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 11.05.2020

Substance name: benzyl(diethylamino)diphenylphosphonium 4-[1,1,1,3,3,3-hexafluoro-2-(4-hydroxyphenyl)propan-2-yl]phenolate
CAS number: 577705-90-9
EC number: 479-100-5
Dossier submitter:

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
20.04.2020	Germany		MemberState	1
Comment received				
In table 5 in section 2.1 of the CLH report ("Proposed harmonised classification and labelling according to the CLP criteria") the CAS No. to identify the substance in the resulting Annex VI entry is missing. Please add the corresponding information.				

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
08.05.2020	France		MemberState	2
Comment received				
Considering that the substance contains 50% of BPAF, read-across to the classification proposal of BPAF is appropriate.				

Date	Country	Organisation	Type of Organisation	Comment number
07.05.2020	Netherlands		MemberState	3
Comment received				
We agree with the proposed classification in Repr. 1B for adverse effects on sexual function and fertility, based on data on Bisphenol AF (EC 216-036-7). Clear effects on fertility were observed in the OECD 422 study, starting at the lowest dose, without marked systemic toxicity. The clear effects on fertility observed in this study alone is considered sufficient for classification as Repr. 1B H360F. The mechanistic studies indicate an endocrine-mediated mechanism is involved, further supporting the proposed classification,. Regarding developmental toxicity, the following was noted: - OECD 422 study, oral, 0-30-100-300 mg/kg bw/day, rats o No significant effects on offspring treated in utero. o No differences in sex ratio and body weights of offspring between treated animals and controls. o Necropsy findings in offspring: no evident effects from BPAF treatment				

o Note: no pups at all produced by animals in the high dose group treated with 300 mg/kg bw/day.

- In vivo study mammary gland, exposure GD 10.5-17.5, follow-up offspring until 16 months, CD-1 mice, 0, 0.05, 0.5, 5 mg/kg bw twice per day:
o BPAF exposure caused accelerated pubertal mammary development.
o By 14 months of age, a significant dose-related increase in non-neoplastic lesions was found in BPAF-exposed groups, including cysts, inflammation, lobuloalveolar hyperplasia and squamous metaplasia.

- In vivo study on effects on offspring, SD rats, exposure GD 3-19 and PND 3-19, 0 and 100 mg/kg/bw/d:
o Lactational exposure caused significantly increased levels of BPAF in serum and in testis, showing that BPAF was transferred via breast milk.
o Gestational and lactational exposure lead to increased testosterone and decreased Inhibin B levels in male offspring. Androgen receptor levels in testes increased following BPAF exposure.

- In vivo study on neurobehaviours in adolescent mice offspring, exposure GD 1-19, 0- 0.4-4 mg/kg bw/day.
o Fetal exposure to BPAF induced anxiety- and depressive-like behaviours in male adolescent offspring. In addition, BPAF exposure impaired memory formation in both sexes.
o Note: no exact numbers given in the research article, no information on parental toxicity.

Perhaps a discussion for classification as category 2 developmental toxicant would be possible, but it seems there is insufficient robust reporting to draw conclusions on possible developmental toxicity.
Overall, there are indications of treatment-related developmental effects, but the evidence is inconclusive for classification and we agree that the available information is insufficient for classification for developmental toxicity and for classification for effect on or via lactation.

Date	Country	Organisation	Type of Organisation	Comment number
20.04.2020	Germany		MemberState	4
Comment received				
The substance addressed in the CLH-report contains ca. 50 % Bisphenol AF as anion. The classification with Repr. 1B, H360F based on the data from Bisphenol AF is supported (see comment on Bisphenol AF). The available data provide clear evidence of an adverse effect on both male and female sexual function and fertility and that the observed effects are considered relevant for humans.				