codex alimentarius commission

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WORLD HEALTH ORGANIZATION

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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

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CONSIDERATION OF DRAFT AND PROPOSED DRAFT MAXIMUM RESIDUE LIMITS IN FOODS AND FEED AT STEPS 7 AND 4

NEED FOR EMRL FOR CAMPHECHLOR IN FISH

- Paper Prepared by Germany Based on Government Comments Submitted in Response to CL 1999/31-PR[1] -

SUMMARY

I) Previous to the principal decision about the need for EMRL for camphechlor in fish, analytical questions and matters of monitoring data should not be discussed.

II) Significant sources for camphechlor residues in fish other than agricultural use of technical camphechlor products most likely do not exist.

III) Germany supports the elaboration of a PTDI[2] for camphechlor. A first estimate of a provisional tolerable intake has been established in Canada. Further, such elaboration seems to be in agreement with the positions of Norway, Slovakia and Spain

IV) Despite the fact that the composition of camphechlor residues in fish is different to that of technical mixtures, which are most often used in toxicological studies, a PTDI can be established and applied to residues in fish.

V) Based on the calculations presented in table 1 and to ensure consumer protection and food safety, fish from heavily contaminated waters should be excluded from trade. Norway and Slovakia support this opinion.

VI) Germany and Austria have set national MRLs for camphechlor in fish, which are lower than residues in highly contaminated fish.

DISCUSSION

Germany received comments to CL 1999/31-PR from Canada, USA, Norway, Slovakia, South Africa, Spain and Thailand. Some of these comments contained principal concerns with the proposal to set an EMRL for camphechlor in fish:

1.1 Paper mill effluents are a highly suspected source of some "camphechlor" contamination of fish additional to agricultural use of toxaphene (USA, Thailand)

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1 This paper contains in an appendix comments from Spain which were received after the publication of CX/PR 00/10.

2 Provisional tolerable daily intake.

1.2 An ADI has never been established and old toxicological data would be inappropriate for establishing an ADI on the proposed three components (USA)

1.3 EMRLs must have a PTDI, a reference dose for camphechlor does not exist (USA)

1.4 Toxicological studies are made with the technical toxaphene mixture which is not present in fish (USA)

1.5 Without a PTDI no risk estimation is possible (USA) and up to now no trade problems were observed (South Africa, Thailand; Spain)

A second group of concerns refers to the analytical method and the quality of monitoring results:

2.1 Lack of information on the portion of the fish analyzed (Canada)

2.2 Limited geographical area from which samples have been drawn (Canada)

2.3 Proposed analytical method quantifies only 3 of the 300 congeners; representativeness of the three indicator congeners remain unclear (USA, Canada, Thailand)

Because there is no general agreement on the ability to establish an EMRL for camphechlor in fish and general acceptance of the need of such EMRL does not exist, other questions seem secondary. Previous to this agreement, analytical questions and matters of monitoring should not be discussed. For that reason Germany comments on the first group of concerns only.

1.1 Paper mill effluents are a highly suspected source of some "camphechlor" contamination of fish additionally to agricultural use of toxaphene (USA, Thailand)

Some literature is cited in the U.S. comment of 1999 (CRD 2 of the 31st Session) in that context. In the first paper Swackhamer [i] does not discuss sources of camphechlor components but proposed other ways of transport than atmospheric transport to the Great Lakes. Scheel [ii] interpreted at least 80% of GC/MS peaks as camphechlor components in his fish extract. Last, Rappe [iii] detected camphechlor components close to paper mills, but the concentration of residues was not correlated to the sampling site (above or below the mill) but to the content of organic matter.

More importantly, in a subsequent paper of Swackhamer [iv] , an atmospheric source of camphechlor for all the Great Lakes with the only exception of Lake Michigan is concluded. Camphechlor component patterns in air over Lake Superior were found to resemble those in lake water[v]. Camphechlor is behaving not differently from other historically banned chemical mixtures, which persists in the Great Lakes[vi]. Additionally, several authors had investigated the concentrations of camphechlor components in effluents of pulp and paper mills and in sediments around the mills. Components of camphechlor were not found in those effluents[vii,viii]. No difference in the camphechlor concentration of sediments downstream and upstream of several US and Canadian pulp mills was found[ix] and sediment concentrations near pulp and paper mills were not extremely high as expected for a 'source' but lower or in the same range than sediment concentrations of Lakes Ontario, Michigan and Superior[x]. As well no decreasing camphechlor concentration as a function of distance to paper mills was found in Sweden[xi], too. Lastly, the camphechlor concentration from representative Great Lake sediment cores of different years correlates with camphechlor usage (maximum between 1970 and 1980)[xii,xiii]. From these results, paper mills should not be a significant second source of camphechlor compounds compared to the technical products (Toxaphene, Strobane, Hercules 3956 etc.) of camphechlor.

1.2 An ADI has never been established and old toxicological data would be inappropriate for establishing an ADI on the proposed three components (USA)

The three components were chosen for analytical reasons as indicators for the total camphechlor concentration in fish, only. Toxicity was not a reason for the selection of proposed indicator compounds. It was never intended to establish an ADI for these three components only, because fish samples usually contain more than 20 individual camphechlor components.

1.3 EMRLs must have a PTDI, a reference dose for camphechlor does not exist (USA)

A substantial database demonstrates that camphechlor may cause acute and chronic toxic effects, including tumour formation, at least at higher concentrations. Therefore, to ensure consumer´s

protection, the available experimental data on camphechlor technical mixtures should be used as a basis for assessing a PTDI.

For the toxicological evaluation of camphechlor the following issues should be considered:

i) A re-evaluation of the genotoxic potential of camphechlor has not demonstrated convincing evidence for a dose-dependent effects in mammalian cells. Additionally, given the reduction of mutagenic effects by metabolic systems in vitro and the lack of evidence for a direct DNA interaction in vivo, the genotoxicity of camphechlor has to be considered as (at least) equivocal. Concerning the carcinogenic effects in rats and mice, mechanistic in vivo- and in vitro-studies suggest that camphechlor can be considered as a tumour promoter allowing the use of threshold values for risk assessment.

ii) Given the concerns regarding the data from chronic studies which suffer from the lack of compliance with current guidelines, the NOAEL for camphechlor should be based on more recent subchronic studies. Data from 13-week studies in dogs and rats show NOAELs of 0.2 mg/kg bw/d and 0.35 mg/kg bw/d, respectively, for a technical-grade mixture of camphechlor.

In conclusion, the NOAEL of 0.2 mg/kg bw/d may be used for the calculation of a PTDI. For the establishment of an appropriate safety factor, the variations in the composition of the different brands or environmental mixtures of camphechlor and the fact that most toxicological studies used the brand toxaphene should be considered. Applying a safety factor of 1000 - as suggested by the Nordic Council of Ministers - the PTDI for camphechlor is 0.2 mg/kg bw. This value is in accordance with the PTDI established by the Health Canada.

A detailed summary of toxicological studies, which should be considered for that estimation and copies of all toxicological studies cited there will be given to the JMPR Secretariat.

1.4 Toxicological studies are made with the technical toxaphene mixture which is not present in fish (USA)

The compositions of camphechlor found within the tissues of animals, particularly those on higher trophic levels, differ from that of the toxaphene technical mixture used as a pesticide. Generally, there is a reduction in the number of congeners along the food chain: about 20 major congeners are found in fish, eight in marine mammals; in humans there are two major congeners, *i.e*. 2-*exo*,3-*endo*,5-*exo*, 6-*endo*, 8,8,10,10-octochlorobornane (Parlar #26) and 2-*exo*,3-*endo*,5-*exo*, 6-*endo*, 8,8,9,10,10-nonachlorobornane (Parlar #50).

The currently available data from various studies (and from different sources) do not suggest a completely different toxicological profile from different environmentally relevant camphechlor mixtures. Although individual camphechlor congeners, i.e. Parlar #26 and #50, may exert some differential toxic effects (i.e. dysmorphogenic effects on cultured rat embryos at high concentrations) the binary mixture of these congeners appears to have similar effects as the toxaphene technical mixture. Moreover, both the camphechlor mixture and the congeners (#26 and #50) had relatively low estrogenic activities (indicated by a proliferative effect on MCF-7 human breast cancer cells). Therefore, the available information on the toxicity of camphechlor congeners in mammals may tentatively indicate that the toxic potential of environmental mixtures of congeners is comparable to that of technical mixtures.

1.5 Without a PTDI no risk estimation is possible (USA) and up to now no trade problems were observed (South Africa, Thailand; Spain)

The German monitoring data presented last year show moderate camphechlor residue concentrations in fish from marine waters of the northern hemisphere. A rough overall mean 0.02 mg/kg camphechlor in the edible part of fish (total camphechlor, wet weight basis) was estimated from these data[xiv]. Based on this mean concentration and a daily fish consumption of 10, 20, 40 or 80 grams, the daily intake of camphechlor is 0.2, 0.4, 0.8 and 1.6 µg, respectively. For a 70 kg person this results in 1%, 3%, 6% and 11% of the tolerable camphechlor intake, when the Canadian estimate of PTDI is applied. As the worst case assumption for daily fish consumption, an amount of 300 g is used in Europe[xv]. In that worst case

the camphechlor intake is 43% of the proposed PTDI, if fish with "normal" residue concentrations is consumed.

On the contrary to that "normal" concentration of 0.02 mg/kg camphechlor (wet weight basis), some fresh water areas with much higher contaminated fish apparently exist. Several authors had reported large residue amounts in fish from the Great Lakes in Northern America, e.g. 4.3 ± 3.7 mg/kg in lake trout (*Savelinus namaycush*) of Lake Michigan[xvi], or 4.9 ± 1.4 mg/kg, 1.5 ± 0.3 mg/kg and 2.4 ± 0.5 mg/kg in lake trout of Lake Superior, Lake Michigan and Huron, respectively[xvii]. Lake Superior trout data had been confirmed recently by Swackhamer[13], too (2.4 ± 1.4 mg/kg). Higher residue concentrations were also reported in fish from the Yucon Territory in Canada. In lake trout of Lake Laberge and Lake Siskewit 0.7 ± 0.6 mg/kg[xviii] and 0.29 mg/kg[xix] were found. Burbot (Lota lota) livers from that region contained up to 54 mg/kg camphechlor on a wet weight basis (fillet was not analysed)[18].

Compared to many other organohalogen compounds there is much lesser information about camphechlor residues in fish. Therefore unknown "hot spots" may exist. If such fish with high residue amounts is consumed, the tolerable daily intake (PTDI of Canada) may be exceeded up to several hundred percent (Table 1).

Table 1: Estimation of camphechlor intake via fish consumption [a)] in dependence of the percentage of high contaminated fish (residue concentration of 3 mg/kg assumed)

percentage of high contaminated fish	daily fish consumption (g/d)	fish consumption per year (kg/a)	total camphechlor intake per day (µg)	% PTDI (person with 70 kg b.w.)
	10	3.7	1.7	12%
	20	7.3	3.4	24%
5%	40	14.6	6.8	48%
	80	29.2	13.5	97%
	300	109.5	50.7	**362%**
	10	3.7	3.2	23%
	20	7.3	6.4	45%
10%	40	14.6	12.7	91%
	80	29.2	25.4	**182%**
	300	109.5	95.4	**681%**
	10	3.7	6.2	44%
	20	7.3	12.3	88%
20%	40	14.6	24.6	**176%**
	40	14.6	24.6	**176%**
	300	109.5	184.8	**1320%**

a) For normal contaminated fish a residue concentration of 0,02 mg/kg is used (total camphechlor, wet weight basis).

To avoid such unacceptable risk at least for selected consumer groups Germany and Austria have set a national MRL for camphechlor in fish.

CONCLUSION

(i) The available data are sufficient to derive a PTDI. The detailed summary of toxicological studies and copies of all toxicological studies will be given to the JMPR Secretariat.

(ii) The sources of contamination of fish are well understood.

(iii) The available data are sufficient to propose an EMRL. Copies of available residue studies will be given to the JMPR Secretariat.

(iv) The Committee should include camphechlor in fish in the Priority List for toxicological and residue evaluation by the JMPR at one of meetings of the JMPR in near future.

[i] D.L. Swackhamer, R.F. Pearson, S.J. Eisenreich, D.T. Long: Organohalogen Compounds **26**, 319-322 (1995)

[ii] R. Scheel: Organohalogen Compounds **33**, 57-62 (1997)

[iii] Ch. Rappe, P. Haglund, R. Andersson, H.-R. Buser: Organohalogen Compounds **35**, 291-294 (1998)

[iv][v] D.L. Swackhamer, R.F. Pearson, S. Schottler, D.G. Symonik: Organohalogen Componds **35**, 303-304 (1998)

[v] D. Muir, G. Stern, H. Karlsson: Organohalogen Compounds 41, 565-568 (1999)

[vi] J.V. DePinto, T. Feist, D. Smith, Organohalogen Compounds **33**, 280-284 (1997)

[vii] T. Rantio, J. Paasvierta, N. Lahtipetä: Chemosphere **27**, 2003-2010 (1993)

[viii] Ch. Rappe, P. Haglund, R. Andersson, H.-R. Buser: Organohalogen Compounds **35**, 295-297 (1998)

[ix] Ch. Rappe, P. Haglund, R. Andersson, H.-R. Buser: Organohalogen Compounds **35**, 287-290 (1998)

[x] J.G. McDonald, K.E. Shanks, R.A. Hites: Organohalogen Compounds **41**, 581-586 (1999)

[xi] Ch. Rappe, P. Haglund, H.-R. Buser, M. Müller: Organohalogen Compounds **31**, 233-237 (1997)

[xii] D.L. Swackhamer, R.F. Pearson, S.J. Eisenreich, D.T. Long: Organohalogen Componds **26**, 319-322 (1995)

[xiii] D.L. Swackhamer, R.F. Pearson, S.P. Schottler: Chemosphere **9**, 2545-2561 (1998)

[xiv] This estimate strongly depends from the percentage of fish with high, moderate and low fat content used in the model. In the presented estimate a relative amount of 25%, 25% and 50% is assumed.

[xv] P.J.C.M. Janssen, F.X.R. Leeuwen: Toxaphene - Risk evaluation actuated by the occurence in fish; Report of National Institute of Public Health and Environmental Protection (1993)

[xvi] J.W. Gooch, F. Matsumura: J. Agric. Food Chem. **33**, 844-848 (1985)

[xvii] S.T. Glassmeyer, D.S. De Vault, T. R. Myers, R.D. Hites: Environ. Sci. Technol. **31**, 84-88 (1997)

[xviii] K.A. Kidd, J.E. Eamer, D.C.G Muir: Chemosphere **27**, 1975-1986 (1993)

[xix] D.L. Swackhamer, M.J. Charles, R.A. Hites: Anal. Chem. **59**, 913-917 (1987)

APPENDIX

COMMENTS FROM SPAIN IN RESPONSE TO CL 1999/31-PR

The Kingdom of Spain is of the opinion that there is presently no need to determine an EMRL for camphechlor in fish because there are no reported problems in international fish trade arising from the presence of camphechlor in fish.

However, studies should be conducted to determine the acceptable daily intake for camphechlor, to define residues and to formulate the related methods of analysis.