Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

Chrysanthemum cinerariaefolium extract from open and mature flowers of *Tanacetum cinerariifolium* obtained with supercritical CO_2

EC Number: 289-699-3
CAS Number: 89997-63-7

CLH-O-0000007335-74-01/F

Adopted

8 June 2023

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON CHRYSANTHEMUM CINERARIAEFOLIUM, EXTRACT FROM OPEN AND MATURE FLOWERS OF TANACETUM CINERARIIFOLIUM OBTAINED WITH SUPERCRITICAL CARBON DIOXIDE

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: Chrysanthemum cinerariaefolium, extract from open and mature flowers of Tanacetum cinerariifolium obtained with supercritical carbon dioxide
EC number: 289-699-3
CAS number: 89997-63-7
Dossier submitter: Spain
GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
22.06.2022	Germany		MemberState	1
Comment received				
Two separate CLH-reports for the extract from chrysanthemum cinerariaefolium have been provided in parallel, which differ by the solvent used for extraction (supercritical CO2 or hydrocarbon solvents). The proposed classification is the same and the chapters on toxicological endpoints are widely identical. In the report on the extract using supercritical CO2 this solvent is explicitly mentioned in the description of the toxicological studies (A2.2.-2.12) while in the report on the extract using hydrocarbon solvents the broader term "pyrethrum extract", which covers both, is used. This might indicate, that nearly all toxicological studies were performed with the extract using supercritical CO2 and a read across was performed to the extract using hydrocarbon solvents. This could be clarified and some more justification for the read across, if performed, would be helpful. As an UVCB of natural origin a variability in the content of the six pyrethrins (pyrethrin 1, cinerin 1, jasmolin 1, pyrethrin 2, cinerin 2 and jasmolin 2) might be possible. Some more general (and non-confidential) information about the variable content (e. g. ranges) would be helpful to understand, that the tested extracts are representative for all extracts in general. It is not clear, whether the DS is of the opinion, that all pyrethrins have similar toxicological properties. Then, some variability in the composition would not be relevant. It is noted, that the toxicological studies were performed with extracts, which included an additional solvent (EC 265-149-8; solvent range: 42.43-50.65%), but as elaborated in the CLH-report, this solvent is likely not the cause for the toxicological effects, which are reflected by the proposed classification.				

Furthermore, we would like to inform you about following formal errors:
• Section 2.1: Please delete the warning statement for pollinators since this is specific for the approval under the BPR and not relevant for the CLH report.
• Section 4.1: Please delete the paragraph about the fate and behavior in the environment based on the representative products' use since this is specific for the approval under the BPR and not relevant for the CLH report.
• Section 4.1: Please delete the effects assessment and summary table of PNEC values since this is specific for the approval under the BPR and not relevant for the CLH report.
• Section A.3.1 & A.3.2: Please delete the boxes "Value used in Risk Assessment" since these boxes are specific for the approval under the BPR and not relevant for the CLH report.

ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment DE-CA Comments CLH-Chrys_cin_CO2 -conf.docx

Dossier Submitter's Response

Thank you for your comment.

First of all, with regard to the first and third paragraphs (which can be considered as related), it should be noted that indeed the two substances only differ in the extraction method. Irrespective of the extraction method, the concentration of pyrethrins was adjusted with the solvent mentioned in the third paragraph (which is not responsible for the observed toxicological effects as it has a harmonised classification only as Asp. Tox. 1 - H304) leaving it in both cases at around 50%. This makes both extracts equivalent, since the same concentrations of active substance can be found in both extracts.

The DS prepared a detailed document for the justification of the read across among the different sources initially submitted (different extracts), which belonged to different active substances, and included this justification for read across and the TE justification between sources of the same active substance, *Chrysanthemum cinerariaefolium*, extract from open and mature flowers of *Tanacetum cinerariifolium* obtained with hydrocarbon solvents. Although it was prepared for the CAR, this DS is willing to provide this document to the RAC Secretariat, if necessary.

According to BPC APCP WG-III-2021, the reference specifications were amended to a maximum concentration of 90% total pyrethrin for *Chrysanthemum* extract from supercritical CO_2. For the (eco)toxicological effects, the endpoints obtained from the studies as total pyrethrins should be converted to the extract considering this updated reference specification.

Regarding the second paragraph, we as DS can only prepare the CLH report on the basis of the information available. This means that the information is eminently provided by the industry, so there are no ranges over which to claim that these extracts are representative of all extracts. However, in our opinion, and without being able to go into more detail due to confidentiality issues, we think that the variability between *Chrysanthemum cinerariaefolium* species found in different regions does not represent a problem for the classification, taking into account that the reference specifications have to be met.

Finally, as regards formal errors, we agree that they should be deleted from the CLH report.

RAC's response
RAC thanks the Member State for the comments and for the Dossier Submitter's clarification.

Date	Country	Organisation	Type of Organisation	Comment number
23.06.2022	United Kingdom	Sumitomo Chemical rep BRA and MGK, SCJ and KPIC	Company-Manufacturer	2

Comment received
Please refer to the attachment ECHA note – An attachment was submitted with the comment above. Refer to public attachment Chrysanthemum Cineranium extract SCF CLH-report commenting table_23.06.2022.pdf

Dossier Submitter's Response
1.1 The appendix was not available for public consultation as the information was confidential. However, it was relevant for ECHA to understand the role of the solvent. 1.2 The exact solvent concentration has not been disclosed in the CLH report at any point. Moreover, as this solvent is not part of the reference specifications of the active substance, this information is not confidential. The solvent identifier (CAS and EC numbers) is necessary to verify that this solvent has a harmonised classification and is not responsible for the effects observed in the (eco)toxicology studies. The concentrations of plant material and BHT have not been disseminated either. This information can also not be considered as confidential and could have relevance for the (eco)toxicological properties of the active substance. 1.3 Thank you for your comment. We hope that it will help to clarify its role in the manufacturing process of the active substance, but not in the alteration of its (eco)toxicological properties. 1.4, 4.1 to 4.3, A.1.1, A.2.1, A.3.1, A.3.3, A.3.5, A.3.6, A.3.8, A.3.10, A.3.12, A.3.13, A.3.15 to A.3.17, A.6.1 to A.6.3 and B.2 We agree that this information should be deleted from the CLH report since this is specific for the approval under the BPR. 1.5 The terminology is already consistent throughout the CLH report. In your example, "total pyrethrins" means pyrethrins+BHT+plant material+water as stated in page 7. Regarding the disclosure of the items listed in the definitions, our opinion can be found in point 1.2 of this comment. 2.1 Since the active substance is an UVCB, all components above a certain concentration are considered relevant, not only the active ones. Furthermore, as the full composition of the plant material has not been disclosed, this partial information cannot be considered confidential. Regarding batches in which the plant material and BHT were determined, we prefer not to go into detail as this information is considered confidential. 3.1, A.2.2 to A.2.8, A.3.2, A.3.4, A.3.7, A.3.9, A.3.11, A.3.18, A.3.19 and B.1 We agree this information should be redacted.

A.3.14 We agree these headings should be amended.

B.1 For DS, the ownership of the data was never completely clear as there were discrepancies between the owners. However, we have consulted the Applicants' contact point for biocides in order to clarify the data ownership, and an amended version will be provided to ECHA.

B.3 and B.4 The information available in the 2008 RAR should not be redacted since it was made public. In the case of the studies after 2008, this information should be redacted.

B.4 This information has been extracted as is from the DAR and has not been altered to keep it true to Italy's assessment of the active substance under PPPR.

RAC's response

RAC thanks the Company for the comments and the Dossier Submitter for the clarification.

Date	Country	Organisation	Type of Organisation	Comment number
24.06.2022	Italy		MemberState	3

Comment received

IT has recently provided the Assessment Report for pyrethrins as PPP active substance. We checked the studies presented for the CLH dossier and we noticed that some studies are missing for the section of mammalian toxicology, environmental fate and behavior and ecotoxicology. In the following one missing study per section is reported as an example: Acute oral toxicity, range finder & LD50 – rats Report No 86-5148A (1986); Degradation of [Cyclopentenone-2-14C]Pyrethrin I in Mußbach soil incubated under aerobic conditions at 20 °C in the dark.
Report No: AS501 (2017); Species Sensitivity Distribution of acute toxicity to fish Acute toxicity of refined pyrethrum concentrate on aquatic organism (fish) - Report No GAB-034/4-32/ SSD (2013).
Has the dossier submitter checked what was presented for pesticide renewal? Please, have a look on Volume 2 of the RAR containing the list of studies and Volume 1, with the proposal for classification, attached to this comment.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Pyrethrins_RAR_Volume 1-2_2022-01-18.pdf

Dossier Submitter's Response

Thank you for your comment.

We are not sure that we have not included all the IT studies in PPP in the CLH report. The studies used as examples are already included in the CLH report. The studies from the RAR are included in Appendix VII of Part B (Appendices). These studies are in a separate appendix because we thought that their location in the CLH report would be simpler, because the CAR prepared under the BPR was used as a template. Moreover, we have not re-evaluated the DAR studies because we consider Italy's opinion to be as valid as ours. For this reason, we have therefore left the information in Volume 3 intact for the RAC to take the decision it deems most appropriate.

For the sake of clarity, we can add here the classification proposed by Italy for PPPs and its comparison with the one proposed in this CLH report:

PPPR	BPR
Acute Tox. 4 (H302 & H332)	Acute Tox. 4 (H302 & H332) ATE_{oral} = 700 mg/kg bw $ATE_{inhalation}$ = 2.5 mg/L (dusts & mists)
Skin Sens. 1B (H317)	Skin Sens. 1B (H317)
STOT SE 1 (H370)	-
Asp. Tox. 1 (H304)	-
Aquatic Acute 1 (H400) M = 1000	Aquatic Acute 1 (H400) M = 100
Aquatic Chronic 1 (H410) M = 100	Aquatic Chronic 1 (H410) M = 10*

*This M-factor is proposed to be changed to 100 (please see comment 7).

RAC's response

Thank you for your comments. Indeed, RAC noted the missing studies and has included them in the opinion document.

Date	Country	Organisation	Type of Organisation	Comment number
24.06.2022	Germany	Pyrethrin Joint Venture	Company-Manufacturer	4

Comment received

Comments concern legally wrong data ownership information stated in the CLH dossier.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment PJV comments_supercritial carbon dioxide_non confidential.zip
ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment PJV comments_supercritial carbon dioxide_confidential.zip
ECHA note: ECHA checks the CLH report as received by the Dossier Submitter (DS) for accordance with the CLP regulation and subsequently publishes the report. Accordance check does not verify and ECHA has no mandate to verify the correctness of the information contained therein, particularly to assess the company's allegation concerning the ownership of the data reported in the reference list. Therefore, ECHA cannot itself make such changes to the CLH Report, nor can act on this allegation. However, the DS will further reply to your comment.

Dossier Submitter's Response

For DS, the relationship between the different data owners was never clear, especially when several of them appeared to be based outside the EU. This resulted in the data coming with the name of different owners in the two dossiers. DS never received clear information on this.

It is not the responsibility of the DS to clarify this information or to intervene in legal problems that the owners of the data have with each other. However, we have asked the Applicants' contact point in order to clarify this issue. We have no objection to the modification of the relevant information once we have received this clarification.

ECHA note – An attachment was submitted with the response from the dossier submitter. Refer to attachment CLH Chrysanthemum extract Supercritical CO2.docx
RAC's response
ECHA note: ECHA has uploaded the revised CLH report with correct data owner information on its website.

CARCINOGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
22.06.2022	Germany		MemberState	5
Comment received				
It is stated in chapter A2.9.1 of the CLH-reports: "In male rats the incidences of adenoma were 5% (3 of 60 males) in both, the highest dose and the mid dose (3000 ppm and 1000 ppm (199 and 66 mg/kg bw/d extract))." However, these incidences could not be easily found in the table on p.123-126 of the report on the CO2-extract (p. 129-132 of the report of the hydrocarbon solvent-extract). It should be added from which data of the table the incidences of 5% are derived. It is mentioned in the CLH-report, that keratoacanthomas in rats and lung carcinomas in mice were increased, but no numeric values of the incidences are available. They should be added for completeness. ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment DE-CA Comments CLH-Chrys_cin_CO2 -conf.docx				
Dossier Submitter's Response				
Thank you for your comment. The data is derived from table showing the microscopic findings in liver (p. 130-131). The combined incidence (SAC + DOS) for hepatocellular adenoma was 5% in males in both mid- and high-dose groups. Regarding the keratoacanthomas in rats and lung carcinomas in mice the highest incidences were 23,3 (males in high-dose group) and 5% (males in mid- and high-dose groups), respectively.				
RAC's response				
RAC thanks the Member State for the comment and the Dossier Submitter for the clarification. These values are included in the RAC background document (section "Supplemental information - In depth analyses by RAC").				

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
24.06.2022	France		MemberState	6
Comment received				
We agree with the aquatic acute and chronic toxicity classification that are proposed.				
Dossier Submitter's Response				

Thank you for your comment. Please see comment 7, some changes have been proposed.
RAC's response
Thank you for your comment

Date	Country	Organisation	Type of Organisation	Comment number
22.06.2022	Germany		MemberState	7
Comment received				
• Section A.3.1.1.1: Please check the reliability of the study "photolysis in water". The CAR states a reliability of 2. • Section A.3.1.2: Please delete the reference to the environmental risk assessment in the text regarding the study by Mori. • Section A.3.2.1: P lease indicate in the tables whether the concentrations are nominal or measured. • Section A.3.2.1.1: In the description of the second acute immobilisation test with D.magna, an EC50 of 272.81 µg/L is mentioned for pyrethrin 1. Please change this to 61.08 µg/L as shown in table A77. • Section A.3.2.1: • The early life stage test with fathead minnow is described as subacute. However, this study is a long-term study. Please revise. • Section A.3.2.1.2: In the text for the acute test with C.riparius, the numbers of immobile daphnids is mentioned instead of chironomids. Please revise. • Section A.3.2.1.2: I n the summary table of acute/short-term toxicity to sediment dwelling organisms, please add that the test was done with the test material FEK-99. • Section 4.1: In Table 4.3, the temperature corrected DT50 in the sediment is 11.2 d at 12 °C (5.27 d at 20 °C) instead of 10 d. Please revise. • Section A 6.1.3: For the P assessment, the temperature corrected DT50 in the sediment is 11.2 d at 12 °C (5.27 d at 20 °C) instead of 10 d. Please revise. • Appendix VII 2): According to the appendix VII, there are studies from the approval as active substances used in plant protection products, which show lower effect concentrations compared to the studies from the approval as biocidal active substance. This could influence the derivation of the M-factors. I.e. for the acute aquatic toxicity, there is a study with				

H.azteca with an LC50 of 0.76 µg total pyrethrins /L =0.00076 mg total pyrethrins /L which is equivalent to 0.00092 mg/l of Chrysanthemum cinerariaefolium extract from supercritical CO2, without solvent (pyrethrins are at a concentration of 82.39% in the composition of the plant extract). This would lead to a M-Factor of 1000. For the chronic aquatic toxicity, there is a study with A.bahia with a NOEC of 0.25 µg total pyrethrins/L = 0.00025 mg total pyrethrins/L which is equivalent to 0.00030 mg/L of Chrysanthemum cinerariaefolium extract from supercritical CO2, without solvent (pyrethrins are at a concentration of 82.39% in the composition of the plant extract). This would lead to a M-Factor of 100. Classification should consider all available data and these studies were judged as reliable in the assessment of the active substance as plant protection product. Therefore, the M-factor should be derived based on these lower effect concentrations. Please adjust the classification accordingly or provide a rationale why these studies should not be considered.

ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment DE-CA Comments CLH-Chrys_cin_CO2 -conf.docx

Dossier Submitter's Response

• Section A.3.1.1.1:
The reliability of the study "photolysis in water" should be changed to 2 as stated in the CAR. Sorry for the mistake.

• Section A.3.1.2:
The reference to the environmental risk assessment in the text regarding the study by Mori should be deleted. Agreed and thank you for the comment.

• Section A.3.2.1:
The concentrations are measured except for the endpoint for algae, which is the solubility limit.

• Section A.3.2.1.1:
Thank you for this correction. The value should be 61.08 µg/L, as shown in table A77.

• Section A.3.2.1:
We agree. It should read "*A flow-through chronic toxicity test*".

• Section A.3.2.1.2:
The following text and the detailed table for **Immobile *Chironomus riparius*** should be deleted from the CLH report:

"*In this specific test, observations on immobilization of the Chironomus riparius were made after 24 and 48 hours. The immobilised Chironomus riparius were counted and abnormal behaviour was noted at test start and every 24 hours thereafter. Water temperature, pH and dissolved oxygen were recorded throughout the exposure period. Chironomus riparius were not fed during the test period. Analytical determinations for total Pyrethrins concentration were made from samples taken from each replicate of each test item group at the start and end of the study. Mortality data as absolute numbers of immobile daphnids and as percent of exposed animals is shown below:*"

• Section A.3.2.1.2:

As it is stated in this section, the tests were not performed with the test material FEK-99. The three acute immobilisation tests with *C. riparius* were performed for the chemical similarity report, using the three available sources.

• Section 4.1:
Thank you for this comment. The value corrected to 12ºC is 11.2 d. This should be amended in table 4.6 as well as in section 4.1 (last paragraph in "Fate and behaviour in aquatic compartment").

• Section A 6.1.3:
Thank you for this comment. The value corrected to 12 ºC is 11.2 d. This should be amended in section A.6.1.3. PBT Assessment.

• Appendix VII 2):
The classification was proposed according to the available studies under BPR (no other studies were available to be evaluated by this DS). Nevertheless, we added some studies that were included in the plant protection product dossier to such Appendix VII but did not change the initial proposal.

The BPR dossier refers to Chrysanthemum extract whereas the PPP dossier refers to Pyrethrins, hence this CLH report refers to the extract from supercritical CO_2 (max. content of 90% pyrethrins, see comment 1). Actually, the endpoints from the studies, estimated in total pyrethrins, need to be converted from total pyrethrins to the extract, considering the APCP WG-III-2021 decision regarding the reference specification (see comment 1).

Nevertheless, being pyrethrins the active biocidal component assessed in the tests, and according to the approach 1S1A, we would accept the evaluation made by Italy under PPP.

Regarding the chronic classification, the study with *A. bahia* has some deficiencies regarding the analytical methods as stated in the DAR ("the expert concluded that the method of this study is not acceptable, is not fully validated - results are not in accordance with RD – two different reference materials were used - materials are not compliant with RD, the composition of batch remained uncharacterized"). Nevertheless, the study has been considered valid for the risk assessment in the RAR. Hence, the DS could consider the higher M factor for the chronic classification (M-Factor 100 for not readily biodegradable substances, based on *A. bahia* study in the interval 0.0001 < NOEC < 0.001 mg/L).

Regarding the acute classification, we are reluctant to accept the M factor of 1000, as it is based on a study with *Hyalella azteca*, and there is no OECD guideline approved for this species, whose behaviour is complicated, hence these studies are not usually considered valid for evaluation in the BPC WG or require an additional further assessment by the competent authorities' experts. Furthermore, there are some deficiencies stated in the RAR such as the not acceptability of the analytical methods, the composition of batch remained uncharacterized, and the study is not accepted by method experts.

The DS could consider for classification the acute study with *M. bahia*, which was accepted in the RAR, and hence the M factor would be 100, same as in the actual proposal.

Considering all the above, and the changes in the reference specification from BPC APCP WG-III-2021 (see comment 1), please find here a comparative table with the environmental classification proposals, including a new proposal which has considered the comments here submitted:

	IT CLH proposal for Pyrethrins under PPP		ES CLH actual proposal for Chrysanthemum extract from hydrocarbon solvents		ES CLH new proposal for Chrysanthemum extract from hydrocarbon solvents after commenting period	
Acute	A1		A1		A1	
M factor	1000	Based on 0.76 µg total pyrethrins/L for *H. azteca**	100	Based on *C. riparius* 0.00311 mg total pyrethrins/L (equivalent to 0.0037 mg *Chrysantemun* extract from supercritical CO_2 without solvent, where pyrethrins are at a concentration of 82.39%)	100	Based on *M. bahia* 0.0014 mg total pyrethrins/L (equivalent to 0.00156 mg/L of *Chrysanthemum* extract from supercritical CO_2, without solvent, where pyrethrins are at maximum concentration of 90% in the composition of the plant extract)
Chronic	C1		C1		C1	
M factor	100	Based on *A. bahia* 0.00025 mg total pyrethrins/L	10	Based on *Daphnia magna* 0.00086 mg total pyrethrins/L (equivalent to 0.00104 mg *Chrysanthemum* extract from supercritical CO_2 without solvent. Considering the substance as total pyrethrins the M factor would be 100 based on a NOEC = 0.00086 mg/L)	100	Based on *A. bahia* 0.00025 mg total pyrethrins/L (equivalent to 0.000278 mg/L *Chrysanthemum* extract from supercritical CO_2, without solvent, where pyrethrins are at a max. concentration of 90% in the composition of the plant extract)

* Studies not submitted under BPR but considered under PPP for classification:

M. bahia	*Pyrethrum extract (FEK-99)*	*96h flow through*	*LC50 = 1.4 µg pyrethrins/L*
Hyalella Azteca	*Pyrethrum Stewardship Blend*	*96h flow through*	*LC50 = 0.76 µg pyrethrins/L*
A. bahia	*Pyrethrum Stewardship Blend*	*28 days, flow through*	*NOEC = 0.25 µg pyrethrins/L*

These values should be converted to C. extract considering the % of total pyrethrins in the extract itself. I.e.: M. bahia LC50 = 0.00156 mg C. extract CO_2/L.

RAC's response

Thank you for the comments and the answers. Regarding the studies with A bahia and H Azteca, RAC has taken them into account and has discussed the validity of the studies in the opinion.

Date	Country	Organisation	Type of Organisation	Comment number
17.06.2022	United Kingdom	Health and Safety Executive	National Authority	8

Comment received

Comments:
Long-term toxicity data are not available for the most sensitive fish species Oncorhynchus mykiss. Equally, at present reliable water phase dosed long-term toxicity data to for the acutely sensitive species Chrironomus riparius are not available. On this basis, the surrogate approach should be considered which would result in a more stringent M-factor of 100.

We note the Heintze, 2001 OECD 219 study with C. riparius is considered supporting information at present. Is there further information regarding analytical verification of the test substance in the water and sediment phases over the study available to consider if a long-term endpoint based mean measured water phase concentrations can be reliably

determined?
Dossier Submitter's Response
We agree to apply a more stringent M-factor for C1 classification (please see comment 7). We consider that the three trophic level chronic studies submitted are valid and enough for classification. Nevertheless, as there is a more stringent NOEC for other invertebrates' study, we agree to the M-factor of 100 for chronic classification (please see comment 7). This would cover the possible higher sensitivity of *O. mykiss*. Regarding water/sediment, only the acute test with chironomids is used for classification, not the chronic one (supporting information). FYI: some additional chronic tests with sediment organisms are being performed by the applicants under BPR.
RAC's response
RAC agrees that for the Heintze, 2001 OECD 219 study with C. riparius, a long-term endpoint based mean measured water phase concentrations cannot be reliably determined on the basis of the data presented in the CLH report.

OTHER HAZARDS AND ENDPOINTS – Physical Hazards

Date	Country	Organisation	Type of Organisation	Comment number
24.06.2022	France		MemberState	9
Comment received				
p52 : Auto-ignition temperature: An auto-ignition temperature of 284 °C has been determined for the pure active substance (Siusiene, E. 2022). However, a DSC screening on pure active substance showed that degradation starts at a temperature of 149 °C. As a consequence, could you please clarify that the measured auto-ignition temperature may not correspond to the auto-ignition temperature of the substance, as it is degraded before ignition ?				
Dossier Submitter's Response				
We noted that this comment is exactly the same that the comment reported in the table for *Chrysanthemumum cinerariaefolium* obtained from hydrocarbon solvents. For the active substance *Chrysanthemumum cinerariaefolium* obtained from supercritical carbondioxide (applicant BRA), values described in the CLH report are: DSC screening: Exotherm onset temp (ºC) 1st: 132.09 2nd: 252.86 AIT: 308 ºC Our explanation is the same:				

DSC has been conducted to provide preliminary thermal stability information on a test substance to screen explosive or self reactive properties. The onset temperature of energetic activity is indicated by examining any deviation in the sample heat flow from the baseline. DSC shows un upward deviation in the sample heat flow from the baseline indicating exothermic activity at the temperature of 132 ºC. A second upward deviation from the baseline indicating exothermic effect has been determined at the temperature of 252ºC. Subsequently, DSC shows a downward deviation indicating endothermic activity. The DSC was conducted in a gold (high pressure, sealed) crucible type in the following conditions: 20ºC to 500ºC at 4ºC/min. In the other hand, the autoignition temperature (AIT) of a substance is defined by the ASTM as "the minimum temperature at which autoignition occurs under the specified conditions of test". This definition highlights the non-fundamental nature of AIT, that is, the measured value depends on the conditions of the experiment. The test is conducted in accordance with the procedure described in EU Regulation 440/2008, test A.15. As determined by this method, the AIT is the lowest temperature at which the substance will produce hot flame ignition in air at atmospheric pressure without the aid of an external ignition source. The AIT changes significantly depending on many conditions (e.g.the volume of the vessel used is particularly important since lower autoignition temperatures will be achieved in larger vessels). Therefore, the AIT by a given method does not necessarily represent the minimum temperature at which a given material will self-ignite. Therefore, the conditions used to conduct the DSC screening and the AIT are very different and may not be comparable. In addition, the test substance is a UVCB substance with multitude of constituents, not only pyrethrins. It means that the energetic activity showed in the DSC and the measured autoignition temperature may be influenced by different constituents present in the same mixture.
RAC's response
Thank you for your comments and answer. RAC supports the conclusion based on the defined AIT

PUBLIC ATTACHMENTS
1. PJV comments_supercritial carbon dioxide_non confidential.zip [Please refer to comment No. 4]
2. Pyrethrins_RAR_Volume 1-2_2022-01-18.pdf [Please refer to comment No. 3]
3. Chrysanthemum Cineranium extract SCF CLH-report commenting table_23.06.2022.pdf [Please refer to comment No. 2]

PUBLIC ATTACHMENTS (Dossier Submitter's response)
1. CLH Chrysanthemum extract Supercritical CO2.docx [Please refer to response to comment No. 4]

CONFIDENTIAL ATTACHMENTS
1. PJV comments_supercritial carbon dioxide_confidential.zip [Please refer to comment No. 4]
2. DE-CA Comments CLH-Chrys_cin_CO2 -conf.docx [Please refer to comment No. 1, 5, 7]