COMPILED COMMENTS ON CLH CONSULTATION

Comments provided during consultation are made available in the table below as submitted through the web form. Please note that the comments displayed below may have been accompanied by attachments which are listed in this table and included in a zip file if non-confidential. Journal articles are not confidential; however they are not published on the website due to Intellectual Property Rights.

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Last data extracted on 31.05.2024

Substance name: 1,3-diphenylguanidine
CAS number: 102-06-7
EC number: 203-002-1
Dossier submitter: France

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
05.05.2024	Norway		Individual	1
Comment received				
As there is no comment field based on the recent PMT/vPvM hazard class category, I wish to provide some comments on this substance that is frequently observed in drinking water and urban stormwater (related to its use as a galvanizing agent in tire production). In my assessment it is likely to meet the Persistence criteria as REACH registered information indicated the majority of biodegradation screen tests said the substances is not readily biodegradable, e.g. OECD Guideline 301 D (Ready Biodegradability: Closed Bottle Test); OECD Guideline 301 D (Ready Biodegradability: Closed Bottle Test); OECD Guideline 301 D (Ready Biodegradability: Closed Bottle Test); OECD Guideline 301 D (Ready Biodegradability: Closed Bottle Test), and this is confirmed by my analysis of QSARs, such as EPIsuit Biowin. Its log Koc reported in REACH dossiers is 2.5 - 3.13 (https://chem.echa.europa.eu/100.002.730/dossier-view/85a7482d-61f5-4625-b9b7-22bbafb256ee/56882166-4005-4e07-b0a5-d94e8a66d431_c09dc9ed-aaad-4502-b308-810bebb4954e?searchText=203-002-1). If the persistency assessment is concerned, and a toxicological hazard is identified, such as Category 2 for reproductive toxicity assessment of toxicity, it should be classified additionally as a PMT substance.				

Date	Country	Organisation	Type of Organisation	Comment number
23.04.2024	Belgium		MemberState	2
Comment received				
In Table 3 (Proposed harmonized classification and labelling according to the CLP criteria), in the row Dossier submitter proposal, it is noted that Eye Irrit. 2 H315 is retained. We assume it should read “Skin Irrit. 2”. Furthermore, STOT SE 3 is not mentioned in this row whereas the classification for this hazard class is also retained.				

Date	Country	Organisation	Type of Organisation	Comment number
14.05.2024	Germany		MemberState	3
Comment received				
The dossier was formally reviewed with regard to classification and labeling.				

It is proposed to classify the substance as Eye Dam. 1, H318 and Acute Tox. 3, H301 instead of Eye Irrit 2, H319 and Acute Tox. 4*, H302.
The classification of the substance as Skin Irrit. 2, H315 remains unchanged.

Therefore, Skin Irrit. 2 has to be included under "Retain" instead of Eye Irrit. 2 in the classification proposal for 1,3-diphenylguanidine.
Due to the stricter classification with regard to acute oral toxicity, the hazard pictogram GHS06 is used for labeling. In accordance with Article 26(1)(b), Regulation (EC) No 1272/2008 (CLP Regulation) stipulates: if the hazard pictogram "GHS06" must be used for labeling, the hazard pictogram "GHS07" does not appear!
Consequently, "GHS07" must be deleted in the proposal for 1,3-diphenylguanidine.

Thus, in the CLH dossier section 2.1 "Proposed harmonised classification and labelling according to the CLP criteria" Table 3
- in row "Dossier submitters proposal" and column "Classification/Hazard Class and Category Code(s)" under "Retain" Skin Irrit. 2 instead of Eye Irrit. 2 has to be included,
- in line "Dossier submitters proposal" and column "Labelling/Pictogram, Signal Word Code(s)" column "GHS07" under "Retain" has to be deleted (see Art. 26 CLP Regulation) and instead GHS07 under Remove to be list
- row "Resulting Annex VI entry if agreed by RAC and COM and column "Labelling/ Pictogram, Signal Word Code(s)" "GHS07" (see Art. 26 CLP) has to be deleted.

Purity:
We would suggest to change the purity of the substance to ≤ 100 %, as DPG is a mono-constituent substance.

Water solubility:
The water solubility is stated as 325 mg/L at pH = 11. However, according to the dissemination page the pH was 10.32. Therefore, we would prefer if a pH of 10 or 10.32 would be stated, instead.

Surface tension:
DPG is a solid substance for which the surface tension was determined at a concentration at ca. 300 mg/L. This information is not stated in the CLH report. We would suggest to add this information to the CLH report. Another option would be to remove the information on the surface tension as it is not a requested data point for solid substances.

HEALTH HAZARDS – Acute toxicity

Date	Country	Organisation	Type of Organisation	Comment number
16.05.2024	Czech Republic	LUČEBNÍ ZÁVODY DRASLOVKA A.S. KOLÍN	Company-Manufacturer	4

Comment received

Lucebni zavody Draslovka a.s. Kolin supports that classification as Acute Toxicity, Category 3 is appropriate for the oral route.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Draslovka public attachments.zip
ECHA note – An attachment was submitted with the comment above. Refer to confidential

attachment Draslovka confidential attachements.zip

Date	Country	Organisation	Type of Organisation	Comment number
16.05.2024	Finland		MemberState	5
Comment received				
The FI CA agrees with the DS that 1,3-diphenylguanidine warrants a classification as Acute Tox. 3; H301 with an ATE (oral) of 110 mg/kg bw.				

Date	Country	Organisation	Type of Organisation	Comment number
14.05.2024	Germany		MemberState	6
Comment received				
Although only one out of several oral studies is considered acceptable, the entire picture is consistent enough to justify Acute Tox. 3 (H301) classification as the lowest ATE of 110 mg/kg bw is based on the only reliable rat study.				

Date	Country	Organisation	Type of Organisation	Comment number
23.04.2024	Belgium		MemberState	7
Comment received				
Acute Toxicity – Oral Based on the results of the acute oral toxicity study performed following OECD TG 401 (Unpublished study report, 2000), LD50 of 111 mg/kg bw in males and 107 mg/kg bw in females, BE CA supports the proposal to classify as Acute Tox. 3 as well as the ATE of 110 mg/kg bw. In Table 7 (Summary table of animal studies on acute oral toxicity), it is mentioned that “Please see annex I for more details” for the Unpublished study report 1977a and 1977b. However, these studies were not available in the Annex I as only reliable studies (Klimish 1 and 2) are described in this Annex I.				

HEALTH HAZARDS – Serious eye damage / eye irritation

Date	Country	Organisation	Type of Organisation	Comment number
16.05.2024	Czech Republic	LUČEBNÍ ZÁVODY DRASLOVKA A.S. KOLÍN	Company-Manufacturer	8
Comment received				
Lucebni zavody Draslovka a.s. Kolin supports that classification as Serious eye damage, Category 1 is appropriate. ECHA note – An attachment was submitted with the comment above. Refer to public attachment Draslovka public attachments.zip ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment Draslovka confidential attachements.zip				

Date	Country	Organisation	Type of Organisation	Comment number
23.04.2024	Belgium		MemberState	9
Comment received				

The results observed in the Unpublished report, 1988, fulfill category 1 criteria “in at least one animal effects on the cornea, iris or conjunctiva that are not expected to reverse or have not fully reversed within an observation period of normally 21 days”. Corneal opacity and arterialisations of the cornea surface were always observed after 21 days and even up to the end of the observation period of 6 weeks.

BE CA agrees to classify as Eye Dam. 1, H318.

Date	Country	Organisation	Type of Organisation	Comment number
14.05.2024	Germany		MemberState	10
Comment received				
The substance fulfils the criteria to classify for irreversible effects on the eye (category 1) according to Table 3.3.1 (a) of the CLP regulation by producing in at least one animal effects on the cornea that have not fully reversed within an observation period of 21 days. In particular, corneal opacity and arterialisations of the cornea surface in three animals up to the end of the observation period at six weeks. Therefore the entry ‘Retain Eye Irrit. 2, H315’ in Table 3 seems superfluous. Maybe ‘Retain STOT SE 3, H335’ is intended here.				

HEALTH HAZARDS – Skin sensitisation

Date	Country	Organisation	Type of Organisation	Comment number
16.05.2024	Czech Republic	LUČEBNÍ ZÁVODY DRASLOVKA A.S. KOLÍN	Company-Manufacturer	11
Comment received				
The proposed classification largely relies on the use of anecdotal and historical epidemiological studies. The available animal studies conducted according to standards do not suggest skin sensitization properties warranting the classification. The presented data is of uncertain reliability, they generally do not include representative individuals, do not sufficiently assess co-founding factors and/or the effects cannot be exclusively linked to DPG. Also, DPG is known as a contact irritant and the presented data do not suggest involvement of the immune system and specific allergic reaction that is a requirement for sensitization classification according to the CLP regulation. We would suggest that the reported effects are covered by the current Skin Irrit. 2 classification and no new sensitization classification is required. ECHA note – An attachment was submitted with the comment above. Refer to public attachment Draslovka public attachments.zip ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment Draslovka confidential attachements.zip				

Date	Country	Organisation	Type of Organisation	Comment number
23.04.2024	Belgium		MemberState	12
Comment received				
Based on the available human information, BE CA supports the proposal to classify as Skin Sens. 1A H317.				

Date	Country	Organisation	Type of Organisation	Comment number

14.05.2024	Germany		MemberState	13
Comment received				
The proposed classification as Skin Sens. 1A appears justified based on the presented human data. However, taking into account the negative maximisation assay according to OECD TG 406 and GLP - albeit conducted with half of the necessary number of guinea pigs and considering only the patch-test data with strong positive reactions (++) and extreme positive reactions (+++), the subcategorization with an exposure score of 4 might be of borderline nature. Additionally, the “frequency of occurrence” might be considered equivocal. The majority of studies selected by the DS show a high frequency (given the selected parameters); however, the studies with larger test populations such as Warshaw et al. (2020), Uter et al. (2016), Dekoven et al. (2017), Geier et al. (2012) and Geier et al. (2003) tend to show a low/moderate frequency, which in combination with the exposure score of 4 could be classified as Category 1 without sub-category.				

HEALTH HAZARDS – Reproductive toxicity

Date	Country	Organisation	Type of Organisation	Comment number
16.05.2024	Czech Republic	LUČEBNÍ ZÁVODY DRASLOVKA A.S. KOLÍN	Company-Manufacturer	14
Comment received				
CONCLUDING STATEMENT ON THE REPRODUCTIVE CLASSIFICATION OF THE 1,3-DIPHENYLGUANIDINE (DPG) FROM THE LEAD REGISTRANT LUCEBNI ZAVODY DRASLOVKA A.S. KOLIN AS RESPONSE TO THE CLH REPORT, PROPOSAL FOR HARMONISED CLASSIFICATION AND LABELLING OF 1,3-DIPHENYLGUANIDINE SUMMARY We suggest using the classification Repr. 2 as harmonised hazard classification of the substance 1,3- diphenylguanidine (DPG) based on the three expert statement documents concerning most recently conducted Extended One-Generation Reproductive Toxicity Study and fourth document with weight of evidence assessment. The presented evidence shows that the effects are not clearly indicative of reproductive toxicity as required by the legislation and the findings are not consistent across the studies. It cannot be concluded that the compound presents a ‘strong capacity for interference with the reproductive system in humans’ as required by the CLP Regulation (EC) No 1272/2008. 1. OVERVIEW OF ATTACHED DOCUMENTATION RELEVANT FOR THE PUBLIC CONSULTATION ON THE CLASSIFICATION OF 1,3-DIPHENYLGUANIDINE: A. EOGRTS_assessment_2022a B. EOGRTS_assessment_2022b C. EOGRTS_assessment_2024 D. DPG_Reprotox_WoE_2024 E. Laboratory_answer_assessment_2024 Highlights of the expert statements				

A. EOGRTS_assessment_2022a
The study OECD 443 EOGRTS test on 1,3-diphenylguanidine (DPG) resulted in findings which are not in line with the previous findings on DPG. Occurrence of female and foetus's mortality, in relatively low concentrations (25 mg/kg bw/day) compared to previous studies where mortality occurred at around 180 mg/kg bw/day in adults, have no explanation in the investigated endpoints. Convulsions and seizures observed indicate a severe state of test animals inappropriate for reproduction study. Frequently occurring sublethal effects seen in previous studies on DPG prior mortality occurrence as weight loss was missing. Available HCD data are not robust for the comparison.

B. EOGRTS_assessment_2022b
In terms of deciding on the appropriate category to assign for reproductive toxicity based on Weight of Evidence, due to the relatively weak findings in the EOGRTS, from findings in previous studies on DPG, it cannot be said that there is a 'strong presumption of a capacity to interfere with reproduction in humans' that would justify a Reproduction Category 1B assignment under CLP. Consistency of results is not observed when comparing the EOGRTS with previous studies using higher dose levels, the level of statistical significance for inter-group differences is questionable, and the number of endpoints affected is limited and subject to reinterpretation as discussed above.

Issues suggested for review include:
- The question on whether the observed neurotoxicity in P generation and Cohort 1B pregnant females is truly an adverse effect based on its transient nature and lack of expected consequences for body weights, food consumption, clinical chemistry and haematological effects.
- The observed mortality and neurological signs were inconsistent between the Cohort 1A, and 1B with no clear explanation suggesting other factors influencing the results beside the tested compound.
- One control female (Cohort 1B) was euthanized on humane grounds, due to the severe clinical signs. No explanation was provided for this finding.
- An unexplained finding is the relatively high number of dead F1 pups (17 in 4 litters). Necropsied pups found dead showed an absence of milk in the stomach and autolysis in all groups, including control group. Although the incidences of both findings were increased in treated groups and dose-related, the relatively high incidence in the control is not 14 satisfactorily explained by the suggestion of nursing difficulties or the absence of maternal care.
- Gestation periods in P females appear to show an increase in the 5 mg/kg/day dose group (two incidences of 24-day gestation) associated with high pup mortality rates (90-100%). At 25 mg/kg/day, and increased number of females with 23-day gestation periods was associated with high post-implantation losses (27.1 vs. 15.6% in controls, $p<0.05$). However, it is questionable if this finding is dose related as there were no 24-day gestation periods and only one 23-day period observed in the 15 mg/kg dose group.
- The percentages of post-implantation losses in PO generation were higher in the control group than in the 15 mg/kg group, but still significantly lower than in the 25 mg/kg group.
- In the P generation females, it was noted that a lower mean percentage (79.2%) of control animals were 'cycling normally' compared to treated groups (95.8% at 5 mg/kg, 91.3% at 15 mg/kg, and 95.8% at 25 mg/kg). The definition of cycling normally in this context, along with the significance of lower normal cycles in control animals vs. treated require further explanation.

C. EOGRTS_assessment_2024
Expert statement recommends CATEGORY 2; Suspected human reproductive toxicant to be suitable classification according to CLP Regulation (EC) No 1272/2008 based on the EOGRTS

study on 1,3-diphenylguanidine.

The CLP states for the developmental toxicity classification “Maternal mortality greater than 10% is considered excessive and the data for that dose level shall not normally be considered for further evaluation. Similar criteria could be applied also for same reproduction toxicity effects (e.g. mating output, gestation length, reproduction troubles).

Cohort 1A
Maternal mortality in the parental generation was 8% at exposure concentrations 5 and 15 mg/kg bw/day. The highest tested dose 25 mg/kg bw/day did not result in mortality, instead severe toxicity was observed/recorded (clonic convulsion, locomotory difficulties, loss of balance, staggering gait and/or tonic seizures). There was also inconsistency in food consumption, weight (gains) and biochemical and haematological parameters (leukocyte counts) among the exposed and unexposed groups as well as compared to the historical control data suggesting compromised overall fitness of the used animals. The increased liver weights and histopathological findings on liver in parental generation and both offspring cohorts also suggest general stress. The mortality and severe toxicity incidence indicate that all concentrations were in the severe toxicity range.

Cohort 1B
Regarding to Cohort 1B, the maternal mortality was dose dependently increasing (3 female deaths in control, 3 at 15 mg/kg bw/day and 6 at 25 mg/kg bw/day – e.g. 12, 12 and 24% mortality. Further 16 females at 15 mg/kg bw/day, and 15 females at 25 mg/kg bw/day displayed clonic/tonic convulsion, half-closed eyes, hypoactivity). This cohort seems therefore unsuitable for judgement on reproductive classification due to high severe toxicity and excessive maternal mortality.

D. DPG_Reprotox_WoE_2024
The weight of evidence assessment evaluated all the relevant data and based on this data assessed concluded that Category 2 reproductive toxicant is adequate based on the assessed data. The main endpoints of the studies were summarised and assessed using the weight of evidence approach. The findings for the key study are assessed in context of the previous studies listing all the relevant findings, some of which were not discussed in detail in the CLH report in which a comprehensive WoE assessment is lacking. Based on the available data the main finding is mortality of the offspring in the key study (EOGRTS). It is noted that the finding is a notable outlier in terms of the concentrations at which the effects occur and also the study contains multiple issues that are putting in question the overall fitness of the study. The weight of evidence assessment evaluated all the relevant data and derived a conclusion that category Repr. 2 is adequate based on lack of specific effects on fertility and the observed effects on development being caused by general toxicity. The comparison of the available data did not yield a convincing pattern, mode of action similar to seen in the OECD 443 EOGRTS test with 1,3-diphenylguanidine or a suggestion of reproductive toxicity. For instance, the endocrine system seems not to be affected, no effects on fertility were observed and inconsistent concentrations. In conclusion several points should be clarified to ensure that classification and consequent mitigation steps are based on sound scientific data and biologically relevant results. Especially indication of reasons of female and foetus’s mortality should be looked for.

E. Laboratory_answer_assessment_2024
The laboratory that conducted the EOGRTS study responded to several issues raised in the expert statement EOGRTS_assessment_2022b. Regarding the absence of milk in stomach of

the pups in all treated groups including controls the laboratory answered that “These findings were potentially the consequence of nursing difficulties or the absence of maternal care” and “the adversity of the clinical signs suggestive of neurologic disorders cannot be ruled out” for these effects. That suggests that the pup mortality was likely caused by overall bad state of the adult animals and the presence of the effects in controls further shows possibly compromised fitness of the tested animals and effects unrelated to the tested compound. The observed transient neurological deficit following the gavage administration (according to the laboratory expert) could also contribute to the lack of care and pup mortality suggesting the study conduct rather than the tested compound as a cause.

2. GENERAL ASSESSMENT

2.1. Development of documentation
Based on Article 41 on Regulation (EC) No 1907/2006 (the REACH Regulation), ECHA requested to submit information on: Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats exposed by oral route in October 2018. Sponsors have chosen Contract research organisation Citoxlab for conducting the study. Citoxlab was acquired by Charles River Laboratories on the onset of the performance of the study. Consequent discussions were with Charles River. EOGRTS_assessment_2022b was sent to Charles River. The reply, Laboratory_answer_assessment_2024 did not focus on the Classification issues raised in the statement (EOGRTS_assessment_2022) due to the declared lack of expertise on the CLP. This is in line with our view that testing contract research organisations should not make conclusions on classification especially in cases of reproductive toxicity where weight of evidence of all available studies is required. Also, other questions were not fully answered. As a result, Draslovka asked again about these topics to Charles River.

2.2. Previous ECHA EOGRTS assessment on DPG

EOGRTS studies were in general recently evaluated and criticised by ECHA (2023) for the methodologies being not well described in the guidance and the methodological limitations and limited experience makes findings of those studies unreliable in many cases. The report published by ECHA in 2023 criticizing the studies included the discussed EOGRTS study on 1,3-diphenylguanidine.

2.3. Self-classification of lead registrant
Regarding the CLH report on classification of 1,3-diphenylguanidine and the Annex 1 of the CLH report prepared by ANSES there is incorrectly listed self-classification as Repro. 1B which is not consistent with the data presented by the lead registrant Lucebni zavody Draslovka a.s. Kolin and it should be removed from the documents. The current harmonised Repr. 2 classification is used by the lead registrant.

The observed effects in the Extended One-Generation Reproductive Toxicity Study are in the line with mode of action of general toxicity and stress – post implementation losses and death pups, no effect in any group on examined pups after post-mortem macroscopic observation or any other relevant endpoint suggesting developmental toxicity. There are no

effects such as malformations indicating developmental mode of action. Therefore, due to uncertainty about the developmental effects and overall performance of the tested animals it would be appropriate to classify with category Repr. 2.

3. CONCLUSION
Based on the limited reliability of the Extended One-Generation Reproductive Toxicity Study and all available data assessed by the weight of evidence approach, the presented evidence shows that the effects are not clearly indicative of reproductive toxicity and the findings are not consistent across the studies. It cannot be concluded that the compound presents a 'strong capacity for interference with the reproductive system in humans' as required by the CLP Regulation (EC) No 1272/2008. We suggest the classification Repr. 2 as harmonised hazard classification of the substance 1,3- diphenylguanidine.

Please see attached documents for more details:
EOGRTS_assessment_2022a.pdf
EOGRTS_assessment_2022b.pdf
EOGRTS_assessment_2024.pdf
DPG_Reprotox_WoE_2024.pdf
Laboratory_answer_assessment_2024.pdf

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Draslovka public attachments.zip
ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment Draslovka confidential attachements.zip

Date	Country	Organisation	Type of Organisation	Comment number
23.04.2024	Belgium		MemberState	15
Comment received				
BE CA supports the proposed classification Repr. 1B H360FD. Indeed clear adverse effects on sexual function and fertility were observed in females in different studies and at doses without severe general toxicity. Sperm parameters were also affected by treatment in several studies. Furthermore, clear signs of developmental toxicity (pups mortality in the OECD TG 443) were also observed.				

Date	Country	Organisation	Type of Organisation	Comment number
14.05.2024	Germany		MemberState	16
Comment received				
A sum of severe adverse effects on sexual function and fertility as well as development (effects on gestation length, difficulties to deliver and dystocia, alteration of oestrous cycle, post-implantation losses and pup mortality) not associated with maternal toxicity from an EOGRTS OECD TG 443 (GLP) as well as from further supporting studies are sufficient for classification as Repr. 1B (H360FD).				

Date	Country	Organisation	Type of Organisation	Comment number
17.05.2024	United Kingdom	Health and Safety Executive	National Authority	17
Comment received				

Developmental Toxicity

'The DS has proposed classification for developmental toxicity category 1B based on severe effects on the development of the offspring, characterised as foetal and/or pup mortality. It has been noted that these effects are seen below 25 mg/kg bw/d, the dose that maternal toxicity appears. However, the pup mortality observed is associated with the females with an extended gestation period, dystocia and difficulty to deliver. Could the DS comment on the possibility that the effects on sexual function and fertility (in particular prolonged parturition) may be directly impacting the survivability of pups?'

HEALTH HAZARDS – Specific target organ toxicity - repeated exposure

Date	Country	Organisation	Type of Organisation	Comment number
16.05.2024	Czech Republic	LUČEBNÍ ZÁVODY DRASLOVKA A.S. KOLÍN	Company-Manufacturer	18

Comment received

The proposed classification for Specific Target Organ Toxicity–repetitive exposure (STOT RE) based on neurotoxicity is based on observed clinical signs and changes in behavior in animals. Those changes, however, are of an uncertain nature and unknown long-term adversity. Most notably, the effects of convulsion and/or staggering/gait observed in the recent study were transient and occurred immediately after the gavage administration (Laboratory_answer_assessment_2024, attachments). Therefore, the link between the observed effects and DPG treatment is unclear. Additionally, the changes in behavior were not accompanied by histopathological findings suggestive of neurological damage which makes a conclusion on the relation of observed effects to the substance and potential adversity difficult. We suggest that the available information does not warrant the new hazard classification STOT RE 2 according to the CLP regulation.

ECHA note – An attachment was submitted with the comment above. Refer to public attachment Draslovka public attachments.zip
ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment Draslovka confidential attachements.zip

Date	Country	Organisation	Type of Organisation	Comment number
23.04.2024	Belgium		MemberState	19

Comment received

Signs of neurotoxicity have been observed in several repeated dose toxicity studies in rodents. As noted in the Table 34 of the CLH, effects were observed in the range to classify in Category 1 in three studies. However, one of these studies is of reliability 3 and the two others have a lower exposure period (only 10 days and during the gestation period). While in the other available studies (reliability 1 or 2), with a longer period of exposure (between 28 and 110 days), clinical signs of neurotoxicity appeared at doses warranted a classification in Category 2.

Based on the available information, BE CA supports the conclusion that it is more appropriate to use subchronic toxicity studies to conclude on the category. Then, BE CA agrees with the proposal to classify as STOT RE Cat. 2 for the nervous system.

Date	Country	Organisation	Type of Organisation	Comment

				number
14.05.2024	Germany		MemberState	20
Comment received				
The subchronic toxicity studies (EOGRTS, OECD TG 421, 90-day NTP) and a 28-day study (OECD TG 407) with the substance show clinical signs of neurotoxicity (locomotion and posture anomalies, convulsion and lethargy) within the corresponding cut-off justify category 2 of specific target organ toxicity of the nervous system.				

ENVIRONMENTAL HAZARDS – Hazardous to the aquatic environment

Date	Country	Organisation	Type of Organisation	Comment number
16.05.2024	Czech Republic	LUČEBNÍ ZÁVODY DRASLOVKA A.S. KOLÍN	Company-Manufacturer	21
Comment received				
Lucebni zavody Draslovka a.s. Kolin supports that classification as Chronic (long term) aquatic hazard, Category 3 is appropriate. ECHA note – An attachment was submitted with the comment above. Refer to public attachment Draslovka public attachments.zip ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment Draslovka confidential attachements.zip				

Date	Country	Organisation	Type of Organisation	Comment number
15.05.2024	Netherlands		Individual	22
Comment received				
Thank you for drafting this CLH proposal. We agree with the overall conclusion on the environmental classification (Aquatic Chronic 3). However, we would like to raise a question regarding the algae study on P. subcapitata. In the report the evaluation of the SIDS is agreed where for algae a NOEC(biomass) of 0.3 mg/L is used as key value instead of 0.013 mg/L. Please be aware that growth rate is the preferred endpoint over biomass when evaluating toxicity to algae (as also indicated in the CLP Guidance). We therefore suggest to either use the ErC10 value of 2.1 mg/L as the key chronic value for algae or provide a clear justification for using the chronic biomass value over the growth rate value. If the key value shifts to 2.1 mg/L, aquatic invertebrates become the most sensitive species, but the classification outcome will remain unchanged.				

PUBLIC ATTACHMENTS
1. Draslovka public attachments.zip [Please refer to comment No. 4, 8, 11, 14, 18, 21]

CONFIDENTIAL ATTACHMENTS
1. Draslovka confidential attachements.zip [Please refer to comment No. 4, 8, 11, 14, 18, 21]