COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during public consultation are made available in this table as submitted by the webform. Please note that the comments displayed below may have been accompanied by attachments which are not published in this table.

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Last data extracted on 09.02.2018

Substance name: hexythiazox (ISO); trans-5-(4-chlorophenyl)-N-cyclohexyl-4-methyl-2-oxo-3-thiazolidine-carboxamide
CAS number: 78587-05-0
EC number: -
Dossier submitter: Finland.

CARCINOGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
01.02.2018	Spain		MemberState	1
Comment received				
The Spanish CA agrees with the dossier submitter that findings in hexythiazox treated rats and mice are considered as weak and inconsistent evidence and not sufficient to warrant carcinogenicity classification.				

Date	Country	Organisation	Type of Organisation	Comment number
01.02.2018	France		MemberState	2
Comment received				
Rat study: - Testicular interstitial cell (Leydig cell) adenoma: While it is acknowledged that strain F344 is not appropriate to investigate this type of tumours in respect to the high spontaneous incidence (almost 100% in control and treated groups at terminal sacrifice), it should however be noted that hexythiazox treatment seems to impact the age at onset. Indeed, at interim sacrifice the interstitial cell tumour incidences were 0/10, 0/10, 2/10 and 3/11 at 0, 60, 430 and 3000 ppm respectively. - Mammary glands tumours In the absence of relevant HCD supporting that the incidences reflect biology variability, it cannot be excluded that the increased incidence mammary gland tumours in males are treatment-related (fibroadenomas: 0, 1, 2 and 6 at 0, 60, 430 and 3000 ppm respectively; 1 adenocarcinoma at 3000 ppm) - Para-follicular cell adenoma In the absence of relevant HCD supporting that the incidences reflect biology variability, it cannot be excluded that the increased incidence C cell tumours in high dose males are treatment-related. Mouse study: - Liver tumours Total number of hepatic tumours was statistically increased at the top dose in both sexes,				

while adenoma was statistically increased only in top dose females.
Furthermore, the incidence of hepatoblastoma (rare tumour) was increased in both sexes at the top dose level of 1500 ppm.

Based on these data and in the absence of appropriate HCD or mechanistic data investigating the potential underlying mechanisms of increased incidences of tumours and their human relevance, it is considered that classification for carcinogenicity cat.2 H351 Suspected of causing cancer is warranted.

While JMPR in 2008 concluded that the increased incidences of tumours in rodents exposed to hexythiazox were likely to be threshold phenomena and that hexythiazox was unlikely to present a carcinogenic risk to humans at exposure levels associated with residues in food, the HED Cancer Assessment Review Committee (USEPA) classified hexythiazox as a "possible human carcinogen" in 1988.

Date	Country	Organisation	Type of Organisation	Comment number
01.02.2018	Germany		MemberState	3
Comment received				
"DE-CA comment on carcinogenicity.pdf" ECHA note – An attachment was submitted with the comment above. Refer to public attachment DE-CA comment on carcinogenicity.pdf				

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
26.01.2018	United Kingdom		MemberState	4
Comment received				
Acute toxicity to Daphnia (Additional Report IIA, 8.2/34 Saito, 2003): Does the study report include observation data for animal inspections? This is important to rule out physical effects for immobilisation given that particles were observed in treatments with mean measured concentrations above the quoted water solubility. In addition, are there any 24/48 hour immobilisation endpoints from the chronic toxicity to Daphnia study which support the 48h EC50 being based on an ecotoxic response? Chronic toxicity to Daphnia (DAR IIA 8.2/21 Lui, 1996): While we note the reduction in oxygen levels over the study, we recognise that levels were above similar test guideline levels. On this basis, we feel additional statistical analysis is required to consider if the immobilisation 21 day NOEC invalid. In addition, can adult immobilisation data available from the other chronic toxicity to Daphnia studies aid interpretation of the Lui, 1996 21-day NOEC for immobilisation?				

Date	Country	Organisation	Type of Organisation	Comment number
01.02.2018	France		MemberState	5
Comment received				
FR agrees with the classification and M factors (acute and chronic) proposals.				

Date	Country	Organisation	Type of Organisation	Comment

				number
01.02.2018	Germany		MemberState	6
Comment received				
We support the proposal for the classification of environmental hazards as Aquatic acute 1 (H400) and Aquatic chronic 1 (H410) and the acute/chronic M-factor of 1. ECHA note – An attachment was submitted with the comment above. Refer to public attachment DE-CA comment on carcinogenicity.pdf				

Date	Country	Organisation	Type of Organisation	Comment number
02.02.2018	Belgium		MemberState	7
Comment received				
BE CA agrees with FI's comparison of available data with the environmental CLP criteria and supports the proposed environmental classification of hexythiazox with Aquatic Acute 1, H400 (M=1) and Aquatic Chronic 1, H410 (M=1).				

PUBLIC ATTACHMENTS
1. DE-CA comment on carcinogenicity.pdf [Please refer to comment No. 3, 6]