codex alimentarius commission E

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

JOINT OFFICE: Viale delle Terme di Caracalla 00153 ROME Tel: 39 06 57051 www.codexalimentarius.net Email: codex@fao.org Facsimile: 39 06 5705 4593

Agenda Item 9(e) **CX/CF 09/3/13**
February 2009

JOINT FAO/WHO FOOD STANDARDS PROGRAMME
CODEX COMMITTEE ON CONTAMINANTS IN FOODS
Third Session
Rotterdam, the Netherlands, 23 – 27 March 2009

DISCUSSION PAPER ON ETHYL CARBAMATE IN ALCOHOLIC BEVERAGES

Prepared by Germany

Introduction

1. Ethyl carbamate (synonyms: urethane or carbamide acid ethylester) occurs at low level, from ng/kg to mg/kg, in many fermented foods and beverages [1]. Ethyl carbamate is genotoxic and a multisite carcinogen in animals as well as probably carcinogenic to humans. It is discussed as consumer risk in fermented food and alcoholic beverages for more than twenty years.

2. Distillated spirits, particularly stone fruit and stone fruit marc spirits, contain ethyl carbamate in manifold higher concentrations than other fermented foods and beverages. The formation of ethyl carbamate in stone fruit spirits is linked to the presence of its precursor - cyanoglycosides - in the stones of the fruits. Cyanoglycosides are hydrolysed by enzymes to sugar and hydrogen cyanide. Thus hydrocyanic acid can be formed quickly in the mash and is then distilled over during the distillation. Hydrocyanic acid can be transferred in catalytic pathways by reaction with ethanol into ethyl carbamate. Certain environmental conditions such as light exposure or copper ions promote the formation process in the distillate. In other alcoholic beverages such as beer and wine different amino acids and urea were identified to be precursors of ethyl carbamate.

3. In the recent past ethyl carbamate and its potential risk for the consumer health were reassessed by different authorities. At its 64th meeting in February 2005, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) considered ethyl carbamate and produced a summary report. JECFA concluded that the intake of ethyl carbamate from foods, excluding alcoholic beverages, was much lower than the amounts shown to cause cancer in laboratory animals and was therefore of low concern. However, compared to this, alcoholic beverages added a much larger amount to the total intake of ethyl carbamate, and this was a concern. JECFA therefore recommended that mitigation measures to reduce concentrations of ethyl carbamate in some alcoholic beverages should be continued. In February 2007 the International Agency for Research on Cancer (IARC) reassessed the carcinogenity of alcoholic drinks and up-graded ethyl carbamate from Group 2B ("possibly carcinogenic to humans") to Group 2A ("probably carcinogenic to humans") [2].

4. Taking these evaluations into account the European Food Safty Authority (EFSA) carried out a risk assessment on ethyl carbamate and concluded that ethyl carbamate in alcoholic beverages was found to be of concern [3]. Particular stone fruit spirits were confirmed to contain high concentrations of ethyl carbamate and

[1] Weber J V and Sharypov V I, Ethyl carbamate in foods and beverages: a review, Environmental Chemistry Letters, 2008 (DOI 10.1007/s10311-008-0168-8)
[2] IARC Monograph Vol. 96 in Press, Consumption of Alcoholic Beverages and Ethyl Carbamate (Urethane), (6-13 February 2007); http://monographs.iarc.fr/ENG/Meetings/96-ethylcarbamate.pdf
[3] Ethyl carbamate and hydrocyanic acid in food and beverages, Scientific Opinion of the Panel on Contaminants

this was therefore regarded to be of particular concern. It should be noted that actually two versions of the assessment were published by EFSA. The high contents of ethyl carbamate in tequila had to be revised by the second version, because preliminary unconfirmed data obtained by a research project have been sent erroneously to EFSA. As a result, in the revision, cited below, all references to tequila have been removed from the opinion as there was no other data available on tequila.

EFSA Evaluation

5. On request of the EU-Commission EFSA started the assessment of ethyl carbamate with the collection of data in the frame of a public call in 2006. 4,203 results were submitted by European Member States of which 4,066 were referring to alcoholic beverages. Furthermore authorities from North America (USA and Canada) submitted 28,858 results from alcoholic beverages (more than 22,000 results on wine) originating in the EU analysed in the years 2002-2006. Based on these very comprehensive data the below given concentration levels of ethyl carbamate in different alcoholic beverages were calculated.

6. Table 1 shows the ethyl carbamate concentrations in different alcoholic beverages:

	[µg/kg] Ethyl carbamate in			
	Beer	Wine	Other spirits	Fruit brandy
Median	0-5[a]	5	20	260
Mean	1-5 [a]	5-7 [a]	64-66 [a]	744-747 [a]
95th percentile of values	6	16	290	3180
Maximum	33	180	6000	22000

a) When two levels are shown, it illustrates values with results set to zero or the limit of detection, respectively, for samples with no detectable levels

7. The margin of exposure (MOE) approach was used for the risk characterisation, comparing animal cancer data with human exposure scenarios. Using this approach, the EFSA Scientific Committee considered previously that an MOE of 10,000 or more, based on a Benchmark Dose Lower Confidence Limit (BMDL) of 10 derived from animal cancer bioassay data, would be of low concern from a public health point of view and might reasonably be considered as a low priority for risk management actions.

8. In combination with consumption data of alcoholic beverages in Europe the median values (see Table 1) have been used to estimate the Margin of Exposure (MOE) for different groups of consumers. Taking the Benchmark Dose Lower Confidence Limit (BMDL) value of 0.3 mg/kg body weight per day following **MOEs** were calculated:

- at 18,000 for food consumption excluding alcoholic beverages,
- for the overall population and for consumers of alcoholic beverages (food consumed with a variety of alcoholic beverages) around 5,000 (because the majority was considered to consume alcohol only little differences between the two groups were observed).
- for consumers of alcoholic beverages at the 95th percentile of the alcohol consumption assuming that only one type - beer, wine and other spirits - is consumed at around 5,000,
- and for high consumers of fruit brandy at less than 600.

9. Based on these findings it was concluded that ethyl carbamate in alcoholic beverages indicates a health concern, particularly with respect to stone fruit brandies. Hydrocyanic acid and its salts are important precursors for ethyl carbamate in this kind of spirits and possible health risks related to the presence of cyanides were also considered in the risk assessment of EFSA.

(Question No EFSA-Q-2006-076), Adopted on 20 September 2007, This opinion, published on 1 August 2008, replaces the earlier version published on 24.October 2007).

10. The EFSA recommended that mitigation measures should be taken to reduce levels of ethyl carbamate in certain alcoholic beverages such as fruit brandies. These measures should include focus on hydrocyanic acid and other precursors of ethyl carbamate.

11. Considering these results and recommendations the presented discussion paper was developed to help figuring out the preferences of action to minimise the content of ethyl carbamate in certain alcoholic beverages.

Product focus of mitigation measures

12. As the MOE of about 600 is almost 10 fold less than for other alcoholic beverages the focus on stone fruit spirits appears to be most relevant by far for an efficient consumer protection. The statistical data of ethyl carbamate in stone fruit spirits indicate - documented in the difference between the arithmetic mean and the median - that it is not normally distributed. This attribute is obviously caused by some severely contaminated products which should be minimised in quantity and concentration firstly.

13. Although the concentrations of ethyl carbamate in beer are the lowest among the alcoholic beverages the calculated MOEs for low consumption and high consumption vary between 17,000 and even 3,000. Lower and upper band ranges were calculated due to the fact that for beer many analytical results were below the limit of quantification. By taking the positive findings (> limit of quantification) and setting the results which were below the limit of quantification to zero the upper band was calculated and by including the results below the limit of quantification with the actual limit consequently the lower band was calculated. In addition the low alcohol content of beer resulted in the highest equivalent of consumption for the same amount of alcohol.

14. Looking at the data of ethyl carbamate in wine (median of 6 µg/kg and a 95th percentile of 16 µg/kg) - apart from any evaluation of the existing limits for ethyl carbamate in wine - the wide majority with 99 % of the wines analysed are apparently already below 30 µg/l (Canadian limit) and even the lower recommendation level of the USA with 15 µg/l is kept by almost 95 % of the wines. A correlation between the age of wine and the ethyl carbamate concentration could not be confirmed by the data available at EFSA. Recommendations of prevention and reduction measures of ethyl carbamate formation in wine are existing [4, 5]; however from a practical point of view it is more complex and difficult to avoid significant ethyl carbamate formation in wine compared to stone fruit spirits.

15. For high consumers of other spirits a MOE in the region of 5,000 was calculated. A broader variety of products was gathered into this group of spirits. Also due to this diversity but also to the lower level of concern it appears to be appropriate to focus first on the group of stone fruit spirits.

16. However ethyl carbamate should be monitored further in alcoholic beverages in order to identify other potential target products for relevant mitigation measures.

Ethyl carbamate and hydrocyanic acid in stone fruit spirits

17. The potential formation of ethyl carbamate in spirit drinks containing cyanide, such as stone fruit spirits, is a well known problem. However the formation of ethyl carbamate is rather complex and not only the concentration of hydrocyanic acid is a relevant factor but also the storage conditions such as temperature, light exposure and other factors are important. Figures from the EFSA evaluation demonstrate that the ethyl carbamate concentration does not really correlate with the concentration of hydrocyanic acid:

18. Based on 266 samples for which both values were available a correlation was modelled. A slight correlation was found, improvement was observed when the log transformation was performed. But it was also found that for products with a concentration of less than 5 mg/l hydrocyanic acid - this level was taken arbitrarily - the ethyl carbamate concentration is below 0.4 mg/l for the majority of products. This relationship was verified to be vice versa, in case of high hydrocyanic acid concentrations (>10 or 20 mg/l) ethyl carbamate concentrations of more than 0.4 mg/l were found in the majority of samples (around 90 % of all samples).

[4] Butzke, C.E. & Bisson, L.F., 2002. Ethyl carbamate preventative action manual. (http://vm.cfsan.fda.gov/~frf/ecaction.html)
[5] Michael Waldner and Ockert Augustyn, Ethyl Carbamate in South African Wine, http://www.wynboer.co.za/recentarticles/200511ethyl.php3)

19. Also by other authors it was established that stone fruit spirits which do not contain detectable amounts of hydrocyanic acid rarely contain increased concentrations of ethyl carbamate, whereas a correlation between both parameters could however not be determined [6].

20. This supports previous findings that concentrations of > 1 mg/l hydrocyanic acid in the distillate indicate an increased risk of ethyl carbamate formation and therefore special measures such as the strict exclusion of light exposure or purification by re-distillation are recommended [7, 8]. According to the group of experts for spirit drinks of the German Society for Food Chemistry based on practical experiences it can be assumed that from 1 mg hydrocyanic acid up to 0.4 mg ethyl carbamate potentially can be formed in a non equimolar relationship[9]. Starting from this relation an estimate of a maximum of 2 mg/l hydrocyanic acid could be deduced to be still in compliance with the German enforcement limit of 0.8 mg/l ethyl carbamate in stone-fruit spirits. For a product with 40 %v/v alcohol this corresponds to a concentration of hydrocyanic acid of 0.5 g/hl pure alcohol.

21. The actual reduction of the limit for hydrocyanic acid in stone-fruit marc and stone-fruit spirits in the European Union [10] from 10 grams to 7 grams per hectolitre of 100 % vol. alcohol – corresponding to 40 and 35 mg/l ethyl carbamate for a 40 % v/v alcohol spirit drink - recently realised in the frame of the revision of the spirit drink regulation, will not effect the ethyl carbamate formation. According to data from the German food control but also as it can be seen from data published by EFSA[3], the huge majority of products (> 99 %) fulfils already this limit. In the EFSA documentation the 95th percentile for hydrocyanic acid in stone fruit spirits was calculated to be at 10.8 mg/kg or corresponding to approximately 2.5 g/hl of 100% alcohol.

22. Thus consequently the regulatory EU limit reflects actually the *status quo* of the cyanide concentration in relevant stone fruit spirits and such a measure will probably not induce any significant change in the production process in order to reduce the ethyl carbamate formation.

23. Taking these conclusions into account it seems to be rather inappropriate to reduce ethyl carbamate by restricting the hydrocyanic acid content, although the parameters are linked.

24. Good manufacturing practice for reducing ethyl carbamate in spirits requires the careful control and monitoring of the hydrocyanic acid in the distillate and therefore reduction of both compounds will be achieved.

Target value

25. From a practical point of view it is established that under Good Manufacturing Practice ethyl carbamte concentrations in stone fruit spirits of below 1 mg/l can be achieved with reasonable measures at certain points in production. Taking into account the existing world wide limits it seems to be justifiable to establish 1 mg/l as a first signal value although further minimisation should be envisaged.

Discussion

26. One crucial point that can be already appointed is the sufficient information of ***all*** the producers. Official objections, at least in Germany due to violations of the national enforcement limit of 0.8 mg/l are focussed often on very small local distilleries, sometimes even “one man” producers. On the other hand rejections of products of leading brands occur only occasionally. This is somehow also reflected in the data published by the EFSA[3], in which the Canadian and American authorities detected generally lower contents of ethyl carbamate in imported products of stone fruit spirits than the EU control authorities. It seems to be rather reasonable that producers which are sizable enough and aware of the ethyl carbamate problem with minimisation management being in force - present the majority of these imports.

27. Although the German control authorities reject samples exceeding the enforcement limit of 0.8 mg/l for many years it appears that not all producers are generally aware of the ethyl carbamate problem. In

[6] Lachenmeier DW, Schehl B, Kuballa T, Frank W, Senn T. Retrospective trends and current status of ethyl carbamate in German stone-fruit spirits. Food Additives and Contaminants 2005; 22(5):397-405.
[7] Christoph N, Bauer-Christoph C. Maßnahmen zur Reduzierung des Ethylcarbamatgehaltes bei der Herstellung von Steinobstbränden (I). Kleinbrennerei 1998; 11:9-13.
[8] Christoph N, Bauer-Christoph C. Maßnahmen zur Reduzierung des Ethylcarbamatgehaltes bei der Herstellung von Steinobstbränden (II). Kleinbrennerei 1999; 1:5-13.
[9] Position paper "Ethylcarbamat in Steinobstbränden" Working Group „Spirit drinks“ German Society for Food Chemistry: (Lebensmittelchemie,60, 26-27 (2006), http://www.gdch.de/strukturen/fg/lm/ag/spirituosen/posi_steinobstbraende.htm
[10] Annex II of REGULATION (EC) No 110/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 15 January 2008 on the definition, description, presentation, labelling and the protection of geographical indications of spirit drinks and repealing Council Regulation (EEC) No 1576/89

addition it must be underpinned that the advices and recommendations to the producers must be - apart from their simple applicability - easily understandable and in order to catch the whole target group of such information.

28. Efficient and also simple measures for good manufacturing practice reducing ethyl carbamate in stone fruit spirits are available for more than 10 years. They are summarised in the ANNEX of this document.

Conclusions

29. The present Discussion Paper on Ethyl Carbamate in Alcoholic Beverages leads to the following conclusions and recommendations for consideration at the Third Session of the CCCF:

- The CCCF should start new work for development of a Codex Code of Practice for the Reduction of Ethyl Carbamate in Stone Fruit Spirits. The Code of Practice should be based on the Annex of this Discussion Paper, including the signal value of 1 mg/l ethyl carbamate.
- The necessity of setting a maximum level for ethyl carbamate in stone fruit spirits should be assessed after the Code of Practice has been implemented.

ANNEX

Technological measures reducing ethyl carbamate

On the national and international level recommendations concerning procedures for the reduction of ethyl carbamate in spirits are available since more then 10 years [11, 12, 13].

Different stages of production, distillation

1. *Mash (avoiding the release of hydrocyanic acid)*
    - Destoning of the fruits [6] (simple measure also for small producers)
    - Avoiding the mechanical damage of the stones
    - Minimized storage time of the mash after end of fermentation
2. *Distillation device (binding of hydrocyanic acid before transferred in the distillate)*
    - Distillation with copper catalyst and cyanide separator
    - Regularly cleaning of the distillation device and activating the copper surface

    In Baden-Wurttemberg it was found by questionnaire that the production year of the distillation device correlates negatively strongly with the ethyl carbamate content, what means that the newer the device was as less ethyl carbamate was detected [14].
3. *Distillation*
    - Use of copper containing agents for distilleries applicable to the mash (specialised trade)
    - Sufficient separation of the first fraction containing hydrocyanic acid
    - Slow distillation and separation of the tailing fraction (possibly containing ethyl carbamate) from 50 % v/v alcohol on

    Additional advices or measures:
    - Isolated distillation of collected tailing fractions
    - Additionally bought distillates shall be proven for their cyanide content respectively ethyl carbamate, if necessary purification by distillation appropriately
4. *Distillate*
    - Test for the content of hydrocyanic acid in main fraction directly after distillation (test kit or by qualified test laboratory), if > 1 mg/l strict exclusion of light exposure
    - Continuous prevention from light exposure, filling into dark bottles or use of covering boxes.

[11] Maßnahmen zur Reduzierung von Ethylcarbamat in Steinobstbränden, BfR Press release 2005 (http://www.bfr.bund.de/cm/234/massnahmen_zur_reduzierung_von_ethylcarbamat_in_steinobstbraenden.pdf)
[12] Maßnahmen zur Reduzierung von Ethylcarbamat in Steinobstbränden, Chemische Untersuchungsämter Baden-Württemberg 2006 (http://www.untersuchungsaemter-bw.de/pdf/merkblatt_ethylcarbamat.pdf)
[13] Ethylcarbamat in Obstbränden, Info-Blatt Nr. C01/1, Gesundheitsdepartement Amt für Gesundheits- und Verbraucherschutz (http://www.kal.ch/dynamic/deepartikel/uploads/1216213319_C01_1.pdf)
[14] Weltring A, Rupp M, Arzberger U et al. Ethyl carbamate: Analysis of questionnaires about production methods of stone-fruit spirits at German small distilleries. Deutsche Lebensmittel-Rundschau 2006; 102(3):97-101