Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

to the Opinion proposing harmonised classification and labelling at EU level of

(3*E*)-dec-3-en-2-one

EC Number: -
CAS Number: 18402-84-1

CLH-O-0000007098-68-01/F

Adopted

18 March 2022

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during consultation are made available in the table below as submitted through the web form. Any attachments received are referred to in this table and listed underneath, or have been copied directly into the table.

All comments and attachments including confidential information received during the consultation have been provided in full to the dossier submitter (Member State Competent Authority), the Committees and to the European Commission. Non-confidential attachments that have not been copied into the table directly are published after the consultation and are also published together with the opinion (after adoption) on ECHA's website. Dossier submitters who are manufacturers, importers or downstream users, will only receive the comments and non-confidential attachments, and not the confidential information received from other parties. Journal articles are not confidential; however they are not published on the website due to Intellectual Property Rights.

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Substance name: (3E)-dec-3-en-2-one
EC number: -
CAS number: 18402-84-1
Dossier submitter: The Netherlands

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
05.08.2021	Netherlands	AMVAC NETHERLANDS B.V.	Company-Manufacturer	1

Comment received

Please note that this active substance is also known as 3-decen-2-one (CAS no. 10519-33-2 / EC no. 234-059-0). It is an approved food flavouring substance (JECFA food flavouring no. 1130; FEMA no. 3532; EU flavouring no. 07.121).
Several literature searches have been conducted with the aim to identify scientific open literature which may affect the assessment on human health, ecotoxicology and environmental fate of the active substance dec-3-en-2-one (CAS 10519-33-2) and its synonyms, along with its two potential metabolites 2-decanol (CAS 1120-06-5) and 2-decanone (CAS 693-54-9) and their synonyms, covering a very wide time span (2004-2021). These searches did not reveal detrimental effects associated with dec-3-en-2-one (AMVAC ref. nos. 965-REV-010, 965-REV-017, 965-REV-025 & 965-REV-027).

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 3-decen-2-one summary.zip
ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment 3-decen-2-one.zip

Dossier Submitter's Response

Noted.
We took note of the new literature search provided (965-REV-027; the other noted documents with literature searches were already included into the DAR and CLH report). In this updated search, conducted in June 2021, 81 articles were retrieved for which 22 were considered to be potentially relevant. Of these, 7 were considered to be relevant and reliable after reference review. The articles found do not influence the already proposed classifications.

RAC's response
Thanks for the information. The QSAR-toolbox and VEGA-CEASAR and VEGA-IRFMN/JRC contain information related to the CAS no. 10519-33-2. All information is included in the Skin Sens. section in the opinion.

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2021	Germany		MemberState	2

Comment received
The dossier has also been formally reviewed with regard to classification and labelling. The present classification and labelling of this substance is plausible and correct. However, we have the following comments: The substance (3E)-dec-3-en-2-one is classified for inhalation toxicity as Acute Tox. 4, H332. As the available data indicate that a corrosive effect has occurred in the respiratory tract, it is proposed to classify the substance. As a corrosivity has occurred in the respiratory tract, it is proposed to assign EUH071 "Corrosive to respiratory tract" (no classification). According to Annex I Part 3 Chapter 3 No. 3.1.2.3.3 in conjunction with Note 1 of Table 3.1.3 in Chapter 3 of the CLP Regulation (EC) No 1272/2008, the following may be used in addition to the appropriate pictogram for acute toxicity (in this case GHS07), the pictogram GHS05 for corrosivity may also be used. GHS05 may also be assigned for corrosivity. Until now, harmonised substances in Annex VI of the CLP Regulation were labelled with EUH071 which were already classified as a Skin Corr. 1, 1A, 1B or 1C (H314), i.e. skin corrosive. Consequently, these substances are then already labelled with GHS05, so that the consideration of assigning the pictogram GHS05 in addition to EUH071 was never discussed. In the classification proposal, the substance (3E)-dec-3-en-2-one is not considered corrosive to skin (Skin Corr. 1, 1A. 1B or 1C H314). However, as it is described in the dossier that in the respiratory tract and therefore also a classification as STOT SE 3, H335 is not being considered, the additional assignment of the pictogram GHS05 (corrosivity) should be considered.
Dossier Submitter's Response
Indeed no classification for corrosiveness to the skin is proposed for this substance, therefore, no GHS05 was proposed. The regulation is clear on the addition of EUH071, but not GHS05 in this case. Normally, GHS05 is required in case of corrosivity to metals or classification for skin/eye corrosion. This is not the case for (3E)-dec-3-en-2-one. GHS07 applies to respiratory tract irritation (STOT SE 3) and skin irritation (proposed for this substance). However, GHS07 is already applied and may not sufficiently reflect the corrosiveness in the respiratory tract. It is correct that Note 1 below Table 3.1.3 of the CLP regulation states that *In addition to an appropriate acute toxicity pictogram, a corrosivity pictogram (used for skin and eye corrosivity) may be added together with the statement 'corrosive to the respiratory tract'*. This could be sufficient basis to apply GHS05. The addition of GHS05 based on the proposed classification with EUH071 'Corrosive to the respiratory tract' can therefore be supported by the DS and could be considered by the RAC.
RAC's response
RAC considers that the addition of the pictogram GHS05 would result in double-classification as the pictogram GHS07 is already applied and the additional EUH071 hazard statement code is also agreed.

CARCINOGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
05.08.2021	Netherlands	AMVAC NETHERLANDS B.V.	Company-Manufacturer	3

Comment received

Page 35 (31) of the CLH report.
Several literature searches have been conducted to identify scientific open literature which may affect the assessment on human health (including carcinogenicity potential), covering a very wide span of time (2004 - 2021). These searches did not reveal any detrimental effects on carcinogenicity associated with dec-3-en-2-one (AMVAC ref. nos. 965-REV-010, 965-REV-017, 965-REV-025 & 965-REV-027).

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 3-decen-2-one summary.zip
ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment 3-decen-2-one.zip

Dossier Submitter's Response

We took note of the new literature search provided (965-REV-027; the other noted documents with literature searches were already included into the DAR and CLH report). In this updated search, conducted in June 2021, 81 articles were retrieved for which 22 were considered to be potentially relevant. Of these, 7 were considered to be relevant and reliable after reference review. None of these articles were related to potential carcinogenic effects. The new literature search does not influence the previous conclusion; classification for carcinogenicity is not considered warranted.

RAC's response

Noted.

MUTAGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
05.08.2021	Netherlands	AMVAC NETHERLANDS B.V.	Company-Manufacturer	4

Comment received

Page 26-35 (22-31) of the CLH report.
No classification is proposed. This is in line with our interpretation of the available data. EFSA's Panel on Food Additives and Flavourings (FAF) also concluded recently that the concern for genotoxicity can be ruled out for Flavouring Group 204 Revision 1 to which dec-3-en-2-one [FL-no: 07.121] belongs (EFSA journal, 2019; https://doi.org/10.2903/j.efsa.2019.5750).

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 3-decen-2-one summary.zip
ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment 3-decen-2-one.zip

Dossier Submitter's Response

Noted.

RAC's response

Noted.

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2021	Germany		MemberState	5
Comment received				
pp. 22-31: In an OECD TG 471 (Ames test with salmonella strains: TA98, TA100, TA102, TA1535, TA1537), (3E)-dec-3-en-2-one does not cause gene mutation. In an OECD TG 476, (3E)-dec-3-en-2-one showed mutagenicity in mouse lymphoma cells (L5178Y) without metabolic activation. However, the follow-up in vivo comet assay (OECD TG 489) in duodenum and liver yielded negative results. In an OECD TG 474 (mammalian erythrocyte micronucleus test), (3E)-dec-3-en-2-one was found to be non-mutagenic with respect to clastogenicity and/or aneugenicity. Additionally the substance was non-genotoxic in an UDS assay according to OECD TG 486. On the basis of the results of these studies the conclusion that (3E)-dec-3-en-2-one is not genotoxic can be supported.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
RAC agrees with this conclusion.				

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
05.08.2021	Netherlands	AMVAC NETHERLANDS B.V.	Company-Manufacturer	6
Comment received				
Page 35-38 (31-34) of the CLH report. Several literature searches have been conducted to identify scientific open literature which may affect the assessment of mammalian toxicology and human health, covering a very wide span of time. These searches did not reveal any detrimental effects on reproductive toxicity associated with dec-3-en-2-one (AMVAC ref. nos. 965-REV-010, 965-REV-017, 965-REV-025 & 965-REV-027). ECHA note – An attachment was submitted with the comment above. Refer to public attachment 3-decen-2-one summary.zip ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment 3-decen-2-one.zip				
Dossier Submitter's Response				
We took note of the new literature search provided (965-REV-027; the other noted documents with literature searches were already included into the DAR and CLH report). In this updated search, conducted in June 2021, 81 articles were retrieved for which 22 were considered to be potentially relevant. Of these, 7 were considered to be relevant and reliable after reference review. None of these articles were related to potential reproductive effects. The new literature search does not influence the previous conclusion; classification for reproductive toxicity is not considered warranted.				

RAC's response
Noted.

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2021	Germany		MemberState	7

Comment received
Adverse effects on sexual function and fertility (p. 31): No data – investigation of reproductive organs in RDT study Adverse effects on development (pp. 32-34): Developmental toxicity was assessed with a prenatal developmental toxicity study according to OECD TG 414. In this study, neither mortality nor clinical signs of toxicity and no effects on macropathology, pregnancy outcome, foetal body weight or foetal development were observed. The only significant effect was a reduced body weight gain (-11.6 %) at the high dose (1000 mg/kg) bw/day). Hence, a classification for developmental toxicity is not warranted.
Dossier Submitter's Response
Thank you for your response and support of the proposal.
RAC's response
RAC agrees with this conclusion.

OTHER HAZARDS AND ENDPOINTS – Acute Toxicity

Date	Country	Organisation	Type of Organisation	Comment number
05.08.2021	Netherlands	AMVAC NETHERLANDS B.V.	Company-Manufacturer	8

Comment received
Page 15-18 (11-14) of the CLH report. The proposal Acute Tox. 4 (H332), which is based on the inhalation tox (ATE = 1.5 mg/L), is in line with our interpretation of the available data. However, we do not agree with the proposed additional EUH071 labelling 'corrosive to the respiratory tract'. The mechanism of toxicity is irritation and not corrosivity. This is further explained in detail in the attached position paper (AMVAC ref. no. 965-REV-026) prepared by an expert pathologist. Additionally, the substance is proposed to be classified as a category 2 irritant (GHS07, H315) and not as corrosive to skin. Moreover, no classification for eye damage and irritation is proposed. ECHA note – An attachment was submitted with the comment above. Refer to public attachment 3-decen-2-one summary.zip ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment 3-decen-2-one.zip
Dossier Submitter's Response
We took note of the position paper submitted regarding the proposed classification as corrosive to the respiratory tract (EUH071). The position paper describes the following points: 3-decen-2-one has generally low toxicity; any substance with intrinsic corrosive properties would be expected to show the same effects in skin and eye as well as respiratory tract, however, the substance is a skin irritant and not an eye irritant; pathological changes in the 5-day inhalation study are indicative of contact irritant

(minimal to moderate severity, not consistent with corrosive mechanism of toxicity, considered to be reversible).

We remain of the opinion that classification as corrosive to the respiratory tract is justified.
In the acute inhalation toxicity study at 0.52 mg/L extremely red lungs were reported in one male and at 2.04 mg/L red edematous lungs were reported in 2 males and dark red extremely edematous lungs were reported in 1 additional male.
In the 5-day inhalation toxicity study, degeneration, erosion and ulceration of several tissues were reported in animals exposed at 531 µg/L but also at 278 µg/L.

RAC's response

RAC agrees to apply the EUH071 and supports the DS in this aspect. The proposal to also apply the GHS05 is rejected by RAC as it would lead to double-classification.

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2021	Germany		MemberState	9

Comment received

Acute toxicity – inhalation:
Acute inhalation toxicity (pp. 13-14):
It is proposed to classify (3E)-dec-3-en-2-one as Acute Tox. 4: H332 with an ATE of 1.5 mg/L and with an additional EUH071 labelling. Based on an acute inhalation study according to OECD TG 403, LC50 of the test substance was found to be between 0.52 - 2.04 mg/L (mortality 1/5 and 3/5) for male rats and > 2.04 mg/L for female rats. Given the incidence of mortality at these dose levels, the DS estimates that the LC50 in males is close to 2 mg/L and > 1 mg/L which would, according to the CLP criteria, warrant an Acute Tox. 4 classification.
The DS states that no LC50 could be estimated. It is proposed to apply the converted acute toxicity estimate of 1.5 mg/L (dusts or mists) as included in table 3.1.2 in Annex I of CLP.

According to the "Guidance Document on Acute Inhalation Toxicity Testing (GD 39)":
In case there are only two data points with mortality close to 0 % and 100 % available (i.e.,a very steep concentration-mortality relationship), they can be used to estimate an "approximate LC50" The approximate LC50 is defined as the geometric mean from these mortalities.

However, a quick manual check shows that the geometric mean will be somewhere around 1.7 mg/L, so the use of the cATpE of 1.5 mg/L can be supported.

Since data indicate that the mechanism of toxicity is corrosivity (lung oedema and discoloration of lungs of dead animals and erosion and ulceration of the respiratory tract in the 5-day inhalation study), labelling with EUH071 'corrosive to the respiratory tract' is required (CLP 3.1.2.3.2).

Overall, the classification of (3E)-dec-3-en-2-one as Acute Tox. 4, H332 with an ATE of 1.5 mg/L and with an additional EUH071 labelling can be supported.

Acute toxicity – dermal:
Acute oral/dermal toxicity (pp. 11-12):
With an LD50 of > 5000 mg/kg bw for acute oral (OECD TG 425) and dermal (OECD TG

402) toxicity, it is agreed that classification is not warranted.
Dossier Submitter's Response
Noted, thank you for your support
RAC's response
Noted and included in the opinion.

OTHER HAZARDS AND ENDPOINTS – Skin Hazard

Date	Country	Organisation	Type of Organisation	Comment number
05.08.2021	Netherlands	AMVAC NETHERLANDS B.V.	Company-Manufacturer	10
Comment received				
Page 18-19 (14-15) of the CLH report. Proposal Skin Irrit. 2 (H315). No comments, since this is in line with our interpretation of the available data. ECHA note – An attachment was submitted with the comment above. Refer to public attachment 3-decen-2-one summary.zip ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment 3-decen-2-one.zip				
Dossier Submitter's Response				
Thank you for your response.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2021	Germany		MemberState	11
Comment received				
Skin irritation (p. 14-15): In an OECD TG 404 in rabbits, a mean value of ≥ 2,3 - ≤ 4,0 for erythema/eschar or for oedema in at least 2 of 3 tested animals from gradings at 24, 48 and 72 hours after patch removal where observed. Therefore, classification of (3E)-dec-3-en-2-one as Skin irritant cat. 2, H315 is supported.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Noted.				

OTHER HAZARDS AND ENDPOINTS – Eye Hazard

Date	Country	Organisation	Type of Organisation	Comment number
05.08.2021	Netherlands	AMVAC NETHERLANDS B.V.	Company-Manufacturer	12
Comment received				
Page 19-20 (15-16) of the CLH report. No classification is proposed. No comments, since this is in line with our interpretation of the available data.				

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 3-decen-2-one summary.zip ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment 3-decen-2-one.zip
Dossier Submitter's Response
Noted. Thank you for your response.
RAC's response
Noted.

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2021	Germany		MemberState	13
Comment received				
Eye irritation (pp. 15-16): In an OECD TG 405 in rabbits, eye irritation scores where outside the ranges of the CLP criteria for classification as eye irritant. Therefore, it is agreed that classification is not warranted.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Noted.				

OTHER HAZARDS AND ENDPOINTS – Skin Sensitisation Hazard

Date	Country	Organisation	Type of Organisation	Comment number
05.08.2021	Netherlands	AMVAC NETHERLANDS B.V.	Company-Manufacturer	14
Comment received				
Page 21-26 (17-22) of the CLH report. Proposal Skin Sens. 1. We do not agree with this interpretation of the available data. Two position papers are provided (AMVAC ref. nos. 965-ACT-006b & 965-REV-024) which support the conclusion from the original study author that this substance should not be classified as a skin sensitizer. Based on the evaluation criteria which were followed by the study director and which were reported in the public literature, the results of the study should indeed be considered negative, despite the increased incidence of the 0.5 scores seen in the test animals compared to the controls. Although such increased incidence may indicate a too low concentration chosen for the challenge, the concentration of 1% used by the study director is considered justified, based on the results of the preliminary irritation study. Therefore, the interpretation of the study director is valid and the results of the study should be considered negative. The proposed read-across substances as weight of evidence for classification are not fit for purpose, because of the differences in the chemical structures. Both substances are not simple straight-chain aliphatic ketones. ECHA note – An attachment was submitted with the comment above. Refer to public attachment 3-decen-2-one summary.zip ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment 3-decen-2-one.zip				
Dossier Submitter's Response				
We took note of the positions papers that were provided. We remain of the opinion that classification as a skin sensitizer is warranted for this substance. Given the doubtful				

reaction in the Buehler assay (score of 0.5 whereas OECD guidance indicates scoring at 0, 1, 2, 3) and the known limited sensitivity of this assay, supported by predictions using DEREK nexus and positive results from substances that are considered to be close analogues, we still propose to classify the substance as Skin Sens. 1.
RAC's response
RAC considers that a score of 0.5 seems to imply a doubtful/negligible erythema so the result may be considered negative or the study equivocal and inconclusive for skin sensitisation potential. The use of predictions and read across from QSAR, DEREK, VEGA etc. databases is appropriate, and most of these predictions concluded skin sensitisation potential. Overall, however, RAC considers the evidence not sufficient for classification based on the CLP Regulation criteria.

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2021	Germany		MemberState	15
Comment received				
pp. 17-22: Skin sensitisation was assessed based on a Buehler test (OECD TG 406) study in Guinea pigs (Induction: 100 % and 75 %, challenge: 1 %). After the challenge "very faint" erythema (score: 0.5) were observed 24 and 48 h later. The score "very faint" erythema was not considered a positive reaction by the study author and the guideline only includes the scores: 0 = no visible change, 1 = discrete or patchy erythema but not 0.5. However, it has to be noted that some kind of reaction was visible which can be an indication for skin sensitizing properties. Because of the inconclusive results of the Buehler test, a read-across evaluation was performed with a prediction of the skin sensitizing potential using DEREK. The prediction for (3E)-dec-3-en-2-one was "PLAUSIBLE" (structural alert and mechanism). Additionally, there is evidence that relevant analogues have skin sensitizing potential. Given the inconclusive reaction in the Buehler test which has a known limited predictivity for sensitisation, the "PLAUSIBLE" prediction from DEREK and the positive results from close analogues, a classification as Skin Sens. 1 (no information on potency) can be supported.				
Dossier Submitter's Response				
Noted, thank you for your support.				
RAC's response				
RAC considers that a score of 0.5 seems to imply a doubtful/negligible erythema so the result may be considered negative or the study equivocal and inconclusive for skin sensitisation potential. The use of predictions and read across from QSAR, DEREK, VEGA etc. databases is appropriate, and most of these predictions concluded skin sensitisation potential. Overall, however, RAC considers the evidence not sufficient for classification based on the CLP Regulation criteria.				

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Single Exposure

Date	Country	Organisation	Type of Organisation	Comment number
05.08.2021	Netherlands	AMVAC NETHERLANDS B.V.	Company-Manufacturer	16
Comment received				
Page 38-40 (34-36) of the CLH report. No classification is proposed. No comments, since this is in line with our interpretation of the available data.				

ECHA note – An attachment was submitted with the comment above. Refer to public attachment 3-decen-2-one summary.zip ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment 3-decen-2-one.zip
Dossier Submitter's Response
Noted.
RAC's response
Noted.

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2021	Germany		MemberState	17
Comment received				
pp. 34-36: Effects in the acute oral and dermal studies were limited and above 2000 mg/kg bw. Moreover, in the Comet assay no specific and significant effects were observed. The acute inhalation study on the other hand showed post-mortem effects that included oedema and discolouring of the lungs. However, since classification as Acute Tox. 4, H332 with an additional EUH071 labelling is proposed (acute inhalation toxicity with the label 'corrosive to the respiratory tract') a STOT SE classification for the inhalation route is not appropriate.				
Dossier Submitter's Response				
Noted. Thank you for your considerations.				
RAC's response				
Noted.				

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Repeated Exposure

Date	Country	Organisation	Type of Organisation	Comment number
05.08.2021	Netherlands	AMVAC NETHERLANDS B.V.	Company-Manufacturer	18
Comment received				
Page 40-45 (36-41) of the CLH report. No classification is proposed. No comments, since this is in line with our interpretation of the available data. ECHA note – An attachment was submitted with the comment above. Refer to public attachment 3-decen-2-one summary.zip ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment 3-decen-2-one.zip				
Dossier Submitter's Response				
Noted.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2021	Germany		MemberState	19

Comment received
pp. 37-41: Based on absence of data, no classification as STOT RE is proposed. A waiver is provided for subchronic testing based on natural occurrence in the diet, the metabolic pathways and the low toxicity in developmental toxicity. Furthermore, structurally related substances have only low oral toxicity or toxic effects that are not applicable to (3E)-dec-3-en-2-one. In a 5-day range-finding study, adverse effects were seen at most dose levels, such as respiratory irritation and olfactory and respiratory epithelium degeneration. However, as effects occurred at concentrations comparable or at lower concentrations that are less than 10-fold lower than those leading to classification as Acute Tox. inhalation Cat. 4 (EUH071), no STOT RE classification is warranted based on these respiratory tract effects.
Dossier Submitter's Response
Noted. Thank you for your considerations.
RAC's response
Noted.

OTHER HAZARDS AND ENDPOINTS – Aspiration Hazard

Date	Country	Organisation	Type of Organisation	Comment number
05.08.2021	Netherlands	AMVAC NETHERLANDS B.V.	Company-Manufacturer	20
Comment received				
Page 45-46 (41-42) of the CLH report. Classification with Asp. Tox. 1 is proposed. The dossier submitter however has already indicated that dec-3-en-2-one actually does not meet criterion 1 (no reliable and good quality human evidence is available) and only partially criterion 2 (kinematic viscosity). However, the substance is not a pure hydrocarbon. The substance should therefore not be classified. ECHA note – An attachment was submitted with the comment above. Refer to public attachment 3-decen-2-one summary.zip ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment 3-decen-2-one.zip				
Dossier Submitter's Response				
The DS remains of the opinion (3E) 3-decen-2-one should be considered an aspiration hazard on the following grounds: -it would obviously be illogical to automatically consider a substance *not* an aspiration hazard because there are simply no reliable and good quality human aspiration toxicity data. Rather, 'criterion 1' must be regarded 'not addressable' due to a lack of data. -RMS considers the deduction that (3E) 3-decen-2-one can reasonably be expected to exhibit aspiration toxicity in humans valid until invalidated: the substance's kinematic viscosity at 40 °C is low enough (substantially below cut-off) to facilitate its entry into the respiratory system. Combined with (3E) 3-decen-2-one's evidenced corrosivity to lung tissue, the criteria to define a substance as likely aspiration hazard are fulfilled. -The criterion that an H304-classified substance can exclusively be a hydrocarbon (i.e., a substance only made up from carbon and hydrogen atoms) should not be considered absolute. As already pointed out in 1272/2008, '*substances in Category 1 include but are not limited to certain hydrocarbons, turpentine and pine oil*'. Interestingly, even pine oil				

itself is a good example of a substance that defies definition as a hydrocarbon, being mainly composed of isomeric tertiary and secondary cyclic terpene alcohols. In conclusion, (3E) 3-decen-2-one *not* being classified H304 would only hinge on the argument that the substance is not strictly a hydrocarbon. As pointed out above, this position is not very strong, especially when set against the stronger arguments in support of classification. Our position therefore remains unchanged.
RAC's response
RAC acknowledges that no human data is available. However, according to the CLP criteria, classification in this category can be based on kinematic visocisty measurement. Based on that, RAC agrees with the DS proposal that classification as Asp. Tox. 1 is warranted.

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2021	Germany		MemberState	21
Comment received				
pp. 41-42: According to CLP, classification in this category is needed when reliable and good quality human data are available or when the substance is a hydrocarbon with a kinematic viscosity of 20.5 mm²/s or less. Human data (case studies) are not available and the kinematic viscosity of dec-3-en-2-one at 40 °C is expected to be between 1.76 mm¬2/s (25 °C) and 2.21 mm2/s (45 °C). Based on the second criteria it is agreed to classify for aspiration hazard. To our view the classification should not be limited to hydrocarbons in a strict sense as dec-3-en-2-one is a hydrocarbon with a single oxygen atom. However, the CLP criteria are seen as fulfilled which warrants classification as Asp. Tox. 1, particularly in light of the irritating or corrosive properties to the lung after inhalation.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Noted and agreed with the argumentation.				

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
05.08.2021	Netherlands	AMVAC NETHERLANDS B.V.	Company-Manufacturer	22
Comment received				
Page 63 (59) of the CLH report. Classification with Aquatic Chronic 2 is proposed. The environmental data clearly show that dec-3-en-2-one is readily biodegradable. Moreover, the environmental toxicity data clearly demonstrate that this substance will not persist in the aquatic environment due to a combination of degradation & very significant volatilisation. A recent 28-day toxicity study on the emergence of chironomids demonstrate low toxicity (NOEC = 103 mg/kg sediment; AMVAC ref. no. 965-AQU-007). Classification with Aquatic Chronic 2 is therefore not warranted. ECHA note – An attachment was submitted with the comment above. Refer to public attachment 3-decen-2-one summary.zip ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment 3-decen-2-one.zip				

Dossier Submitter's Response
Dec-3-en-2-one is classified as readily biodegradable, failing the 10 day window. In the ready biodegradability test (OECD 301F) the criteria were not met at 10 days and were met at 28 days. According to CLP guidance V4.1 June 2015, p 564, the 28 day time window should only be considered for tests where the 10 day window is not applicable (OECD 301C), difficult to evaluate (14 day window sometimes applied in 301D), no information is present to evaluate (e.g., old or public literature studies) or for complex multicomponent substances (e.g., oils, UVCBs). Since none of these apply in this case, the information at the 10 day time window was applied and the substance was considered not rapidly degradable for the CLH assessment. Please note that the study with *Chironomus riparius* was not submitted to the Netherlands until after the CLH report was submitted to the ECHA (the study was submitted to the Netherlands on July 6th, 2021) and has not yet been evaluated. The study report indeed concludes a NOEC of 103 mg/L. However, it is noted that even if the NL evaluation confirms this endpoint, a chronic endpoint for fish is not available and the "most stringent" classification would be used (according to CLP guidance V4.1 June 2015, Figure 4.1.1). Since this classification would still be Chronic 2 for fish, the overall classification should not change based on this study.
RAC's response
RAC notes that during the test, the degradation of (3*E*)-dec-3-en-2-one did not meet the 10-day window thus the substance is not demonstrated to be readily biodegradable in a 28-day test for ready biodegradability as the pass level of the test must be achieved within 10 days from the onset of biodegradation according to Section 4.1.2.9.5 of the CLP Regulation. Therefore, RAC does not agree with the DS to consider the substance as readily biodegradable but failing the 10-day window. The 10-day window condition may be waived as discussed in the CLP Regulation Annex II.2.3. If this is not possible, then the pass level should be evaluated within a 14-day window if possible, or after the end of the test. RAC concludes that there is currently not sufficient justification that the 10-day window condition may be waived. Based on the available data on the hydrolytic behaviour of the substance in the water demonstrating stability, the additional justifications on the unreactive nature of the structure of the substance and due to the degradation of (3*E*)-dec-3-en-2-one amounting to 60 % after 28 days, RAC agrees with the DS to consider (3*E*)-dec-3-en-2-one as not rapidly degradable for classification purpose. RAC also notes that the study with *Chironomus riparius* mentioned during the consultation round has not been evaluated and taken into account as part of this proposal. Taking into account that reliable chronic data is not available for all trophic levels, RAC agrees with the DS proposal is to classify the substance as Aquatic Chronic 2; H411, the substance being not rapidly degradable, based on the surrogate approach and the lowest EC_{50} obtained with *O. mykiss* (1.50 mg/L, mm).

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2021	Germany		MemberState	23
Comment received				
We thank the RMS for the evaluation. We agree to the classification as aquatic chronic 2. However, we kindly ask the RMS to provide some further explanation concerning the identity and CAS number of the substance. The CLH-dossier refers to the CAS number 18402-84-1. The DAR, from which the relevant data is taken, refers to the CAS number 10519-33-2. Please clarify if both CAS numbers refer to the same substance or if there are differences. The subchapter 3 "History of the previous classification and labelling" gives some information, but additional clarification would be very helpful. Preferably, both CAS numbers should be directly mentioned and explained in the text.				

Dossier Submitter's Response
Thank you for indicating an issue that will require correction. CAS no. 18402-84-1 specifically relates to the '*3-Entgegen*'-isomer (3E) 3-decen-2-one that is the actual active substance, whereas CAS no. 10519-33-2 simply refers to '3-decen-2-one', i.e., no stereoisomer in specific, which is unnecessarily inaccurate. Wherever reference is made to the active substance in particular, the CAS no. should therefore be 18402-84-1. Correction pending.
RAC's response
RAC appreciates and takes into account the additional information.

OTHER HAZARDS AND ENDPOINTS – Physical Hazards

Date	Country	Organisation	Type of Organisation	Comment number
05.08.2021	Netherlands	AMVAC NETHERLANDS B.V.	Company-Manufacturer	24
Comment received				
No classification is proposed. No comments, since this is in line with our interpretation of the available data. ECHA note – An attachment was submitted with the comment above. Refer to public attachment 3-decen-2-one summary.zip ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment 3-decen-2-one.zip				
Dossier Submitter's Response				
Noted				
RAC's response				
RAC agrees with the rational of the DS and that no classification and labelling with regards to the physical hazards are warranted for (3*E*)-dec-3-en-2-one.				

PUBLIC ATTACHMENTS
1. 3-decen-2-one summary.zip [Please refer to comment No. 1, 3, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24]

CONFIDENTIAL ATTACHMENTS
1. 3-decen-2-one.zip [Please refer to comment No. 1, 3, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24]