

**Committee for Risk Assessment**  
**RAC**

Annex 2  
**Response to comments document (RCOM)**  
to the Opinion proposing harmonised classification and  
labelling at EU level of

**theophylline; 1,3-dimethyl-3,7-dihydro-1*H*-  
purine-2,6-dione**

**EC Number: 200-385-7**

**CAS Number: 58-55-9**

CLH-O-0000006848-58-01/F

**Adopted**  
**17 September 2020**

**ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON THEOPHYLLINE; 1,3-DIMETHYL-3,7-DIHYDRO-1H-PURINE-2,6-DIONE**

**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.

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**Substance name: theophylline; 1,3-dimethyl-3,7-dihydro-1H-purine-2,6-dione**

**EC number: 200-385-7**

**CAS number: 58-55-9**

**Dossier submitter: The Netherlands**

**GENERAL COMMENTS**

Date	Country	Organisation	Type of Organisation	Comment number
05.12.2019	Germany		MemberState	1
Comment received				
In part B of section 1.3 the unit for the density has to be corrected from mg/cm <sup>3</sup> to g/cm <sup>3</sup> . Also references to tables in the text are not correct (shifted, e.g. table 7 in text refers to table 6).				
Dossier Submitter's Response				
The unit for density should indeed be g/cm <sup>3</sup> . Regarding your second comment, table 7 in text (page 19) refers to table 7 (Body weight data) and does not refer to table 6 (as suggested). However, we further checked other references to tables and it is noted that 'table 10' in text (page 21; section 'cross-over mating trial') should be 'table 11'.				
RAC's response				
Noted.				

**TOXICITY TO REPRODUCTION**

Date	Country	Organisation	Type of Organisation	Comment number
05.12.2019	Germany		MemberState	2
Comment received				
The classification of theophylline as Repr. 1B (H360D) is based on effects in mice (reduced numbers of live pups/litter, and increased number of resorption) and rats (reduced live fetuses/litter). We agree that the observed effects are unlikely to be secondary due to maternal toxicity. Consequently, the proposed classification is supported.				
Dossier Submitter's Response				
Thank you for your support.				

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RAC's response				
The RAC supports the proposal made by the DS. Thanks for the support.				

Date	Country	Organisation	Type of Organisation	Comment number
11.12.2019	France		MemberState	3
Comment received				
<p>The present dossier describes in details the available reproductive toxicity data about theophylline and explains the observed differences in toxicity between the studies.</p> <p>Based on available data, the proposed classification for reproductive toxicity as Repro 1B H360D is supported.</p>				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
The RAC supports the proposal made by the DS. Thanks for the support.				

Date	Country	Organisation	Type of Organisation	Comment number
10.12.2019	Sweden		MemberState	4
Comment received				
<p>The Swedish CA supports the classification of theophylline as Repr. 1B, H360D.</p> <p><b>Fertility</b> The Swedish CA agrees that available animal data on theophylline do not meet the classification criteria for adverse effects on fertility or sexual function.</p> <p><b>Developmental toxicity</b> The Swedish CA agrees that the severe developmental effects seen in mice (i.e. stat. sign. dose-dependent increased number of resorptions and reduced number of live pups/litter) and rats in the absence of, or presence of limited maternal toxicity are clear evidence of adverse effects on the development of the offspring of theophylline, which warrant classification in Category 1B.</p>				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
The RAC supports the proposal made by the DS. Thanks for the support.				