Justification for the selection of a substance for CoRAP inclusion

Substance Name (Public Name):	Acetone oxime
Chemical Group:	--
EC Number:	204-820-1
CAS Number:	127-06-0
Submitted by:	AT
Date:	17/03/2015

Note

This document has been prepared by the evaluating Member State given in the CoRAP update.

Contents

1 IDENTITY OF THE SUBSTANCE

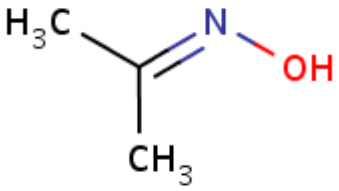
1.1 Other identifiers of the substance

Table 1: Substance identity

EC name:	Acetone oxime
IUPAC name:	Acetone oxime
Index number in Annex VI of the CLP Regulation	--
Molecular formula:	73.0943
Molecular weight or molecular weight range:	C_3H_7NO
Synonyms/Trade names:	*Acetoxime, 2-Propanone oxime, beta-Isonitrosopropane*

Type of substance ☒ Mono-constituent ☐ Multi-constituent ☐ UVCB

Structural formula:



1.2 Similar substances/grouping possibilities

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Structural formula:
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2 CLASSIFICATION AND LABELLING

2.1 Harmonised Classification in Annex VI of the CLP

There is no harmonised classification of acetone oxime according to the entry in table 3.1 in Annex VI of CLP.

2.2 Self classification

- In the registration

The self-classification of the substance is different in the two submitted registrations; one registrant has made an option out for different endpoint classifications. While registrant A self-classifies acetone oxime additionally for its sensitizing effects (Skin Sens. 1) and carcinogenic effects (Carc. 2), registrant B does not self-classify for these endpoints. A detailed list of self-classification in the registration of registrant A and registrant B and the hazard statement codes are given below:

Registrant A self-classifies the substance as:

Flam. Solid 1 H228: Flammable solid
Acute Tox. 4 H312: Harmful in contact with skin.
Eye Damage 1 H318: Causes serious eye damage.
Skin Sens. 1B H317: May cause an allergic skin reaction.
Carc. 2 H351: Suspected of causing cancer <state route of exposure if it is conclusively proven that no other routs of exposure cause the hazard>.

Registrant B self-classifies the substance as:

Flam. Solid 1 H228: Flammable solid.
Eye Damage 1 H318: Causes serious eye damage.
STOT Rep. Exp. 2 H373: May cause damage to organs

- The following hazard classes are in addition notified among the aggregated self classifications in the C&L Inventory:

  Acute Tox. 4 (H302)
  Eye Dam. 1 (H318)
  Carc. 2 (H351)
  Flam. Sol. 1 (H228)
  STOT RE 2 (H373)
  Skin Sens. 1B (H317)

2.3 Proposal for Harmonised Classification in Annex VI of the CLP

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3 INFORMATION ON AGGREGATED TONNAGE AND USES

From ECHA dissemination site		
☐ 1 – 10 tpa	☐ 10 – 100 tpa	☒ 100 – 1000 tpa
☐ 1000 – 10,000 tpa	☐ 10,000 – 100,000 tpa	☐ 100,000 – 1,000,000 tpa
☐ 1,000,000 – 10,000,000 tpa	☐ 10,000,000 – 100,000,000 tpa	☐ > 100,000,000 tpa
☐ <1 . . . . . >+ tpa (e.g. 10+ ; 100+ ; 10,000+ tpa)		☐ Confidential

☒ Industrial use	☒ Professional use	☐ Consumer use	☐ Closed System

Inter alia use for preparation of paints, coatings, toners, printing, inks.

4 OTHER COMPLETED/ONGOING REGULATORY PROCESSES THAT MAY AFFECT SUITABILITY FOR SUBSTANCE EVALUATION

☐ Compliance check, Final decision	☐ Dangerous substances Directive 67/548/EEC
☐ Testing proposal	☐ Existing Substances Regulation 793/93/EEC
☐ Annex VI (CLP)	☐ Plant Protection Products Regulation 91/414/EEC
☐ Annex XV (SVHC)	☐ Biocidal Products Directive 98/8/EEC ; Biocidal Product Regulation (Regulation (EU) 528/2012)
☐ Annex XIV (Authorisation)	☐ Other (provide further details below)
☐ Annex XVII (Restriction)	

5 JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE

5.1 Legal basis for the proposal

☒ Article 44(2) (refined prioritisation criteria for substance evaluation)

☐ Article 45(5) (Member State priority)

5.2 Selection criteria met (why the substance qualifies for being in CoRAP)

☒ Fulfils criteria as CMR/ Suspected CMR

☒ Fulfils criteria as Sensitiser/ Suspected sensitiser

☐ Fulfils criteria as potential endocrine disrupter

☐ Fulfils criteria as PBT/vPvB / Suspected PBT/vPvB

☐ Fulfils criteria high (aggregated) tonnage (*tpa > 1000*)

☐ Fulfils exposure criteria

☐ Fulfils MS's (national) priorities

5.3 Initial grounds for concern to be clarified under Substance Evaluation

Hazard based concerns		
CMR ☐C ☐M ☐R	Suspected CMR[1] ☒C ☒M ☐R	☐ Potential endocrine disruptor
☐ Sensitiser	☒ Suspected Sensitiser[1]	
☐ PBT/vPvB	☐ Suspected PBT/vPvB[1]	☐ Other (please specify below)
Exposure/risk based concerns		
☒ Wide dispersive use	☐ Consumer use	☐ Exposure of sensitive populations
☒ Exposure of environment	☒ Exposure of workers	☐ Cumulative exposure
☒ High RCR	☐ High (aggregated) tonnage	☐ Other (please specify below)

Human health

Irritation&Corrosion: The substance is self-classified based on GHS criteria as Eye damage 1 (by registrant A and B). No skin irritating or corrosive properties of acetone oxime were encountered. The appropriate classification based on GHS criteria has to be verified.

Sensitisation: Registrant B does not classify the substance for its skin sensitising properties based on a negative local lymph node assay. However, there is evidence that acetone oxime possess sensitizing potential based on guinea pig maximization assays submitted by registrant A. All the submitted studies have to be verified if the substance meets the classification criteria or not.

Repeated dose toxicity: The evaluation of the repeated dose toxicity data leads to two different classification. Registrant B classifies the substance based on the GHS criteria as STOT RE 2 (affected organ: spleen, red blood cells), whereas the other registrant does not classify the substance. An evaluation of the endpoint related to the GHS criteria is necessary.

[1] CMR/Sensitiser: known carcinogenic and/or mutagenic and/or reprotoxic properties/known sensitising properties (according to CLP harmonized or registrant self-classification or CLP Inventory)
Suspected CMR/Suspected sensitiser: suspected carcinogenic and/or mutagenic and/or reprotoxic properties/suspected sensitising properties (not classified according to CLP harmonized or registrant self-classification)
Suspected PBT: Potentially Persistent, Bioaccumulative and Toxic

Mutagenicity & Carcinogenicity: Results of *in vitro* and *in vivo* mutagenicity studies are partly ambiguous. A detailed evaluation of the test results is necessary and warranted to evaluate and determine possible mutagenic effects. The carcinogenicity studies which are due to the registrants categorized as not assignable (Klimisch 4) or not reliable (Klimisch 3) for evaluation demonstrate neoplastic effects. Acetone oxime application induced benign hepatocellular tumors in male rats. Furthermore, a major metabolite of acetone oxime 2-nitropropane (CAS: 79-46-9) is harmonized classified as Carc. 1B. The relevance of formation of mutagenic and tumorigenic secondary nitro-alkanes in humans has to be verified. It has to be further determined whether the submitted studies are sufficient to evaluate the potential hazard or if further data are required.

Toxicity for reproduction: Read across approach has been applied for the endpoint fertility and reproductive effects of acetone oxime. It has to be verified within substance evaluation if the read across approach is justified.

Distinct self-classification: The two registrants interpret the application of the GHS criteria differently. A detailed list of self-classification (registrant A and registrant B) and the hazard statement codes are given below:

Registrant A self-classifies the substance as:

Flam. Solid 1, H228: Flammable solid
Acute Tox. 4, H312: Harmful in contact with skin.
Eye Damage 1, H318: Causes serious eye damage.
Skin Sens. 1B, H317: May cause an allergic skin reaction.
Carc. 2, H351: Suspected of causing cancer.

Registrant B self-classifies the substance as:

Flam. Solid 1, H228: Flammable solid.
Eye Damage 1, H318: Causes serious eye damage.
STOT Rep. Exp. 2, H373: May cause damage to organs.

Human exposure

Regarding the registration of this substance, only industrial and professional uses are registered. Based on that, the registrants assessed exposure of industrial workers and professionals only. The substance is used inter alia for the preparation of coatings, paints, inks and toners. The exposure assessments given in the registration dossiers are performed in a quantitative way using the exposure assessment tool ECETOC TRA. The descriptions of the uses and risk management are not explained/discussed in detail. Regarding the identified potential toxicological concerns (e.g.: CMR? Yes?/No?)and the given exposure assessment in the registration dossiers, it is not clear, if the risk management measures used in practice are sufficient for ensuring safe use. A risk for human health cannot be ruled out for industrial workers and professionals at this stage. Regarding uses like preparation of coatings, paints, inks and toners, it is uncertain, if exposure to consumers might be also a concern (e.g. exposure to treated articles). Based on the outcome of the evaluation of the human health concerns, if the risk management indicated in registration dossiers are sufficient.

Environmental hazard

Although the substance is not readily biodegradable (9.1% degradation of test substance (O2 consumption) after 28 day, according to OECD Guideline 301 D, no further assessment of degradation was performed. No metabolites or transformation products of the rather slow hydrolysing substance (half-life of ~18days at ph 7 and 20°C based on data provided in the registration dossiers) were identified, hampering conclusions on environmental risk assessment.

Unlikely exposure was used as a waiving argument for soil and sediment although the substance is persistent. According to Table R.7.11-2 of Guidance on information requirements and chemical assessment Chapter R.7c (ECHA, 2008)the substance is in hazard category 3. Here, as risk to soil organisms cannot be excluded by use of Equilibrium Partitioning Method only, also confirmatory long-term soil toxicity testing is necessary for risk assessment.

Regarding chronic aquatic toxicity, there are some QSAR indications for chronic aquatic toxicity (ChV for fish 0.624mg/L and 0.01 mg/L for daphnids according to ECOSAR class Aliphatic Amines, ECOSAR v1.00). No experimental long term data for fish or invertebrates are available.

Regarding the assessment of the microbial activity in sewage treatment systems a weight of evidence approach was provided, which needs thorough evaluation as the provided justifications are not easily followed: For acetone oxime itself only a value of 2.5mg/L from the toxicity control of the ready biodegradability test is provided .

Read across was performed with two multi-constituent substances: Wasox-VMAC2 (acetone O,O'-[methoxy(vinyl)silanediyl]oxime; acetone O,O',O''-(vinylsilanetriyl)oxime and acetone O-[dimethoxy(vinyl)silyl]oxime, CAS 797751-44-1, Molecular weight: 231.627) and Wasox-MMAC2 (Propan-2-one-O-(dimethoxymethylsilyl)oxime; Propan-2-one-O,O'-(methoxymethylsilandiyl) dioxime, Propan-2-one-O,O',O''-(methylsilantriyl)trioxime, CAS number: 797751-43-0, Molecular weight: 223.893). 3h EC_{50}-values between > 192.31 mg/L and >300mg/L were gained. For further evaluation the value of > 198.96 mg/L (3h EC_{50})was taken by the registrants. Obviously by mistake a value of 298.96 mg/L was taken for PNEC derivation.

These read-across substances are nevertheless hydrolytically unstable, comprise a much higher molecular weight (about 3 times higher than acetone oxime) and have a rather different molecular structure than acetone oxime.

Environmental exposure

Referring to the risk assessments of the registration dossiers, the registrants do not expect any risks for the environment. Calculated exposure levels (PECs) and input parameter like amount used, efficiency of STP, etc. are provided. Nevertheless, the descriptions of the uses, justification of model and parameters and risk management are not explained/discussed in detail. As the ecotoxicological properties still need to be clarified and no relevant exposure was used as justification for waiving of ecotoxicological data, the environmental exposure assessment needs to be evaluated, if it is valid and justified.

Conclusion:
Acetone oxime is a candidate substance to be listed on the CoRAP. There is evidence from *in vitro* and *in vivo* studies that acetone oxime possesses mutagenic and carcinogenic potential. The different reliability conclusions of certain tests are reflected in the distinct classification of the two registrants based on GHS criteria (data lacking and Carc. 2). Furthermore, the possible sensitizing potential and the potential to damage organs after repeated exposure have to be clarified. The read across approach for the development and fertility effects has to be evaluated. Regarding the environment potential risks need to be evaluated – particularly microbial activity in sewage treatment systems.

5.4 Preliminary indication of information that may need to be requested to clarify the concern

☒ Information on toxicological properties	☐ Information on physico-chemical properties
☐ Information on fate and behaviour	☒ Information on exposure
☒ Information on ecotoxicological properties	☐ Information on uses
☐ Information ED potential	☐ Other (provide further details below)

Required tests will be decided based on outcome at the end of the first year of evaluation.

5.5 Potential follow-up and link to risk management

☒ Harmonised C&L	☐ Restriction	☒ Authorisation	☐ Other (provide further details)

Depending on the outcome of substance evaluation a harmonized classification and/or authorization might be required.