Committee for Risk Assessment

RAC

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

tris(2-methoxyethoxy)vinylsilane; 6-(2-methoxyethoxy)-6-vinyl-2,5,7,10-tetraoxa-6-silaundecane

EC Number: 213-934-0
CAS Number: 1067-53-4

CLH-O-0000001412-86-207/F

Adopted

8 June 2018

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during public 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 public 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 public 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: tris(2-methoxyethoxy)vinylsilane; 6-(2-methoxyethoxy)-6-vinyl-2,5,7,10-tetraoxa-6-silaundecane
EC number: 213-934-0
CAS number: 1067-53-4
Dossier submitter: Austria

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
03.08.2017	Belgium		MemberState	1
Comment received				
BE CA welcomes this proposal for harmonized classification and labelling. As a general comment, we would point out the actual lack of information on vinylsilanetriol, a possible tris(2-methoxyethoxy)vinylsilane) metabolite.				
Dossier Submitter's Response				
Thank you for your comment. As you have pointed out, vinylsianetriol (CAS No: 143-48-6) is a possible metabolite of tris(2-methoxyethoxy)vinylsilane. However, no toxicological information on this substance was found in data searches.				
RAC's response				
Thank you for your input.				

MUTAGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
03.08.2017	Belgium		MemberState	2
Comment received				
BE CA agrees with the conclusion of the Austrian Authorities not to classify tris(2-methoxyethoxy)vinylsilane as a mutagenic chemical according to the CLP regulation. All in vitro tests on mutagenicity/genotoxicity showed negative results for this compound, including after a primary metabolic activation (bacterial reverse mutation assay). Furthermore, 2-methoxyethanol, its main metabolite, is currently not classified for mutagenicity.				
Dossier Submitter's Response				
Thank you for your input and comment.				

RAC's response
Agree. Thank you for your comment.

Date	Country	Organisation	Type of Organisation	Comment number
02.08.2017	Germany		MemberState	3
Comment received				
The German CA agrees that the available data on tris(2-methoxyethoxy)vinylsilane are not sufficient for classification as a germ cell mutagen.				
Dossier Submitter's Response				
Thank you for your comment.				
RAC's response				
Agree. Thank you for your comment.				

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
03.08.2017	Belgium		MemberState	4
Comment received				
BE CA supports the tris(2-methoxyethoxy)vinylsilane classification proposal as a presumed human reproductive toxicant (1B) concerning both sexual function, fertility and development. The combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD guideline 422, reliability 1) showed clear evidence of an adverse effect on sexual function and fertility, especially seminiferous tubule degeneration, hypospermia and prostate atrophy in males, reduced fertility index and changes in gestational duration in females. Those results are not likely to be secondary to a general toxicity, as first adverse effects on fertility and development were observed at a dose without systemic toxic effects in females (75 mg/kg bw/d). In males, BECA is of the opinion that reproductive effects at 75 mg/kg bw/d cannot be explained by the clinical findings on the spleen. Those observations support the classification proposal. The same experimental animal testing also showed a developmental toxicity, through reduced postnatal survival, increased resorption and decrease in the mean number of pups born and life litter size at PND 0 in females exposed to 75 mg/kg bw/d. At 250 mg/kg bw/d, entire litter resorption was observed in 5 out 9 females exposed. These findings are not presumed to be secondary to maternal toxicity. Moreover, 2-methoxyethanol, a reported tris(2-methoxyethoxy)vinylsilane) metabolite (OECD 2006, ECHA 2017b) has a well-known developmental toxicity. In the present CLH report, the Nelson et al. study (1989) showed 92% of dead or resorbed litters when exposed to 73 mg/kg bw/d 2-methoxyethanol. Furthermore, this substance is already classified as Repr. 1B (H360FD), which gives credit to the present classification proposal. The resulting classification as Repr. 1B (H360FD) is thus supported.				
Dossier Submitter's Response				
Thank you for your input and comment. We agree with your remarks.				

RAC's response
Agree. Thank you for your input and comment.

Date	Country	Organisation	Type of Organisation	Comment number
02.08.2017	Germany		MemberState	5

Comment received

The effects on sexual function and fertility in male and female rats as seen in an OECD TG 422 screening study are sufficient for classification of tris(2-methoxyethoxy)vinylsilane as reproductive toxicant category 1B (H360F).

However, the toxicological data in rats are mainly presented in a qualitative manner (e.g. „Mean number of days between pairing and coitus increased", „mean number of implantation sites reduced"). It is stated in the CLH report that access to the original study was not available. Still, improvement of quantitative toxicological data on reproductive toxicity regarding tris(2-methoxy¬ethoxy)vinylsilane in the CLH report would ensure a more comprehensive assessment of the substance's potential to cause reproductive toxic effects based on the information given in the report.

Although quantitative data on litter losses are limited for animals at the mid dose group (75 mg/kg bw/d), the observed embryotoxic effect (total litter resorption/loss in 6/9 litters) at the high dose (250 mg/kg bw/d) should be considered as sufficient to justify classification in Category 1B for developmental toxicity. This effect is considered as unlikely to be secondary to lower body weight gain and haematology effects seen in the absence of clinical symptoms in dams at the high dose only. As default it is assumed that the resorptions are responsible for the lower body weight gain (22 % in comparison to the controls), as no information on corrected body weights was given.
Supporting evidence is given by the high rate of absorption/dead pups (at 73 mg/kg bw/d without maternal toxicity) observed for the assumed metabolite 2-methoxyethanol which is a classified reproductive toxicant affecting fertility as well as development (H360FD).

Therefore, we support the classification of tris(2-methoxyethoxy)vinylsilane as Repr. 1B (H360FD).

Dossier Submitter's Response

Thank you for your comment. We share your opinion that the report would benefit from better quantitative data on reproductive toxicity (data from the OECD TG 422 study). However, since the original study was not accessible, we presented as much information as possible and think that classification of tris(2-methoxyethoxy)vinylsilane as Repr. 1B (H360FD) is justified based on the available data.
As noted by Germany we mainly have access to qualitative descriptions of the observed effects, however, also some quantitative information can be derived from the data:
We agree with Germany that detailed information on number of total resorptions in the high dose dams is available and allows to conclude on the severity of the effect.
In addition detailed information is also presented on gestation length. Although the degree of increase and the number of affected dams in the mid dose is not known, it is relevant that this effect was seen in the mid as well as in the high dose. In the high dose, the only female that delivered, also had increased gestation length. In the mid dose one possible case of dystocia is described, which is a severe and quite rare effect, which is often associated with prolonged gestation time on a group basis and therefore adds to the biological relevance of the finding.
The fertility index in the high dose was reduced to 60%, as compared to 90% in the control group. It is plausible that the observed decrease in the fertility index is a

consequence of the effects on male reproductive organs described in a qualitative way (i.e. small and / or soft testes and / or epididymides, reduced absolute and relative testes and epididymal weights, seminiferous tubule degeneration in males with small/soft testes, hypospermia and luminal cellular debris in epididymides, reduced mean absolute and relative prostate weight which correlated with dereased section and/or atrophy, mean absolute and relative seminal vesicle weights reduced). It is known that rats can compensate effects on sperm production rather effectively, therefore a reduced fertility index by 30% is meaningful in relation to the effects observed on male reproductive organs. Overall we believe that the available information is sufficient to clearly demonstrate adverse effects on reproduction and development supporting a classification as Repr 1B, H360 DF.
RAC's response
Agree. Thank you for your input and comment.

Date	Country	Organisation	Type of Organisation	Comment number
31.07.2017	France		MemberState	6
Comment received				
We agree with the proposed harmonized classification: Repr.1B H360FD				
Dossier Submitter's Response				
Thank you for your comment.				
RAC's response				
Agree. Thank you for your opinion.				