Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

ethametsulfuron-methyl (ISO); methyl 2-[(4-ethoxy-6-methylamino-1,3,5-triazin-2-yl)carbamoylsulfamoyl]benzoate

EC Number: 619-290-0
CAS Number: 97780-06-8

CLH-O-0000006714-71-01/F

Adopted

20 September 2019

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON ETHAMETSULFURON-METHYL (ISO); METHYL 2-({[4-ETHOXY-6-(METHYLAMINO)-1,3,5-TRIAZIN-2-YL]CARBAMOYL}SULFAMOYL)BENZOATE

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during public 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 public 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 public 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.

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Substance name: ethametsulfuron-methyl (ISO); methyl 2-({[4-ethoxy-6-(methylamino)-1,3,5-triazin-2-yl]carbamoyl}sulfamoyl)benzoate
EC number: -
CAS number: 97780-06-8
Dossier submitter: United Kingdom

CARCINOGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
01.03.2019	Spain		MemberState	1
Comment received				
The Spanish CA agrees with the dossier submitter that there was no treatment-related increase in tumour incidence (including in the mammary gland observed in rat) and therefore, ethametsulfuron-methyl does not meet the criteria for classification for carcinogenicity.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Thank you very much for your comment. Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
25.02.2019	United States	FMC Corporation	Company-Manufacturer	2
Comment received				
The carcinogenic potential of ethametsulfuron-methyl has been investigated in standard studies in rats and mice. No evidence of tumour induction was observed in any tissue for either species or gender. The applicant agrees with the RMS that ethametsulfuron-methyl does not meet the classification criteria for carcinogenicity.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Thank you very much for your comment. Noted.				

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON ETHAMETSULFURON-METHYL (ISO); METHYL 2-({[4-ETHOXY-6-(METHYLAMINO)-1,3,5-TRIAZIN-2-YL]CARBAMOYL}SULFAMOYL)BENZOATE

Date	Country	Organisation	Type of Organisation	Comment number
20.02.2019	Germany		MemberState	3
Comment received				
We agree to the DS proposal.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Thank you very much for your comment. Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
27.02.2019	Sweden		MemberState	4
Comment received				
The section on carcinogenicity in the CLH report is very brief. Considering that there were no differences with respect to mortality, food consumption, body weight or body weight gain between treated animals and controls in the rat study, it may be discussed if dose levels selected were too low for a carcinogenicity study.				
Dossier Submitter's Response				
We agree that dose selection may be an issue with the rat chronic/carcinogenicity study. However, it can be concluded that there was no treatment related increase in tumour incidence in this study and, therefore, the criteria for classification as a carcinogen are not met based on the available data.				
RAC's response				
RAC notes that the dosing in both studies (doses separated in steps of 10x and probably starting at a very low dose) might be questionable. But nevertheless, there are no evidences suggesting that ethametsulfuron-methyl might display any carcinogenic potential.				

MUTAGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
25.02.2019	United States	FMC Corporation	Company-Manufacturer	5
Comment received				
The genotoxicity potential of ethametsulfuron-methyl has been investigated in standard *in vitro* and *in vivo* studies. Negative responses were observed *in vitro* in bacterial and mammalian cell culture systems, and *in vivo* in mice. No evidence of genotoxicity was observed. The applicant agrees with the RMS that ethametsulfuron-methyl does not meet the classification criteria for germ-cell mutagenicity.				
Dossier Submitter's Response				
Thank you for your comment and support.				
RAC's response				
Thank you very much for your comment. Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
20.02.2019	Germany		MemberState	6
Comment received				
Inconclusive. No classification of the substance is needed on the basis of available studies but there is data lacking. Justification Regarding the data provided by the DS DAR and CLH report, several deviations from the test guideline for the bacterial reverse mutation test were confirmed. In the submitted Ames test, only four Salmonella Typhimurium strains were used and a test with either Salmonella Typhimurium TA102 or an appropriate E. coli strain was not conducted. Accordingly, the endpoint for ROS induced genotoxicity was not assessed. Although the test results were negative for all other genotoxicity studies conducted, the database is still considered as insufficient for a classification on genotoxicity.				
Dossier Submitter's Response				
We agree that the submitted bacterial gene mutation (Ames) tests have not investigated gene mutations induced via ROS generation. However, there is sufficient *in vitro* and *in vivo* information from well conducted standard studies to conclude on the mutagenic potential of ethametsulfuron-methyl. We also note that ethametsulfuron-methyl did not cause an increase in tumour incidence in rat and mice lifetime studies, reducing concern that this substance is mutagenic.				
RAC's response				
Thank you very much for your comment. Noted. RAC supports the DS's position on this issue.				

Date	Country	Organisation	Type of Organisation	Comment number
27.02.2019	Sweden		MemberState	7
Comment received				
Neither the CLH report nor annex I contain a presentation of results (frequencies etc) in the in vitro and in vivo tests. Consequently, the reviewer must rely on the DS and an independent assessment of this endpoint cannot be made.				
Dossier Submitter's Response				
The results of the aviable mutagenity studies were clearly negative and, as such, it is our opinion that sufficient information is provided in the CLH report to enable RAC to conclude on germ cell mutagenicity. Further information on the studies can be provided should RAC consider it necessary.				
RAC's response				
Thank you very much for your comment. Noted. RAC also performed the assessment with the CLH report and no additional information was provided for assessment.				

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
01.03.2019	Spain		MemberState	8
Comment received				
Fertility No adverse effects on fertility have been observed. Therefore no classification is warranted for sexual function and fertility.				

Development
Ethametsulfuron-methyl did not induce any structural or visceral malformations/variations in standard studies conducted in rats or rabbits.
A small increase in early resorptions was observed in the absence of marked maternal toxicity at doses of up to 1000 mg/kg/day in a standard rabbit developmental toxicity study. However, in a second rabbit developmental toxicity study, specifically conducted to investigate pre/post implantation loss, the incidence of early resorptions was comparable between treated and control groups up to 1000 mg/kg/day, the highest dose tested. There were no other treatment-related effects on late resorptions, or visceral malformations/variations. We agreed with the dossier submitter that the failure to confirm the increase in early resorptions in a second study in the same strain of rabbit, even at the limit dose of 1000 mg/kg/day reduces concern that the late resorptions observed in the first rabbit study are treatment-related. Besides, similar changes were not observed in rats. Therefore, it can be concluded that ethametsulfuron-methyl is not a developmental toxicant and No classification is required.

Dossier Submitter's Response

Thank you for your comments and your support.

RAC's response

Thank you very much for your comment. Noted.

Date	Country	Organisation	Type of Organisation	Comment number
25.02.2019	United States	FMC Corporation	Company-Manufacturer	9

Comment received

Reproductive effects
No toxicologically significant adverse effects on sexual function or fertility were observed in male or female parental rats in either a one-generation reproduction pilot study or in the two-generation reproduction study. In addition, no test-substance-related effects on litter size, pup survival, pup growth and development, and clinical observations were observed in either study. The applicant agrees with the RMS that ethametsulfuron-methyl does not meet the classification criteria for sexual function and fertility.
Developmental Effects
Ethametsulfuron-methyl did not induce any structural or visceral malformations or variations in rat and rabbit developmental studies. In the original rabbit developmental study, a slight increase in early resorptions were observed. However, this observation was not confirmed in a second study in which ethametsulfuron-methyl was administered to the same rabbit strain at the limit dose of 1000 mg/kg/day for the gestation period of GD 7-28, which was 9 days longer than the dosing period in the original study. The applicant agrees with the RMS that no effects were observed in these studies that meet the requirements for classification.

Dossier Submitter's Response

Thank you for your comments and your support.

RAC's response

Thank you very much for your comment. Noted.

Date	Country	Organisation	Type of Organisation	Comment number
20.02.2019	Germany		MemberState	10

Comment received

Classification as reproductive toxicant in Category 2 with hazard statement H361d is suggested.
Justification
In the developmental toxicity study in the rabbit, an increase in the number and percentage of total and early resorptions per litter was observed at all dose levels. The resorption rate exceeded the historical control range. In addition, heart and heart vessels malformations were seen in two foetuses in two different litters at a dose level of 250 mg/kg bw/day. Even though no dose response was obvious, this finding is of concern since it is rare and was clearly above the historical control range.
Unfortunately, no meaningful evaluation of resorption rate or malformations was feasible in the highest dose group receiving 4000 mg/kg bw/day. Due to excessive toxicity with maternal deaths and abortions, the number of litters and foetuses was too small. Therefore, we can rely only on what observed at the low and mid dose levels.
Based on a higher resorption rate in both dose groups and supported by the potentially teratogenic findings in the low dose group, classification for developmental toxicity should be at least considered. According to the ”Guidance on the application of the CLP Criteria”, developmental effects which occur in the presence of maternal toxicity (as it is the case here) must not be ignored but might result in a less severe classification. On balance, we think that Category 2 would be appropriate.

In its 2014 conclusion on the substance the EFSA also proposed classification Repr 2.

There is new data in the CLH report coming from a follow-up study in which no significant increase in resorptions and no heart malformations were observed up to 1000 mg/kg bw/day. Unfortunately, this study was not guideline-compliant because only a small number of animals were used (10 rabbits instead of 20 per dose group). According to the OECD TG 414, groups with fewer than 16 female animals may be inappropriate to evaluate the developmental toxicity. In addition, the rate of resorptions was rather high (in particular when compared to the previous study) in nearly all groups including the concurrent control but was highest at the top dose level (i.e., 5.9 total resorptions/litter at 1000 mg/kg bw/day as compared to 3.4 in the controls).
Regarding its limitations it is questionable whether the negative results obtained in this study should be used to weaken the findings of the standard study.
The presented time frame (2006-2017) for historical controls for late resorptions in the study Anonymous 2018 is too broad. The time frame should contain only data of the last five years in this case.

Dossier Submitter’s Response

Cardiovascular Malformations - Rabbits

The only malformations were cardiac and great vessel malformations, observed in 2 fetuses from two separate litters at the lowest dose of 250 mg/kg/day only in the 1991 study. Similar changes were not observed in either controls or other treatment groups. No skeletal or visceral variations were observed in this study. The observation of cardiac and great vessel malformations would be of concern. However the absence of similar changes at the higher dose levels, especially at 1,000 mg/kg/day which was not maternally toxic and sufficient foetuses were available for a rigorous examination reduces concern that these changes are treatment-related findings. If the substance were a

developmental toxicant, causing such malformations, it would have been anticipated that variations would also have been observed. That no treatment-related increases in variations were observed further reduces concern that the cardiac and vascular malformations were treatment-related.

No cardiac or great vessel malformations were observed in the supplemental study (2018), conducted with 10 does using a top dose of 1,000 mg/kg/day.

It is also noted that no treatment-related increases in skeletal or visceral variations or malformations were observed in a standard rat developmental toxicity study, at dose levels of up to 4,000 mg/kg/day. This dose is well in excess of the modern limit dose of 1,000 mg/kg/day.

In our opinion, the cardiovascular changes are considered chance findings and should not be used to support classification for developmental toxicity.

Increased Early Resorptions – Rabbits

We agree that the increase in early resorptions observed in rabbits at doses of up to 1,000 mg/kg/day are of limited concern. The changes at the top dose are of questionable value given the severe maternal toxicity and lethality observed at that dose (4,000 mg/kg/day).

In the supplemental study conducted specifically to investigate increased resorptions, there was no clear treatment-related increase in early resorptions. There was an increase in late resorptions of 4.3%, which was within the provided historical control. It is usual practice to use historical control data of +/- 5-years, however, we feel that the use of a longer time period gives a much more robust value for the late resorptions from this test facility. Therefore we are confident the increase in late resorptions observed at the top dose of 1,000 mg/kg/day is within the expected natural variation and not likely to be treatment-related.

In relation to differences in resorption rates between the standard and supplemental rabbit studies, it is noted that the studies were conducted 17-years apart and it is not altogether surprising there are differences in resorption rates.

Although the supplementary study is limited, compared to the statistical power of a standard guideline developmental toxicity study, we consider it provides reliable and relevant information on the potential of ethametsulfuron-methyl to increase the early resorption rate in rabbits.

Overall, taking a weight of evidence approach, it is our view that the results of the second study reduce concern that the findings are treatment related. As such, we remain of the opinion that classification for developmental toxicity based on increased early resorptions is not justified.

RAC's response

Thank you very much for your comment. Noted. RAC supports the DS's position as regard as the lack of robustness of the early and total resorptions reported in the main study in rabbits. However, RAC disagrees with DS with regards to the reliability of the HCD because it must be addressed to the standard period of ±5 years.

Date	Country	Organisation	Type of Organisation	Comment number
27.02.2019	Sweden		MemberState	11
Comment received				
The developmental study in rabbits performed in 2018 to follow up the findings in the 1991 study did not show the increased frequency of early resorptions clearly shown in the first study. However, the follow-up study was a non-standard study performed with only 10 dams/group in contrast to the 1991 study which was performed according to OECD 414 (1983) with 22 dams/group. Therefore, we do not consider the results from the new study to overrule the findings in the first. The increase in resorptions in the 1991 study occurred at doses where also a reduced bodyweight gain was observed. In the absence of further information, it is not possible to assess if the effects were restricted to outliers with severely reduced bodyweight gains. Nevertheless, according to HCD, early resorptions are rare events in rabbits and the CLP states "In rabbits, the body weight gain may not be useful indicators of maternal toxicity because of normal fluctuations in body weight during pregnancy." Therefore, we do not find it safe to exclude that the early resorptions observed in rabbits may be related to treatment and we suggest that classification in category 2 should be considered by RAC.				
Dossier Submitter's Response				
Please see our response to comment 10 We do not use the findings of the non-standard study to overrule the earlier standard rabbit study but consider the findings together in a weight of evidence assessment. However, we agree that the decision on no classification/Cat 2 is not a straightforward one.				
RAC's response				
Thank you very much for your comment. Noted. RAC supports the DS's position on this issue.				

Date	Country	Organisation	Type of Organisation	Comment number
20.02.2019	Netherlands		MemberState	12
Comment received				
Reproductive toxicity The NL CA agrees with the proposed 'no classification' for adverse effects on sexual function and fertility and the 'no classification' for adverse effects on/via lactation. With respect to adverse effects on developmental toxicity, the following is noted. In a rat developmental study, up to 1000 mg/kg/day no statistically significant developmental effects were observed (NOAEL 1000 mg/kg/day). We agree with the Dossier Submitter that the findings in rat do not warrant classification of ethametsulfuron-methyl for developmental toxicity. However, based on the effects observed in the 1991 rabbit study (as mentioned in CLH report as "Anonymous (1991m)" in table 27, page 27), a concern for developmental toxicity was raised by EFSA and they suggested that a classification as reproductive toxicant, category 2 (H361d) may be required (EFSA Journal 2014;12(7):3787). In the EFSA report, it is stated that, in addition to reduced number of live foetuses and increased resorptions, also an increase in heart-related malformations from 250 mg/kg/day on is observed which is not specifically mentioned in the CLH report. The Dossier Submitter is requested to clarify this issue and to discuss the relevance of these				

findings with respect to classification for developmental toxicity. As the EFSA report is from 2014, the non-standard follow-up study is not included in their conclusion.
Dossier Submitter's Response
Cardiovascular Malformations - Rabbits The only malformations were cardiac and great vessel malformations, observed in 2 fetuses from two separate litters at the lowest dose of 250 mg/kg/day only in the 1991 study. Similar changes were not observed in either controls or other treatment groups. No skeletal or visceral variations were observed in this study. The observation of cardiac and great vessel malformations would be of concern. However the absence of similar changes at the higher dose levels, especially at 1,000 mg/kg/day which was not maternally toxic and sufficient foetuses were available for a rigorous examination reduces concern that these changes are treatment-related findings. If the substance were a developmental toxicant, causing such malformations, it would have been anticipated that variations would also have been observed. That no treatment-related increases in variations were observed further reduces concern that the cardiac and vascular malformations were treatment-related. No cardiac or great vessel malformations were observed in the supplemental study, conducted with 10 does using a top dose of 1,000 mg/kg/day. It is also noted that no treatment-related increases in skeletal or visceral variations or malformations were observed in a standard rat developmental toxicity study, at dose levels of up to 4,000 mg/kg/day. This dose is well in excess of the modern limit dose of 1,000 mg/kg/day. In our opinion, the cardiovascular changes are considered chance findings and should not be used to support classification for developmental toxicity.
RAC's response
Thank you very much for your comment. Noted. RAC supports the DS's position on this issue.

OTHER HAZARDS AND ENDPOINTS – Acute Toxicity

Date	Country	Organisation	Type of Organisation	Comment number
25.02.2019	United States	FMC Corporation	Company-Manufacturer	13
Comment received				
The oral LD50 of >5000 mg/kg bw for rats is above the value for classification, the dermal LD50 of >2000 mg/kg in rats and rabbits is above the value for classification, and the inhalation LC50 of >5.7 mg/L in rats is above the value for classification. The applicant agrees with the RMS that these values do not meet the criteria for classification.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Thank you very much for your comment. Noted.				

OTHER HAZARDS AND ENDPOINTS – Skin Hazard

Date	Country	Organisation	Type of Organisation	Comment number
25.02.2019	United States	FMC Corporation	Company-Manufacturer	14
Comment received				
No evidence of skin irritation was observed in two separate rabbit studies. The applicant agrees with the RMS that these results do not meet the criteria for classification.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Thank you very much for your comment. Noted.				

OTHER HAZARDS AND ENDPOINTS – Eye Hazard

Date	Country	Organisation	Type of Organisation	Comment number
01.03.2019	Spain		MemberState	15
Comment received				
Based on the observed corneal opacity with a score of ≥ 1 in 4/6 animals in the unwashed group of the rabbits study (Anonymous, 1991e) the Spanish CA supports the dossier submitter proposal to classify ethametsulfuron-methyl as Eye Irritation 2: H319 – 'Causes serious eye irritation'.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Thank you very much for your comment. Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
25.02.2019	United States	FMC Corporation	Company-Manufacturer	16
Comment received				
Ethametsulfuron-methyl caused reversible eye irritation (with a score of >1 for corneal opacity in 4 of 6 animals in the unwashed group and 2 of 3 animals in the washed group. All irritation reversed by observation day 10. The applicant agrees with the RMS that the observations meet the classification criteria for Category 2 (H319 "causes serious eye irritation").				
Dossier Submitter's Response				
Thank you for your comment and support.				
RAC's response				
Thank you very much for your comment. Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
20.02.2019	Germany		MemberState	17
Comment received				
The proposal for classification with Eye Irrit. 2 is supported based on cornea effects that were fully reversible after at maximum 10 days in the study Anonymous 1991e.				
Dossier Submitter's Response				
Thank you for your support.				

RAC's response
Thank you very much for your comment. Noted.

OTHER HAZARDS AND ENDPOINTS – Skin Sensitisation Hazard

Date	Country	Organisation	Type of Organisation	Comment number
25.02.2019	United States	FMC Corporation	Company-Manufacturer	18
Comment received				
Skin sensitization was investigated in a LLNA study in mice, and in two Buehler assays in guinea pigs. No positive responses were noted in any assay. The applicant agrees with the RMS that ethametsulfuron-methyl does not meet the requirements for classification.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Thank you very much for your comment. Noted.				

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Single Exposure

Date	Country	Organisation	Type of Organisation	Comment number
25.02.2019	United States	FMC Corporation	Company-Manufacturer	19
Comment received				
No deaths, clinical signs of toxicity, respiratory tract irritation, narcotic effects, or other findings of specific target organ toxicity were noted in any of the acute toxicity studies for any relevant route of exposure. The applicant agrees with the RMS that there are no observations that meet the criteria for classification for specific target organ toxicity.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Thank you very much for your comment. Noted.				

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Repeated Exposure

Date	Country	Organisation	Type of Organisation	Comment number
25.02.2019	United States	FMC Corporation	Company-Manufacturer	20
Comment received				
The repeated dose toxicity of ethametsulfuron-methyl has been evaluated in 90-day studies in rats, mice, and dogs, lifetime studies in rats and mice, and in a one-year dog study. Increased absolute and relative spleen weights observed in male mice at 3.5 mg/kg/day and above in the 2-year mouse study did not correlate with any functional or microscopic changes, and therefore did not meet the criteria for classification. The applicant agrees with the RMS that none of the observations in these studies meets the classification criteria for STOT-RE.				
Dossier Submitter's Response				
Thank you for your comment and your support.				
RAC's response				
Thank you very much for your comment. Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
01.03.2019	Spain		MemberState	21
Comment received				
The only treatment-related change observed at or below any repeated dose classification guidance value was a statistically significant increase in absolute and relative spleen weights in male mice at a dose of 3.5 mg/kg/day and above in a lifetime oral dosing study. There were no supporting histopathological changes, or clinical chemistry/haematology findings to suggest that the spleen function was perturbed. Therefore, although dose-related, the lack of evidence of perturbed spleen function in mice, and absence of similar changes in standard studies in rats or dogs reduces the overall level of concern. The Spanish CA agreed with the dossier submitter that no classification for STOT-RE is required.				
Dossier Submitter's Response				
Thank you for your comments and your support.				
RAC's response				
Thank you very much for your comment. Noted.				

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
25.02.2019	United States	FMC Corporation	Company-Manufacturer	22
Comment received				
Ethametsulfuron-methyl should be classified for the environment as Aquatic Acute 1 with an acute M-factor of 1000 based on Lemna ErC50 data in the range 0.0001 mg/l < EC50 ≤ 0.001 mg/l. The applicant agrees with the RMS conclusion that Ethametsulfuron-methyl is not a rapidly degradable compound. Ethametsulfuron-methyl and should be classified for the environment as Aquatic Chronic 1 with a chronic M-factor of 100 based on Lemna NOEC data in the range 0.0001 mg/l < NOEC ≤ 0.001 mg/l.				
Dossier Submitter's Response				
Thank you for your comments and support.				
RAC's response				
Thank you very much for your comment. Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
20.02.2019	Netherlands		MemberState	23
Comment received				
Agreed to base the aquatic classifications on the selected effect concentrations obtained for Lemna gibba and agreed with the proposed Aquatic Acute 1 (M=1000) and Aquatic Chronic 1 (M=100) classifications.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Thank you very much for your comment. Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
20.02.2019	Germany		MemberState	24
Comment received				
Page 39, point 11.1 Rapid degradability of organic substances, Table 29: As stated under point 11.1.4.3 the study by Sarff (2010) was according to the Method described in OECD 308 and not OECD 309. The study is therefore not a "freshwater aquatic biodegradation simulation study" but an "aerobic sediment/water study". Please correct the stated method for this study in the Table 29. Page 42; 11.1.4.3 Water, water-sediment and soil degradation data (including simulation studies): The study by Sarff (2010) was conducted according to OECD 308 and is therefore an aerobic sediment/water study and not a freshwater aquatic biodegradation simulation study. Please correct the study-type. Page 48, point 11.5.3 Acute toxicity to algae or other aquatic plants (Table 34): Actually the EC50 (shoot length, 10 days) is > 23 mg a.s./L (mm) instead of 0.23 mg as./L for the aquatic macrophyte Myriophyllum spicatum (Hoberg, 2010c). But there is no influence on classification and labelling as Aquatic acute 1 and M-factor of 1000, because the relevant study is the study with Lemna gibba (Porch et al., 2009) with ErC50 (7 days) of 0.000808 mg a.s./L (mm).				
Dossier Submitter's Response				
Thank you for your comment. We confirm there is a slight editorial omission and confirm the Sarff (2010) study was an aerobic aquatic-sediment study following OECD test guideline 308 [Reference: Sarff, P. 2010. Aerobic aquatic metabolism of 14C ethametsulfuron-methyl (DPX A7881) in two aerobic aquatic sediment systems]. This does not impact the proposal. We are unable to update the CLP report but the edit is noted. Table 34 includes the *Myriophyllum spicatum* 10-day EC50 based on shoot length which is considered to be approximately 0.23 mg a.s./l (mm) given 50% inhibition of shoot length from this concentration. The 10-day EC50 based on shoot dry weight is not presented in the CLH report as it is not as sensitive but based on the below exert from the DAR considered to be > 23mg a.s./l (mm) given a maximum of 15% inhibition in shoot dry weight at the highest treatment. Summary text from DAR 'The EC_{50} value for *Myriophyllum spicatum* exposed for 10-days to ethametsulfuron methyl based on shoot dry weight is >23 mg a.s./L. No EC_{50} has been calculated for shoot length and this parameter appears to be more sensitive – there was > 50 % inhibition of shoot length at 0.23 mg a.s./L and above.'				
RAC's response				
Thank you very much for your comment. Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
01.03.2019	France		MemberState	25
Comment received				
FR agrees with the classification proposal and the M factors (acute and chronic) proposed in the CLH report.				

Dossier Submitter's Response
Thank you for your support.
RAC's response
Thank you very much for your comment. Noted.

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Ozone Layer

Date	Country	Organisation	Type of Organisation	Comment number
25.02.2019	United States	FMC Corporation	Company-Manufacturer	26
Comment received				
Agree with RMS. Although no specific data have been provided for this hazard, considering the chemical structure and other available information on the physicochemical properties, ethametsulfuron-methyl is not expected to be hazardous to stratospheric ozone.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Thank you very much for your comment. Noted.				

OTHER HAZARDS AND ENDPOINTS – Physical Hazards

Date	Country	Organisation	Type of Organisation	Comment number
25.02.2019	United States	FMC Corporation	Company-Manufacturer	27
Comment received				
Sufficient study data is available to assess the potential physical hazards of Ethametsulfuron-methyl. The compound is a solid that exhibits no evidence of explosive, flammability, self-reactive, pyrophoric or oxidative hazards. The applicant agrees with the RMS that ethametsulfuron-methyl does not meet the classification criteria for any physical hazards.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Thank you very much for your comment. Noted.				