULATORY RISK MANAGEMENT

3.1. NEED FOR FOLLOW UP REGULATORY ACTION AT EU LEVEL

Butanone oxime is a high production volume chemical. The substance is produced/imported at high tonnage (> 1000 t/a) and is widely used with high exposure for workers in the EU.

Risks from occupational uses

DNELs calculated by the eMSCA were lower than the values given by the registrants. For calculation of RCRs eMSCA used air monitoring data for butanone oxime collected in Germany between 1998 and 2011 and modelled dermal exposure data. Based on these data, risks were identified. A DMEL for carcinogenicity was not provided by the registrants and thus newly derived by the eMSCA. The cancer risk of 1:100 000 is associated with exposure values even lower than the DNELs.

The eMSCA considers that the available air monitoring data do most likely not reflect the current situation at the working place due to significant changes in the currently used formulations of paints and varnishes containing butanone oxime. These changes go back to adaptation of the formulations to the provisions of the Decopaint Directive (2004/42/EC) which aims at the reduction of volatile organic compounds. In Germany a

newly derived national occupational exposure limit value was implemented. Currently a new measurement field campaign is carried out.

The eMSCA will await the discussion on the classification of butanone oxime as carcinogen category 1B before a conclusion on the most appropriate risk management option will be drawn. The data generated by the new measurement field campaign in Germany will be taken into account for this decision.

Risks from consumer uses

Consumer DNELs calculated by the eMSCA were lower than the values given by the registrants. For the calculation of RCRs, the eMSCA used modelled data for exposure by dermal application and by inhalation. Based on these data, risk characterisation ratios well above 1 were identified for several contributing consumer exposure scenarios. Therefore, there is concern on health risks from consumer use of butanone oxime.

3.1.1. Need for harmonised classification and labelling

The SEV leads to the need of an update of the existing harmonised classification and labelling of butanone oxime and of new entries in CLP-Annex VI.

The eMSCA proposes the following classification and labelling:

Current entry in Annex VI, CLP Regulation	Proposal for harmonised classification and labelling by the eMSCA
Carc. 2 H351: Suspected of causing cancer	Carc. 1B H350: May cause cancer
-	Acute Tox. 3 H301: Toxic if swallowed
-	STOT SE 3 H336: May cause drowsiness or dizziness
Skin Sens. 1 H317: May cause an allergic skin reaction	Skin Sens. 1B H317: May cause an allergic skin reaction
Acute Tox. 4* H312: Harmful in contact with skin	Acute Tox. 4 H312: Harmful in contact with skin
Eye Dam. 1 H318: Causes serious eye damage	Eye Dam. 1 H318: Causes serious eye damage

Pictograms, Signal Word	Pictograms, Signal Word
GHS08: Health hazard, Warning GHS07: Exclamation mark, Warning GHS05: Corrosion, Danger	GHS08: Health hazard, Danger GHS06: Skull and crossbones, Danger GHS07: Exclamation mark, Warning GHS05: Corrosion, Danger

Butanone oxime is legally classified as carcinogen category 2 according to the CLP Regulation. The substance evaluation of butanone oxime has verified the concern that a more severe classification regarding carcinogenicity is needed. The available data for carcinogenicity of butanone oxime do not comply with the legal classification of butanone oxime as carcinogen category 2. Based on the available data on carcinogenicity butanone

oxime fulfils the criteria for classification and labelling as category 1B carcinogen, H350 but not as category 2 according to the CLP Regulation.

In combined chronic toxicity/carcinogenicity studies in rats and mice exposed by inhalation to butanone oxime sufficient evidence of animal carcinogenicity was demonstrated. Two animal experiments using two species (rat and mouse) resulted in clear evidence for carcinogenicity. A causal relationship has been established between butanone oxime and a statistically significant increased incidence of a combination of benign and malignant tumours. Being similar to OECD TG 453 both studies are well conducted and do not cast doubts about the relevance of the results. Tumour development was noted by inhalation of relatively low concentrations in rats and mice.

The data from a developmental toxicity study in rabbits have shown that butanone oxime induces acute intoxication, e.g. lethality in rabbits from oral doses given in a short time (on two days). Mortality was observed in all 5 female rabbits which were treated with butanone oxime on gestations day (GD) 6 and 7 with 80 mg/kg bw (cumulative 160 mg/kg bw). The animals were found dead between GDs 8-10. In the main study, treatment with 40 mg/kg bw during GD6 to GD10, five days (cumulative 200 mg/kg bw) induced mortality in 8/18 females (GDs 11-24). Taken together, from experiments with single and repeated exposure, rabbits appear more sensitive than rats to toxic effects of butanone oxime. According to the Guidance on the application of the CLP criteria, classification should be based on the lowest acute toxicity estimates (ATE) value available i.e. the lowest ATE in the most sensitive appropriate species tested. Based on the ATE values in rabbits derived between 160 and 200 mg/kg bw butanone oxime fulfils the criteria for classification as Acute Tox. 3, H301: Toxic if swallowed according to the CLP Regulation (Annex I, Part 3, Table 3.1 Acute toxicity category 3: 50 < ATE ≤ 300 mg/kg bw).

Further substance evaluation has verified the concern that butanone oxime caused transient target organ effects. There were changes in neurobehavioral function including narcotic effects. In acute oral, inhalation and dermal toxicity studies and also in studies with repeated exposure to butanone oxime in different animal species, transient and reversible changes in neurobehavioral function consistent with central nervous system depression, but no evidence of cumulative neurotoxicity was detected. Based on these data there is reasonable concern that butanone oxime should be classified additionally due to its narcotic effects according to the CLP Regulation.

In rats single oral doses of ≥ 300 mg/kg bw butanone oxime administered by gavage produced narcotic effects. In the acute inhalation toxicity study with rats a strong transient narcotic effect occurred in both sexes at 4.83 mg/L/4h. In a dermal acute toxicity study in rabbits butanone oxime produced significant effects on the central nervous system (CNS) at single doses of 185 mg/kg bw and higher, and transient narcosis occurring during the first 48 hours following exposure at the low dose level of 18 mg/kg bw. Also in specific investigations transient and reversible functional disturbances in nervous system function consistent with CNS depression were observed in rats after single or repeated oral application of butanone oxime. Based on these data, butanone oxime meets the criteria for classification and labelling as a specific target organ toxicant (single exposure) of category 3 for narcotic effects (STOT SE 3, H336: May cause drowsiness or dizziness) according to the CLP Regulation (Annex I, Part 3.8.2.2.2).

Butanone oxime has shown a clear evidence of skin sensitisation in guinea pigs (GPMT and Buehler assay). The results of a mouse ear swelling test (MEST) with butanone oxime have shown a sensitising response of 40 % and a swelling rate of 120 % for the mouse ear. Based on this animal model system a moderate potency for skin sensitisation is determined for butanone oxime. Based on available data, butanone oxime is classified as skin sensitizer category 1 (legal classification).

In comparison to the given criteria for the hazard category and sub-categories for skin sensitisation according to the CLP Regulation butanone oxime fulfils the criteria for

classification in the hazard class as skin sensitizer sub-category 1B, H317: May cause an allergic skin reaction, because a skin sensitisation response of ≥ 30 % at > 1.0 % i.d. induction dose was observed in the adjuvant type test method (GPMT); and of ≥ 15 % at > 20 % topical induction dose in the non-adjuvant type test method (Buehler assay).

In addition, butanone oxime meets the criteria for classification and labelling for acute dermal toxicity as Acute Tox. 4, H312 according to the CLP Regulation and it seems that the reference indicating minimum classification (*) is no longer necessary. The legal classification of butanone oxime can be confirmed for Acute Tox. 4, H312. The available data on eye irritation do fulfil the criteria laid down in the CLP Regulation, and the legal classification as 'Irreversible effects on the eye' Category 1, H318 is warranted.

3.1.2. Need for Identification as a substance of very high concern, SVHC (first step towards authorisation)

Currently butanone oxime is classified for carcinogenicity as carcinogen category 2 according to the CLP Regulation. The available data suggest that butanone oxime meets the criteria for classification and labelling as carcinogen category 1B, H350 according to the CLP Regulation. The SEV leads to the need of an update of the existing harmonised classification and labelling of butanone oxime.

If butanone oxime was reclassified as carcinogen category 1B, the substance would fulfil the criteria for identification as SVHC according to Article 57(a). The eMSCA will await the discussion on the classification of butanone oxime as carcinogen category 1B before a conclusion on the most appropriate risk management option will be drawn. Currently a field campaign is conducted in Germany. The data generated during this campaign will be taken into account for this decision.

3.1.3. Need for restrictions

During the substance evaluation the eMSCA has evaluated the risks resulting from consumer use of butanone oxime in coatings by performing exposure assessments and risk characterisation for different coating product types. This risk assessment showed RCRs above 1 for short-term/acute systemic effects by inhalation, long-term effects by dermal administration and long-term local and systemic effects by inhalation, indicating that the corresponding risks are not adequately controlled.

These risks could require a community-wide restriction. However, if butanone oxime will be classified as carcinogen 1B, H350, as proposed by the eMSCA this will imply a generic restriction according to entry 28 of Annex XVII of the REACH Regulation which will affect sales to the general public of butanone oxime as a substance, as a constituent of other substances or in mixtures. The registered concentrations of butanone oxime in coatings for consumer use all exceed the generic concentration limits of ingredients of a mixture classified as carcinogen that trigger classification of the mixture according to the CLP Regulation. Therefore it is expected that a classification of butanone oxime as carcinogen 1B, H350 will lead to changes in consumer uses that may result in control of risks. This process should be awaited for before deciding whether consumer uses of butanone oxime have to be additionally restricted or not.

3.1.4. Proposal for other Community-wide regulatory risk management measures

The eMSCA will await the discussion on the classification of butanone oxime as carcinogen category 1B before a conclusion on the most appropriate risk management

option will be drawn. Currently a measurement field campaign is conducted in Germany. The data generated during this campaign will be taken into account for this decision.

4. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS

Follow-up action	Date for intention	Actor
CLH dossier for classification as: *Carc. 1B, H350* And also as: *Acute Tox. 3, H301;* *Acute Tox. 4, H312;* *Skin Sens. 1B, H317;* *STOT SE 3, H336*	2015-2016	German CA