ECHA
European Chemicals Agency

Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

tetrahydrofuran

ECHA/RAC/DOC no CLH-O-0000000954-69-03/A2

Adopted
25 May 2010

Annex 2 - Comments and response to comments on CLH PROPOSAL for TETRAHYDROFURAN

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Substance name: Tetrahydrofuran
CAS number: 109-99-9
EC number: 203-726-8

General comments

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
2009/09/30	Belgium / Walter Cremers / Cefic	Re: Response to the French Classification Proposal for Tetrahydrofuran (THF, CAS Number: 109-99-9, EC Number: 203-726-8) Dear Sir or Madam: On behalf of the Cefic BDO and Derivatives Sector group we submit the following comments on the Annex VI report, the Proposal For Harmonised Classification And Labelling of Tetrahydrofuran (CAS Number: 109-99-9; EC Number: 203-726-8). France has proposed to classify Tetrahydrofuran (THF) as a Category 3 carcinogen. However, a recent reanalysis (2009) by a Pathology Working Group (PWG), of the key study used to classify THF, supports the conclusion that THF does not meet the criteria for classification as a carcinogen by either EC or GHS criteria. **This is available separately in the RAC CIRCA IG.** As summarized in the C&L Dossier, THF is not genotoxic. The French authorities have proposed to classify THF as a Category 3	FR: Thank you for your comments. Since a document [The PWG (Pathology working Group) review of selected histologic changes in the kidneys of male rats assigned to a 2-year inhalation carcinogenicity study of tetrahydrofuran (NTP study NO. 05181-03) 2009 Biotechnics] has been provided by Cefic, additional arguments have been provided in the proposal for harmonized classification and labelling to support a classification as Carc. Cat. 3 for THF.	France has amended the proposal to include the PWG data and discussed their relevance with regards to the proposed Carc. Cat. 3 classification.

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
		carcinogen based on weakly positive findings in male rat kidneys, female mouse liver tumors, and some slightly higher incidences of two benign tumor types at high exposure concentrations in a 2-Year Inhalation Carcinogenicity Study of THF (NTP Study No. 05181-03) by the National Toxicology Program (NTP,1998). The French proposal did not consider the female mouse liver tumor findings to be relevant to humans since it has been demonstrated that THF induced cell proliferation in female mouse liver (Gamer et al., 2002, Van Ravenzwaay et al., 2003). Likewise, the slight increases in incidences of mammary fibroadenoma, testicular adenoma, and prostate epithelial hyperplasia were noted by NTP but were within or very close to historical control values (NTP, 1998). Therefore, this French classification proposal is based primarily on the male rat kidney tumors. The diagnosis of these kidney tumors was the subject of a recent PWG evaluation (Biotechnics, 2009). The PWG report, which was not available to the French competent authorities at the time of their classification, suggests a mode of action that is not relevant to humans. Both NTP and the PWG pathologists confirmed that renal tumors (adenomas) were slightly more		

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
		prevalent in the kidneys of animals exposed to high concentrations of THF compared with the control group. The PWG confirmed that there was no significant difference in the incidence of renal changes (neoplastic and pre-neoplastic combined) between control and THF-exposed groups when applying state of the art diagnostic criteria. Additionally, there was no evidence of early tumor occurrence or of tumor progression to carcinoma. The PWG was composed of experts in the field of rat kidney pathology including the area of chronic progressive nephropathy (CPN). The PWG participants applied refined, current diagnostic criteria that distinguished between "reactive" tubular hyperplasia, which is associated with CPN, and atypical tubular hyperplasia. The original NTP report data did not make a distinction between these two phenomena as the knowledge of CPN was less developed at the time of the 1998 assay. Furthermore, PWG members agreed that, based upon the absence of experimental results that would implicate genotoxic mechanisms for the observed renal changes, it was likely that the atypical hyperplasia and adenomas seen in the control group resulted from regenerative processes associated with advanced CPN, and in the high exposure group, these proliferative changes resulted from either CPN and/or low-grade a2u-globulin nephropathy. The extremely high background of CPN seen in male rats (in addition to weak, low-grade, a2u-globulin		

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
		nephropathy) likely may have influenced the tumor analysis by NTP for THF. Neither of these changes have counterparts in humans. The PWG concluded that the mechanisms that likely contributed to the formation of renal tumors in male rats in the NTP study pose no risk for humans. There are several publications, published after the 1998 NTP report, which show that CPN is widespread in laboratory rats, especially the strain used by NTP. Hard et al., 2009, noted that various chemicals exacerbate CPN. Hard et al., 2009, states that CPN is a single renal disease of unknown etiology, occurring at high incidence in laboratory rats. CPN can confound subchronic and chronic carcinogenicity interpretation, and no known equivalent chemical interactions are seen with human nephropathies. Seely, et al., 2002, has also found an increase in the xenobiotic-increased severity of CPN in the F344 strain of rats used in the NTP bioassays. Based on the new information generated by the PWG report, and the subsequent peer-reviewed publications, the Cefic BDO and Derivatives Sector Group believe that THF lacks sufficient evidence to warrant carcinogen classification for following reasons: 1) There was no significant difference in the incidence of renal changes (neoplastic and pre-		

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
		neoplastic combined) between control and THF-exposed groups when applying state of the art diagnostic criteria. 2) Proliferative changes, in experimental animals, resulted from either CPN and/or low-grade a2u-globulin nephropathy and have no counterpart in humans. Carcinogenicity Classification Conclusion: THF is not genotoxic, nor does THF cause an increase in human-relevant tumor types in experimental animals. According to EC and GHS regulatory criteria (REGULATION (EC) No 67/548 and REGULATION (EC) No 1272/2008), THF not only lacks sufficient evidence to warrant carcinogen classification, but also seems to fit the clear criteria for non-classification. Since THF lacks sufficient evidence to warrant carcinogen classification according to EC and GHS regulatory criteria, Cefic suggests that the Carc. Category 3 proposal should be withdrawn. Additional C&L Dossier Comments - additionally, Cefic would like to provide the following comments or corrections for consideration, by section: Section 1.3: Autoflammability is listed as 321°C. The accepted industry value is 215°C.	The report will be amended (autoflammability and uses).	The value of 321°C has not been amended. Instead, a reference to a safety data sheet to support this value has been added, together with new values of 230°C and 215°C. Greater clarity of this issue is required.

Annex 2 - Comments and response to comments on CLH PROPOSAL for TETRAHYDROFURAN

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
		Section 2.1: The report currently states: THF is used as aerosol paint concentrates, furniture polish and cleaners, laundry starch preparations, lubricating oils, paint and varnish removers, synthetic resin and rubber adhesives … The report should state: THF is used as a solvent in aerosol paint concentrates, furniture polish and cleaners, laundry starch preparations, lubricating oils, paint and varnish removers, synthetic resin and rubber adhesives … Section 5.3.2: France is proposing a Note - Code H, for skin irritation, which is used to indicate that it may be necessary to complement the harmonised classification for some endpoints. France notes that the IUCLID irritation studies are old and poorly reported. The IUCLID studies are, however, fairly consistent and thus France is still proposing R36/37, which is generally accepted. It is doubtful that additional animal testing will be requested or allowed, under REACH, to make the irritation dataset more robust. The current information seems adequate for REACH and other classification efforts; therefore the Code H note should be withdrawn. Sincerely, Walter Cremers, Secretary General BDO and Derivatives Sector Group.	France is not proposing a R36/37 classification as these endpoints are not re-evaluated in this dossier. Regarding eye and respiratory system irritation endpoints, France keeps Annex I entrance unchanged. Data regarding eye irritation are provided for SCL discussions. Note H is proposed for informing industry that they are expected to complement the harmonised classification, especially for skin irritation, depending on their substance impurity profile and other relevant information that may be available to them (e.g. data). Note H has no mean to request more information.	The general public uses have been changed to those indicated by Cefic. Classification for skin irritation was not proposed and there was no justification for action on a community-wide basis. Therefore the rapporteur has not assessed the irritant potential of THF.

Annex 2 - Comments and response to comments on CLH PROPOSAL for TETRAHYDROFURAN

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
		References Gamer AO, Jaeckh R, Leibold E, Kaufmann W, Gembardt C, Bahnemann R, and van Ravenzwaay B. (2002). Investigations on Cell Proliferation and Enzyme Induction in Male Rat Kidney and Female Mouse Liver Caused by Tetrahydrofuran. Toxicol. Sci. 70, 140-149. Hard GC, Johnson KJ, Cohen SM. (2009). A comparison of rat chronic progressive nephropathy with human renal disease-implications for human risk assessment. Crit Rev Toxicol. 39(4):332-46. National Cancer Institute/National Toxicology Program. NTP Toxicology and Carcinogenesis Studies of Tetrahydrofuran (CAS No. 109-99-9) in F344/N Rats and B6C3F1 Mice (Inhalation Studies). NCI/NTP Carcinogenesis Technical Report Series 1998; 475: 1-244. Biotechnics. (2009). Pathology Working Group Review of Selected Histological Changes in the Kidneys of Male Rats Assigned to a 2-Year Inhalation Carcinogenicity Study of Tetrahydrofuran (NTP Study Number: 05181-03). Publication in a peer review journal in preparation. Seely JC, Haseman JK, Nyska A, Wolf DC, Everitt JI, Hailey JR. (2002). The effect of chronic progressive nephropathy on the incidence of renal tubule cell neoplasms in		

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
		control male F344 rats. Toxicol Pathol. 30(6):681-6. Van Ravenzwaay B, Gamer AO, Leibold E, Kaufmann W. (2003). Effect of cytochrome P-450 inhibition on tetrahydrofuran induced hepatocellular proliferation in female mice. Arch. Toxicol. 77 (8): 459-464		
2009/10/13	Germany / Mark Schwägler / MSCA	German CA: France suggests the classification of the substance Tetrahydrofuran, based on regulation (EC) No 1272/2008 in category 2 as a suspected human carcinogen with the hazard statement H351. The proposal for classification follows from the results of a two 2-year carcinogenicity-study in rats and mice. In this study a higher incidence of renal tubule epithelial adenoma and carcinoma in male rats and tumour formation in female mouse liver was observed. We support the opinion of France that the relevant tumours for a decision are the renal rat tumours. However, to give a final judgement a more detailed description of the experimental results and argumentation whether the criteria for an alpha 2µ- globulin-associated response are fulfilled, would be necessary. Based on the provided information in the CLH Report we agree with the conclusion to classify THF as carcinogenic cat. 2 - H351, additionally	FR: Thank you for your comments. Since a document [The PWG (Pathology working Group) review of selected histologic changes in the kidneys of male rats assigned to a 2-year inhalation carcinogenicity study of tetrahydrofuran (NTP study NO. 05181-03) 2009 Biotechnics] has been provided by Cefic, additional arguments have been provided in the proposal for harmonized classification and labelling to support a classification as Carc. Cat. 3 for THF.	Noted. Since the proposal was submitted, additional information on the carcinogenicity histopathology results has been provided, which France has incorporated into the report. These demonstrate that an α 2u-globulin mechanism does not fully explain the induction of the observed kidney tumours.

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
		to the current classification, provided that the argumentation that the alpha 2μ- globulin nephropathy is the responsible mode of action could be followed in sufficient detail. Reference to IUCLID (2000): In version 2 of the CLH report reference was made to the IUCLID data set of 2000 in several cases. Please, replace these by the original references and add "cited in IUCLID 2000" as it is difficult to track down these studies in the IUCLID by the often little information. In version 1 of the report the original citations were given but have apparently been replaced during revision.	The IUCLID references will be corrected as suggested.	Noted.
2009/10/15	United Kingdom / Tim McArragher / International Specialty Products	Dear Sir or Madam: On behalf of International Specialty Products we submit the following comments on the Annex VI report, the Proposal For Harmonised Classification And Labelling of Tetrahydrofuran (CAS Number: 109-99-9; EC Number: 203-726-8). First, we fully support the comments of the CEFIC BDO Sector Group regarding the French proposal submitted under separate cover. We urge ECHA to adopt those comments. In addition to the minor corrections noted by the CEFIC Group, we also support the results of the 2009 Pathology Working Group (PWG). Based on new information generated by the PWG,	FR: Thank you for your comments. Since a document [The PWG (Pathology working Group) review of selected histologic changes in the kidneys of male rats assigned to a 2-year inhalation carcinogenicity study of tetrahydrofuran (NTP study NO. 05181-03) 2009 Biotechnics] has been provided by Cefic, additional arguments have been provided in the proposal for harmonized classification and labelling to support a classification as Carc. Cat. 3 for THF.	France has incorporated the PWG data into its report and discussed the relevance of the findings with regards to the proposed classification for carcinogenicity. With regards to the specific concerns of International Specialty Products, it is recognised by the Society for Toxicologic Pathology that it is not appropriate to combine hyperplasia and neoplasia for the purposes of statistical analysis (reference included in background document). Also, the PWG and Hard (2005) demonstrated that THF did not exacerbate CPN, since the incidence and severity of CPN was not increased in the high-

Annex 2 - Comments and response to comments on CLH PROPOSAL for TETRAHYDROFURAN

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
		THF lacks sufficient evidence to warrant a carcinogen classification. The PWG found that there was no significant difference in the incidence of renal changes (neoplastic and pre-neoplastic combined) between control and THF-exposed groups when applying the latest refined diagnostic criteria. In addition, proliferative changes in laboratory animals resulted from either chronic progressive nephropathy (CPN) and/or low-grade a2u-globulin nephropathy and have no counterpart in humans. We therefore suggest that the Carcinogen Category 3 proposal should be withdrawn. Additionally, we also feel that the irritation dataset in IUCLID is robust and, due to the animal testing restrictions under REACH, further refinement is unlikely. Therefore the Code H Note should likewise be withdrawn. We agree with the R36/37 assignment. We request that ECHA revise the French THF Proposal by incorporating the foregoing comments along with those comments from CEFIC.	Code H Note has no mean to require further animal testing rather than using information available to each producer/ importer taking into account substance specificities such as impurities.	dose compared with the control group; therefore, effects on CPN did not explain the increased incidence of tumours. Classification for skin irritation was not proposed and there was no justification for action on a community-wide basis. Therefore the rapporteur has not assessed the irritant potential of THF.
2009/10/15	Ireland / Health & Safety Authority	The Irish CA notes that the existing Annex VI entry for tetrahydrofuran lists a specific concentration limit for irritation to eyes and the respiratory system (R36/37) of C $\geq$ 25%. This specific concentration limit is not included in the Annex VI report. We propose that this should be included for completeness.	FR: Thank you for your comments. Explanation on SCL was added.	The Rapporteur has added the SCL for eye/respiratory sensitisation to the report.

Annex 2 - Comments and response to comments on CLH PROPOSAL for TETRAHYDROFURAN

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
		We are in agreement with the proposal to apply Note H for skin irritation.		There was no justification for action on a community-wide basis. Therefore the rapporteur has not assessed the irritant potential of THF.
2009/10/16	United States / Kathleen Roberts / Tetrahydrofuran Task Force	Appended are comments from the Tetrahydrofuran Task Force (document number 51623) in response to the French classification proposal for tetrahydrofuran (THF, CAS Number: 109-99-9, EC Number: 203-726-8). As indicted in our comments, the Tetrahydrofuran Task Force endorses the comments of the CEFIC BDO Sector Group and the findings of the 2009 Pathology Working Group (PWG). I have included copies of both the CEFIC comments (document number 51898) and the PWG report (document number 48961) with this submission. If you have any questions regarding this submission, please do not hesitate to contact me. Kind regards, Kathleen Roberts Tetrahydrofuran Task Force Manager <u>Re: Response to the French Classification Proposal for Tetrahydrofuran (THF, CAS Number: 109-99-9, EC Number: 203-726-8)</u> Dear Sir or Madam: The Tetrahydrofuran Task Force (THF Task	FR: Thank you for your comments. Since a document [The PWG (Pathology working Group) review of selected histologic changes in the kidneys of male rats assigned to a 2-year inhalation carcinogenicity study of tetrahydrofuran (NTP study NO. 05181-03) 2009 Biotechnics] has been provided by Cefic, additional arguments have been provided in the proposal for harmonized classification and labelling to support a classification as Carc. Cat. 3 for THF (see also response to CEFIC, second row of the table).	France has incorporated the PWG data into its proposal and discussed the relevance of the findings with regards to the proposed classification for carcinogenicity. With regards to the specific concerns of the THF Task Force, it is recognised by the Society for Toxicologic Pathology that it is not appropriate to combine hyperplasia and neoplasia for the purposes of statistical analysis (reference included in the revised report). Also, the PWG and Hard (2005) investigations demonstrated that THF did not exacerbate CPN, since the incidence and severity of CPN was not increased in the high-dose compared with the control group; therefore, effects on CPN did not explain the increased incidence of tumours.

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
		Force or Task Force) is pleased to submit these comments on the Annex VI report, the Proposal for Harmonised Classification and Labelling of Tetrahydrofuran (CAS Number: 109-99-9; EC Number: 203-726-8). The Task Force represents U.S. manufacturers and users of tetrahydrofuran (THF). Its mission is to address scientific, regulatory, and product stewardship issues concerning the health, safety, or environmental aspects of THF or products using THF. Given that many of our members' products can and are used in Europe, we have a vested interest in this classification proposal. First, we strongly endorse the comments submitted by the CEFIC BDO Sector Group regarding the French proposal. We urge the European Chemicals Agency (ECHA) to adopt those comments. We also support the findings of the 2009 Pathology Working Group (PWG). As detailed in the CEFIC BDO comments, the new information generated by the PWG demonstrates that there is insufficient evidence to support a carcinogen classification. The PWG found that there was no significant difference in the incidence of renal changes (neoplastic and pre-neoplastic combined) between control and THF-exposed groups when applying the latest refined diagnostic criteria. In addition, proliferative changes in laboratory animals resulted from either chronic progressive		

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
		nephropathy (CPN) and/or low-grade a2u-globulin nephropathy. Neither mechanism is relevant to humans. We therefore urge that the proposed Carcinogen Category 3 designation be withdrawn. Additionally, we also feel that the irritation dataset in IUCLID is robust and, due to the animal testing restrictions under the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH), further refinement is unlikely. Therefore the Code H Note should likewise be withdrawn. We agree with the R36/37 assignment. We request that ECHA revise the French THF Proposal by favorably considering the foregoing comments along with those from the CEFIC BDO Sector Group. Sincerely,  Kathleen M. Roberts Manager Tetrahydrofuran Task Force		
2009/13/10	Netherlands / Simon Goswell / Lyondell Chemie Nederland B.V.	Note: The comments included in the attachment below arrived by letter dated on 13/10/2009 and registered as item A(2009)3606 in ECHA's Mail Registration system.	FR: Thank you for your comments. Based on the document provided by CEFIC (The PWG (Pathology working Group) review of selected histologic changes in the	See the Rapporteur's comments to the THF Task Force and International Specialty Products submissions and MS's response.

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
		Re. Response to the French classification proposal for Tetrahydrofuran (THF, CAS Number: 109-99-9, EC Number: 203-726-8) Dear Sir or Madam: On behalf of Lyondell Chemie Nederland B.V. we submit the following comments on the Annex VI report, the proposal for harmonised classification and labelling of Tetrahydrofuran (CAS Number: 109-99-9; EC Number: 203-726-8). First, we fully support the comments of the CEFIC BDO Sector Group regarding the French proposal submitted under separate cover. We urge ECHA to adopt those comments. In addition to the minor corrections, noted by the CEFIC Group, we also support the results of the 2009 Pathology Working Group (PWG). Based on new information generated by the PWG report, we believe that THF lacks sufficient evidence to warrant a carcinogen classification. The PWG found that there was no significant difference in the incidence of renal changes (neoplastic and pre-neoplastic combined) between control and THF-exposed groups when applying the latest refined diagnostic criteria. In addition, proliferative changes, in laboratory animals, resulted from	kidneys of male rats assigned to a 2-year inhalation carcinogenicity study of tetrahydrofuran (NTP study NO. 05181-03) 2009 Biotechnics), additional data have been provided to support a classification as Carc. Cat. 3.	

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
		either chronic progressive nephropathy (CPN) and/or low-grade a2u-globulin nephropathy and have no counterpart in humans. We therefore suggest that the Carcinogen Category 3 proposal should be withdrawn. Additionally, we also feel that the irritation dataset in IUCLID is robust and, due to the animal testing restrictions under REACH, further refinement is unlikely. Therefore the Code H Note should likewise be withdrawn. We agree with the R36/37 assignment. We urge ECHA to revise the French THF Proposal by incorporating the foregoing comments along with those comments from CEFIC. Sincerely, Simon Goswell Director		

Carcinogenicity

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
2009/10/05	Hungary / Zsuzsanna Kiss / National Institute of Chemical Safety	On the basis of the controversial information appended, we agree that the proposed classification (Directive 67/548/EEC) of tetrahydrofuran is: Carcinogen Category 3; R40. In one test in E.coli showed mutagenicity using	FR: Thank you for your support. .	Noted. Since Hungary made its comments, France has amended the report to include additional data and discussion to support the Carc. Cat. 3 classification.

Annex 2 - Comments and response to comments on CLH PROPOSAL for TETRAHYDROFURAN

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
		the Ames' reverse mutation test, in the NTP study renal adenomas and nephrosis was reported in male rats. No human data available.		
2009/10/08	Denmark / Christina Ihlemann / Danish EPA (MS competent Authority)	Regarding the proposed classification of Tetrahydrofuran for cancer in category 3 Denmark agrees with the proposed classification for carcinogenic effects in category 3. We find the data from male rats on renal tumours justifies this classification. Although there is data to clarify the mechanism of the renal tumours in rats it is not established that the mechanism is in fact via the α 2u-globulin mechanism. So the carcinogenicity seen in male rats cannot at this stage be ruled out as irrelevant in humans.	FR: Thank you for your support.	Noted. Since Denmark made its comments, France has amended the report to include additional data and discussion to support the Carc. Cat. 3 classification.
2009/10/13	Germany / Mark Schwägler / MSCA	German CA: 1998 NTP mouse study; p 29: Typo: The highest dose was given as 1800 ppm. In the description of effects it reads, however, 1200 ppm twice - please correct	FR: Thank you for your comments. The typographical errors have been corrected.	Noted.
2009/10/13	Netherlands / Bureau REACH	We agree with the proposed classification carcinogen category 3 (Xn, R40) based on the increase in renal adenomas/carcinomas in the male rat and the increase in mammary gland fibroadenomas in female rats. The available information does not indicate that the increase in renal tumors in the rat is caused by α 2u-globulin nephropathy. We evaluated the available information using the criteria	FR: Thank you for your support. Since a document [The PWG review of selected histologic changes in the kidneys of male rats assigned to a 2-year inhalation carcinogenicity study of tetrahydrofuran (NTP study NO. 05181-03) 2009 Biotechnics] has been provided by Cefic, additional arguments have been provided in the proposal for harmonized	Noted. Since the public consultation, the proposal has been revised to include additional information on the likelihood of an α 2u-globulin mechanism being involved in the tumour induction.

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
		established by the IARC Working Group and the RIVM criteria as laid down in the factsheet on Alpha2u-globulin associated nephropathy and renal cell neoplasms. (Turkstra GH, van Raaij MTM, 2001, Alpha2u-globulin associated nephropathy and renal cell neoplasms. Factsheet FSV/006/00, available at http://www.rivm.nl/bibliotheek/rapporten/601516009.pdf)	classification and labelling to support a classification as Carc. Cat. 3 for THF.	
2009/10/15	Ireland / Health & Safety Authority	The Irish CA is in agreement with the proposal of France to amend the existing Annex VI entry for tetrahydrofuran to include classification as Carc. Cat 3 R40 [Carc. 2 H351]	FR: Thank you for your support.	Noted.

Other hazards and endpoints

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
2009/10/13	Germany/Mark Schwägler / MSCA	German CA: Flashpoint: The entry "Open cup: -20°C" is invalid. The German national institute PHYSIKALISCH-TECHNISCRE BUNDESANSTALT. (PTB) recommended „Close cup: -20°C". (Data base PTB-Lab. 3.43, 2008/Chemsafe) Flammabillity(Gas): Vapour-air mixtures are explosive within flammable limits noted above. upper flammable limit/ upper explosive limit (UFL): 46g/m3 (±10%) or 1,5 Vol% (±10%):	FR: Thank you. The proposal will be amended	Noted. The amendments have been made.

Date	Country/Person/ Organisation/ MSCA	Comment	Response	Rapporteur's comment
		Data base PTB-Lab. 3.43, 2008/Chemsafe lower flammable limit/lower explosive limit (LFL): 370g/m3 (±5%) cr12,4 Vol% (±5%): Data base PTB-Lab. 3.43, 2008/Chemsafe Explosive properties: The substance has not explosive properties in the sense of EEC-Method A.14. May form explosive organic peroxides when exposed to air or light or with age. Auto flammability: 230 °C (DIN 51 794/IEC 60079-4), Data base PTB-Lab. 3.43, 2008/Chemsafe		

ATTACHMENTS

CEFIC:
Re: Response to the French Classification Proposal for Tetrahydrofuran (THF, CAS Number: 109-99-9, EC Number 203-726-8).
Attachment:
Pathology Working Group review of selected histologic changes in the kidneys of male rats assigned to a two-year inhalation carcinogenicity study of tetrahydrofuran (NTP study No. 05181-03), 2009. (Enclosed as a separate pdf file to this table).
Tetrahydrofuran Task Force:
Re: Response to the French Classification Proposal for Tetrahydrofuran (THF, CAS Number: 109-99-9, EC Number: 203-726-8)
Attachment 1: Letter from Cefic to ECHA regarding 'Response to the French classification proposal for tetrahydrofuran', dated 29 September 2009 (Refer to General Comments from CEFIC in this table).
Attachment 2: Pathology Working Group review of selected histologic changes in the kidneys of male rats assigned to a two-year inhalation carcinogenicity study of tetrahydrofuran (NTP study No. 05181-03), 2009. (Enclosed as a separate pdf file to this table).
Attachment 3: Letter from the Tetrahydrofuran Task Force to ECHA regarding 'Response to the French classification proposal for tetrahydrofuran', dated 16 October, 2009.

Annex 2 - Comments and response to comments on CLH PROPOSAL for TETRAHYDROFURAN