Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

trimethyl phosphate

EC Number: 208-144-8
CAS Number: 512-56-1

CLH-O-0000007318-70-01/F

Adopted

8 June 2023

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: Trimethyl phosphate
EC number: 208-144-8
CAS number: 512-56-1
Dossier submitter: Austria

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
25.08.2022	Germany		MemberState	1
Comment received				
The DE CA supports the AT CA's conclusion on the proposed harmonised classification.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Noted				

CARCINOGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
25.08.2022	Germany		MemberState	2
Comment received				
Significantly dose-related increased incidences of subcutaneous fibromas in male rats and adenocarcinoma in female mice (uterus/endometrium), as well as occurrence of rare tumours and dose-related occurrence of tumours in the lung (lung alveolar/bronchiolar adenoma/carcinoma) and the adrenals (pheochromocytoma) indicate carcinogenic potential for humans. Based on the available data, classification as Carc. 1B is warranted.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Noted				

MUTAGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
25.08.2022	Germany		MemberState	3
Comment received				
Many studies document the mutagenic effects of trimethyl phosphate in vitro (bacterial and mammalian cell systems), mutation assays in Drosophila melanogaster, as well as in vivo - in mice, rats, and rabbits - inducing chromosomal aberrations in somatic cells and spermatocytes. The transmission of mutations to F1 offspring has been demonstrated. Thus, classification as Muta. 1B is justified.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Noted				

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
25.08.2022	Germany		MemberState	4
Comment received				
Concerning fertility effects, an OECD TG 422 study demonstrates a clearly reduced fertility up to complete sterility at higher doses presumably caused by genotoxic effects on spermatocytes. However, a contribution of other modes of action cannot be excluded. A developmental toxicity study is missing for this substance, but an increased intrauterine mortality in the OECD TG 422 study indicates developmental effects. Hence, a contribution of other modes of action than germ cell mutagenicity to the observed effects cannot be excluded. Thus, classification as Repr. 1B, H360FD, is warranted				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Noted				

OTHER HAZARDS AND ENDPOINTS – Acute Toxicity

Date	Country	Organisation	Type of Organisation	Comment number
25.08.2022	Germany		MemberState	5
Comment received				
The lowest available oral LD50 of 840 mg/kg bw from a rat study (NIH national library, cited by DFG, 1983) would justify a classification as Acute Tox. 4, H302. However, this study cannot be located and essential background information regarding the method, including strain, sex (number/group), dose levels and exposure duration is missing. In view of this problem, it is possible to refer to a comprehensive study by Deichmann & Witherup (1946) in rats, rabbits and guinea pigs for derivation of an LD50. Although this is an older study, the study provides background information on the previously mentioned missing parameters of the method. In the study by Deichmann & Witherup (1946) the lowest determined LD50 in rabbits amounts to 1257 mg/kg bw. This value is acceptable for the ATE.				
Dossier Submitter's Response				
Thank you for your support.				

RAC's response
Noted

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Repeated Exposure

Date	Country	Organisation	Type of Organisation	Comment number
25.08.2022	Germany		MemberState	6
Comment received				
Neurotoxic effects have been observed in several repeated-dose toxicity studies in rats, rabbits, and dogs, with effective doses > 10 mg/kg bw/d and < 100 mg/kg bw/d, indicating that STOT RE 2 classification H373 (nervous system) is warranted. Neurotoxic effects include e.g. progressive decrease of central motor maximum nerve conduction velocity (MNCV), decreased muscle force as well as persistent abnormal posture, tremors, and unsteadiness.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Noted				