Vitenskapskomiteen for mattrygghet
Norwegian Scientific Committee for Food Safety

Opinion of the Panel on Contaminants of the Norwegian Scientific Committee for Food Safety

New WHO TEFs for dioxins and dioxin-like PCBs:

Assessment of consequence of altered TEF values for dioxins and dioxin-like PCBs on current exposure in the Norwegian population

14 November 2007

SUMMARY

Dioxins and dioxin-like PCBs (dl-PCBs) exhibit a broad range of toxic and biological effects and act via the same mechanism. There is a general acceptance of an additive model for risk assessment of such compounds. Since their potencies vary over several orders of magnitude, the toxic equivalency concept was developed in order to simplify risk assessment of mixtures of dioxins and dl-PCBs. Each of the dioxins and dl-PCBs with similar mechanisms of action have been assigned a toxic equivalency factor (TEF), ranging their potencies relative to the most potent dioxin. TEF values in combination with analytical data are used to calculate and express the concentrations as toxic equivalencies (TEQs) in food.

Different TEF values were in use until the WHO TEF values were published in 1998. In 2005 the WHO 1998 TEF values were revised, resulting in increased, decreased or unchanged TEF values for individual congeners of dioxins and dl-PCBs.

The Norwegian Food Safety Authority has asked the Norwegian Scientific Committee for Food Safety (Vitenskapskomiteen for mattrygghet, VKM) to evaluate how the revised TEF values for dioxins and dl-PCBs influence the dietary exposure expressed as TEQ in relation to tolerable weekly intake (TWI). Based on this evaluation, The Norwegian Food Safety Authority would like VKM to comment if there is a need to re-calculate the previously estimated dietary intake of dioxins and dl-PCBs in Norway.

The request has been answered by the Panel on Contaminants (Panel 5) of VKM.

Panel 5 has calculated total TEQs for some foods known to be important sources for dioxins and dl-PCBs in the Norwegian diet by using both the old and the revised TEFs. In all samples the revised TEFs reduced the total TEQ by 5 to 45%. The highest reduction was seen for cod liver oil, in which mono-*ortho*-PCBs contributed more than 50% to the total TEQ calculated with the 1998 TEFs. For fish, the reduction was 15-19%. For dairy products and pork the reduction was 11-15%, whereas for mutton the reduction in total TEQ was only 5%.

Panel 5 has not re-calculated the previously estimated dietary intake of dioxins and dl-PCBs in the Norwegian population using the revised TEFs. However, since calculations with the revised 2005 TEFs result in lower total TEQ in some important dietary sources for these compounds than calculations with the WHO 1998 TEFs, Panel 5 deduces that the dietary TEQ-exposure to dioxins and dl-PCBs will be lower when using the revised TEFs. This indicates that a lower proportion of the population will be exceeding the TWI. It should be kept in mind that changes in TEFs, resulting in lower TEQ in food, do not imply reduced exposure to the absolute concentration of dioxin-like compounds.

Panel 5 is of the general opinion that there is a need for regular monitoring of food contamination and dietary habits because both dietary habits and contaminant profiles in food change with time. It is now 10 years since the last national dietary survey. A re-calculation of the previously estimated dietary intake of dioxins and dl-PCBs with the revised TEFs would be based on possibly outdated consumption data. Panel 5 is therefore of the opinion that a new estimation of dietary intake of dioxins and dl-PCBs in Norway should await new consumption data. Furthermore, Panel 5 recommends that in the next national assessment of dietary exposure to dioxins and PCBs the exposure should be calculated with both the 1998 and the 2005 TEFs in order to better investigate the impact of the new TEFs on calculated exposure. This will also be important when documenting the exposure time-trends.

SAMMENDRAG

Dioksiner og dioksinliknende PCB (dl-PCB) kan gi mange toksiske og biologiske effekter via den samme virkningsmekanismen. For å risikovurdere disse forbindelsene er det en generell enighet om å bruke en additiv modell. Siden virkningsstyrken av dioksiner og dl-PCB går over flere størrelsesordner, ble prinsippet om toksiske ekvivalent faktorer (TEF) utviklet for å forenkle risikovurdering av blandinger av dioksiner og dl PCB. For hver forbindelse er det fastsatt en TEF som står i forhold til virkningsstyrke sammenliknet med det dioksinet som har størst virkningsstyrke. Sammen med analytiske data brukes TEF til å beregne og uttrykke det totale innholdet av dioksiner og dioksinliknende PCB som toksiske ekvivalenter (TE) i mat.

Ulike TEF-verdier var i bruk inntil WHO publiserte TEF-verdier i 1998. I 2005 revurderte Verdens helseorganisasjon (WHO) TEF-verdiene for dioksiner og dioksinliknende PCB fra 1998, noe som resulterte i at TEF-verdier ble hevet, senket, eller forble uendret.

Mattilsynet har bedt Vitenskapskomiteen for mattrygghet (VKM) om å vurdere hvordan de reviderte TEF-verdiene vil påvirke eksponeringen fra mat i forhold til tolerabelt ukentlig inntak. Basert på resultatene fra denne vurderingen, ønsker Mattilsynet at VKM kommenterer om de nye TEF-verdiene gjør det nødvendig å gjøre nye inntaksvurderinger av dioksiner og dioksinliknende PCB i det norske kostholdet.

Oppdraget er besvart av VKMs faggruppe for forurensninger, naturlige gifter og medisinrester (Faggruppe 5).

Faggruppe 5 har beregnet sum TE for dioksiner og dioksinliknende PCB for et lite utvalg av matvarer som er viktige kostkilder for disse kontaminantene, både med TEF fra 1998 og de

reviderte verdiene fra 2005. Sum TE ble redusert i alle prøvene når TEF-verdier fra 2005 ble brukt i beregningene istedenfor TEF-verdier fra 1998. Reduksjonen varierte fra 5-45 %. Størst reduksjon ble funnet i fiskelever, der mono-*orto*-PCB bidro til mer enn 50 % av det totale innholdet av dioksiner og dioksinliknende PCB i prøvene (sum TE) når TEF-verdiene fra 1998 ble benyttet. Nivåene av TE i fisk ble redusert med 15-19 %, mens de for melkeprodukter og svinekjøtt ble redusert med 11-15 %. For fårekjøtt var reduksjonen kun på 5 %.

Inntaket av dioksiner og dioksinliknende PCB fra det norske kostholdet er ikke beregnet med de nye TEF-verdiene fra 2005. Siden mengden av total TE i et utvalg av matvarer som er viktige kostkilder for disse kontaminantene reduseres ved bruk av de reviderte TEF-verdiene fra 2005, mener Faggruppe 5 at det er sannsynlig at de nye TEF-verdiene vil medføre at eksponering for dioksiner og dioksinliknende PCB i befolkningen uttrykt som toksiske ekvivalenter blir lavere. Det er viktig å være klar over at endrede TEF-verdier som resulterer i et lavere innhold av dioksiner og dioksinliknende PCB i mat uttrykt i TE, ikke reduserer eksponeringen for absolutte konsentrasjoner av dioksiner og dioksinliknende PCB.

Faggruppe 5 mener det er et generelt behov for kontinuerlig overvåking av miljøgifter og eksponering fra mat, fordi både kostholdet og innholdet av miljøgifter i mat endrer seg over tid. Det er nå ti år siden den forrige nasjonale kostholdsundersøkelsen ble gjennomført. Faggruppe 5 er av den oppfatning at nye inntaksbergninger av dioksiner og dioksinliknende PCB fra mat bør vente til nye kostholdsdata er tilgjenglige. Videre mener faggruppen at når den neste nasjonale vurderingen av eksponering av dioksiner og dioksinliknende PCB fra mat skal gjennomføres, bør beregningene gjøres med TEF-verdiene både fra 1998 og 2005. Dette vil både gjøre det lettere å vurdere effekten av de endrede TEF-verdiene og gjøre det mulig å dokumentere tidstrender.

CONTRIBUTORS

Persons working for VKM, either as appointed members of the Committee or as *ad hoc* experts, do this by virtue of their scientific expertise, not as representatives for his/her employers. The Civil Services Act instructions on legal competence apply for all work prepared by VKM.

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BACKGROUND

Dioxins and dioxin-like PCBs (dl-PCBs) exhibit a broad range of toxic and biological effects and act via the same mechanism. There is a general acceptance of an additive model for risk assessment of such compounds. Since their potencies vary over several orders of magnitude, the toxic equivalency concept was developed in order to simplify risk assessment of mixtures of dioxins and dl-PCBs. Each of the dioxins and dl-PCBs with similar mechanisms of action have been assigned a toxic equivalency factor (TEF), ranging their potencies (Van den Berg *et al.*, 1998). These factors were meant to be revised as more toxicological knowledge of the congeners became available.

In 2006 a re-evaluation of TEF for dioxins and dl-PCBs was published in Toxicological Sciences, with the title "*The 2005 World Health Organization Reevaluation of Human and Mammalian Toxic Equivalency Factors for Dioxins and Dioxin-Like Compounds*" (Van den Berg *et al.*, 2006). In this paper the toxicity data for the different congeners were discussed and evaluated. In conclusion, there was a need to alter TEF values for four dioxins/furans, two non-*ortho* PCBs and all the mono-*ortho*-PCBs.

TERMS OF REFERENCE

In official control of maximum levels for dioxins and dl-PCBs in food in the European Economic Area (EEA) the old WHO TEF values from 1998 (Van den Berg *et al.*, 1998) should still be used until the next revision of the EU Regulation on maximum levels for dioxins and dl-PCB in food. Even though the revision not will take place before the end of 2008, the Norwegian Food Safety Authority (Mattilsynet) would like to know how the altered TEF values would affect the estimated exposure of dioxins and dl-PCBs among Norwegians.

- The Norwegian Food Safety Authority has asked the Norwegian Scientific Committee for Food Safety (Vitenskapskomiteen for mattrygghet, VKM) to evaluate how the altered TEF values for dioxins and dl-PCBs influence the estimated exposure from food in relation to tolerable weekly intake (TWI).
- Based on this evaluation, The Norwegian Food Safety Authority would like VKM to comment if there is a need to re-calculate the previously estimated dietary intake of dioxins and dl-PCBs in Norway.

ASSESSMENT

Several congeners of dioxins (chlorinated dibenzo-p-dioxins, chlorinated dibenzofurans) and dioxin-like PCBs (non-*ortho* substituted PCBs (no-PCBs) and mono-*ortho* substituted PCBs (mo-PCBs)) share the ability to bind and activate the intracellular aryl hydrocarbon receptor (also called the dioxin receptor) which regulates transcription of numerous genes. Most of the toxic effects of these substances are believed to be exerted via the dioxin receptor. The toxicity equivalence factor (TEF) principle was developed in order to obtain a tool to assess risk connected to exposure to a mixture of these substances in food. The TEF values indicates an order of magnitude estimate of the toxicity of a compound relative to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) which is assigned the TEF value 1. TEF values in combination with chemical concentration data can be used to calculate toxic equivalency (TEQ) concentrations in food.

Exposure to dioxin-like compounds can also be expressed as absolute concentrations of each compound. When TEFs are re-evaluated, there is a change in how the toxicity of the different

congeners is regarded in relation to TCDD. A change in total TEQ calculated with new TEFs should not be confused with altered exposure to the absolute concentrations of dioxin-like compounds.

Different TEF values were used until the WHO TEF values were published in 1998 (Van den Berg *et al.*, 1998). In 2005 the TEF values for dioxins and dioxin like PCBs were revised, resulting in increased, decreased or unchanged TEF values for individual congeners.

The WHO 1998 and WHO 2005 TEF values and the relative difference between them are shown in table 1 (Van den Berg *et al.*, 2006).

An indication of the quantitative impact of the 2005 changes of the TEF values in some selected food samples were presented in Van den Berg *et al.* (2006). They concluded that in general, the changes in 2005 values have limited impact on the total TEQ in the samples with an overall decrease in TEQ ranging between 10 and 25%.

Table 1. WHO 1998 and WHO 2005 TEF values and the ratio between them

Compound	WHO 1998 TEF	WHO 2005 TEF	Ratio 2005 TEF/1998 TEF
Chlorinated dibenzo-p-dioxins			
2,3,7,8-TCDD	1	1	1
1,2,3,7,8-PeCDD	1	1	1
1,2,3,4,7,8-HxCDD	0.1	0.1	1
1,2,3,6,7,8-HxCDD	0.1	0.1	1
1.2.3.7.8.9-HxCDD	0.1	0.1	1
1,2,3,4,6,7,8-HpCDD	0.01	0.01	1
OCDD	0.0001	0.0003	3
Chlorinated dibenzofurans			
2,3,7,8-TCDF	0.1	0.1	1
1,2,3,7,8-PeCDF	0.05	0.03	0.6
2,3,4,7,8-PeCDF	0.5	0.3	0.6
1,2,3,4,7,8-HxCDF	0.1	0.1	1
1,2,3,6,7,8-HxCDF	0.1	0.1	1
1,2,3,7,8,9-HxCDF	0.1	0.1	1
2,3,4,6,7,8-HxCDF	0.1	0.1	1
1,2,3,4,6,7,8-HpCDF	0.01	0.01	1
1,2,3,4,7,8,9-HpCDF	0.01	0.01	1
OCDF	0.0001	0.0003	3
Non-ortho-substituted PCBs (noPCBs)			
PCB 77	0.0001	0.0001	1
PCB 81	0.0001	0.0003	3
PCB 126	0.1	0.1	1
PCB 169	0.01	0.03	3
Mono-ortho-substituted PCBs (moPCBs)			
PCB 105	0.0001	0.00003	0.3
PCB 114	0.0005	0.00003	0.06
PCB 118	0.0001	0.00003	0.3
PCB 123	0.0001	0.00003	0.3
PCB 156	0.0005	0.00003	0.06
PCB 157	0.0005	0.00003	0.06
PCB 167	0.00001	0.00003	3
PCB 189	0.0001	0.00003	0.3

The impact of the new TEFs on total TEQ is dependent on the congener profiles (relative concentrations of the different compounds) in different food items. In order to evaluate the impact of the revised TEFs on total TEQ in Norwegian food, the lower bound level[1] (LB) total TEQ has been calculated with both TEFs from 1998 and from 2005 in farmed salmon, herring, mackerel, cod liver oil, dairy products, sheep meat and pig meat (figure 1). TEQ with 2005 TEFs have been calculated by multiplying the average TEQ based on 1998 TEFs from individual congeners in each food item with the ratio between new and old TEFs (shown in table 1). Calculations with upper bound values would probably give the same result in fish samples, since most congeners are detected in fish. In meat samples, calculation of upper bound TEQ with the new TEF values may be different, since the concentration of several congeners may be below the level of quantification. This has not been calculated in the present assessment.

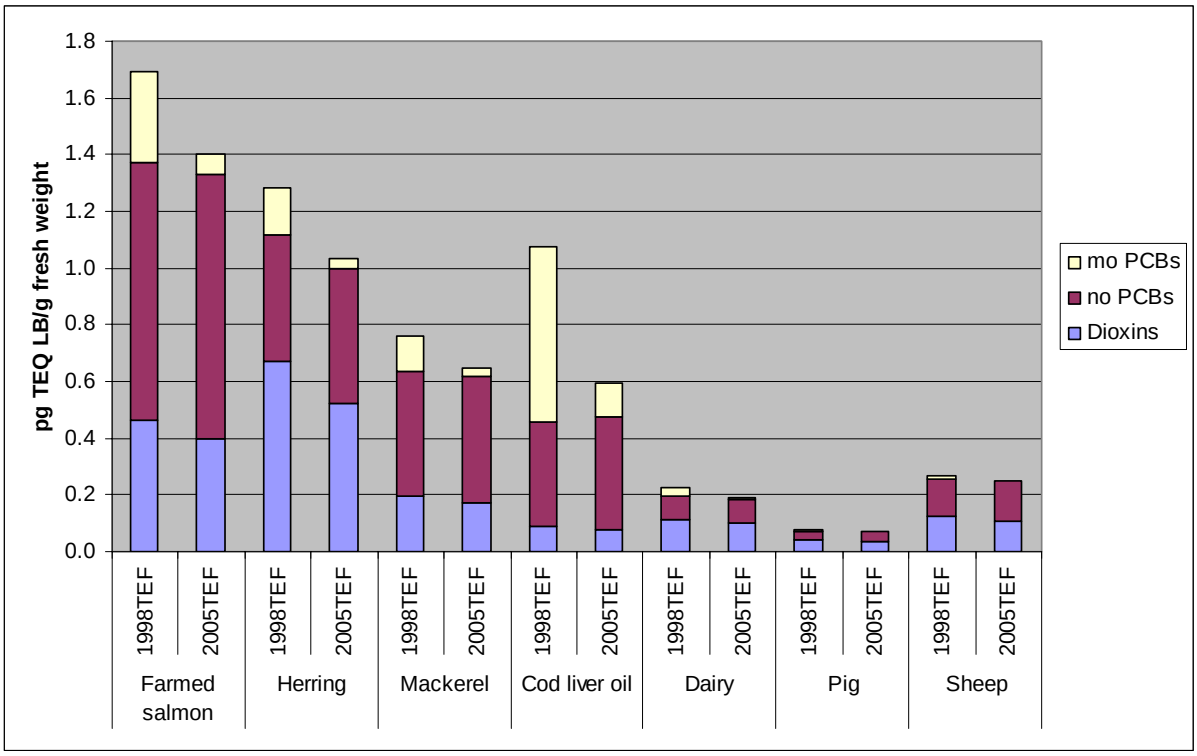

Figure 1. Average total TEQ in some Norwegian foods calculated with WHO 1998 TEF and with WHO 2005 TEF. *Sample details:* Data are from a database on dioxins and PCBs in food at The Norwegian Institute of Public Health. Data are based on analyses performed for the Norwegian Food Safety Authority in different laboratories. Salmon: n = 78 dioxins and no PCBs, 57 mo-PCBs, 2002 - 2005. Herring: n = 21 for dioxins and no PCBs, n = 20 mo-PCBs, 2002 - 2005. Mackerel: n = 22, 2003 - 2005. Cod liver oil: n = 10, 2003-2005. Dairy: n = 23 for dioxins and no-PCBs, n = 13 for mo-PCBs, 2003 – 2006. Pig: n = 13 for dioxins and no-PCBs, n = 5 for mo-PCBs, 2000 – 2004. Sheep: n = 11 for dioxins and no PCBs, n = 4 for mo-PCBs, 2001 – 2004.

[1] TEQ can be calculated as lower bound, medium bound or upper bound levels. Using lower bound levels, the concentrations of all non-detected congeners in a sample are set to 0. For medium bound calculations, the concentrations of non-detected congeners are set to ½ the level of quantification. Using upper bound calculations, the concentrations of non-detected congeners are set equal to the level of quantification.

Total TEQ calculated with 2005 TEFs was reduced in all samples compared with total TEQ calculated with 1998 TEFs. The % reduction in TEQ for each congener group is shown in table 2. The TEQ from dioxins was reduced by 12-22%. This could be surprising since the TEFs for the octa-chlorinated PCDD/Fs have been increased by a factor of three. These congeners constitute however small proportions of the total PCDD/F concentrations in fish. Furthermore, the octa-chlorinated congeners are assigned TEFs that are much lower than the TEFs of the less chlorinated PCDD/Fs. Therefore, the increased TEFs for the octa-PCDD/Fs do not have an important impact on the total TEQ in fish. Organisms such as crabs and mussels may contain higher proportions of the octa-chlorinated PCDD/Fs than fish. However, since these congeners still are assigned TEFs that are orders of magnitude lower that the TEFs of the less chlorinated PCDD/Fs, the octa-PCDD/Fs do not contribute in any important extent to the total TEQ in these organisms either.

The TEQ from no-PCBs was increased from 1 to 11% whereas the reduction of TEQ from mo-PCBs was 77-81%. The mo-PCBs contributed least to the total TEQ calculated with the WHO 1998 TEFs. Although the TEQ from this congener group as such shows the largest reduction, this does not have a high impact on the reduction of total TEQ, due to the low contribution.

The reduction in total TEQ varied from 5 to 45%. Highest reduction was seen in cod liver oil, in which mo-PCBs contributed more than 50% to the total TEQ calculated with the 1998 TEFs. For fish the reduction was 15 – 19%. For dairy products and pork, the reduction was 11 – 15%, whereas for mutton the reduction in total TEQ was only 5%.

The new 2005 TEF values will probably affect calculation of total TEQ in food from specially contaminated areas differently, as the congener profiles may be different from those in foods contaminated at the background level.

In general, the altered 2005 TEF values will reduce the total TEQ in the Norwegian food samples, especially in foods where mo-PCBs contribute substantially to the total TEQ.

Table 2. % changes in total TEQ for some Norwegian foods* when TEQ is calculated from analytical data with WHO 2005 TEFs instead of WHO 1998 TEFs.

	Dioxins	no-PCBs	mo-PCBs	Total TEQ
Farmed salmon	-15 %	3 %	-78 %	-17 %
Herring	-22 %	6 %	-77 %	-19 %
Mackerel	-12 %	1 %	-78 %	-15 %
Cod liver oil	-12 %	8 %	-81 %	-45 %
Dairy	-12 %	3 %	-79 %	-15 %
Pig	-13 %	11 %	-87 %	-11 %
Sheep	-15 %	8 %	-84 %	-5 %

*based on the same data as in figure 1

Impact of WHO 2005 TEFs on exposure in the Norwegian population

The dietary exposure in the Norwegian population has not been calculated using the WHO 2005 TEFs. However, since total TEQ are lower with the WHO 2005 TEFs than with the WHO 1998 TEFs in the food samples calculated here, Panel 5 of VKM deduces that the WHO 2005 TEFs will result in lower exposure in the population when exposure is expressed

as dioxin equivalency. Impact of the lower total TEQ in food on calculated dietary exposure will probably vary individually, depending on the diet. Calculation of total dietary exposure can not be performed, since total TEQ with new TEFs has not been calculated for all food items. The putative impact can therefore only be evaluated on a general basis.

Fish is the main contributor to dioxin and PCB exposure in Norway followed by dairy products (Kvalem *et al.*, 2005; VKM, 2007). A 15-19% reduction in total TEQ for fish will have high impact on the calculated total dietary TEQ intake in the general population. People with high fish consumption are also in the group having the highest dioxin and PCB exposure. The impact of the 2005 TEF values on total dietary TEQ intake for people having low fish consumption, may be lower, because the reduction of TEQ in meat seems to be a little lower than in fish. However, this population group is believed to have low exposure overall.

A 45% reduction in total TEQ in cod liver oil may have high impact on calculated exposure among small children.

Based on the calculations expressed as dioxin toxicity in the present assessment, it is expected that the calculated intake in the Norwegian population will be approximately 10-20% lower when TEQ is calculated with the WHO 2005 TEFs.

Need for new assessment of dietary exposure to dioxins and dl-PCBs

It has previously been estimated that approximately 85 % of the Norwegian population do not exceed the TWI (14 pg TEQ/kg body weight/week) for dioxins and dl-PCBs when TEQ is calculated with the WHO 1998 TEFs (VKM, 2007). Preliminary calculation of total TEQ in food known to be important sources of dioxins and dl-PCBs with the new TEF values indicate that the calculated exposure will be lower, implying that a lower proportion of the population will be exceeding the TWI. However, there is a general need for regular monitoring of food contamination and dietary habits. This is important because both dietary habits and congener profiles in food change with time. It is now 10 years since the previous national dietary survey. A re-calculation of these data with the WHO 2005 TEQs would be based on possibly outdated consumption data. Panel 5 is of the opinion that a new dietary survey is needed to address this question.

In the next national assessment of dietary exposure to dioxins and PCBs the exposure should be calculated with both the 1998 TEFs and with the 2005 TEFs, in order to better investigate the impact of the new TEFs on calculated exposure. This will also be important when documenting the exposure time-trends. It should be kept in mind that changes in TEFs, resulting in lower TEQ in food, do not imply reduced exposure to the absolute concentration of dioxin-like compounds.

CONCLUSION

Panel 5 has not re-calculated the previously estimated dietary intake of dioxins and dl-PCBs in the Norwegian population using the revised TEFs. However, Panel 5 has calculated total TEQ for some important dietary sources for dioxins and dl-PCBs by using both the old (1998 TEFs) and the revised TEFs (2005 TEFs). Total TEQ with the 2005 TEFs was reduced in all samples, varying from 5 to 45%. Since these TEFs give lower total TEQ than the WHO 1998 TEFs in some important dietary sources for these compounds, Panel 5 deduces that the exposure to dioxins and dl-PCBs expressed as TEQ will be lower when using the revised TEFs. The use of the new TEF values indicates a lower dietary exposure to dioxins and dl-PCBs, implying that a lower proportion of the population will be exceeding the TWI. It

should be kept in mind that changes in TEFs, resulting in lower TEQ in food, do not imply reduced exposure to the absolute concentration of dioxin-like compounds.

Panel 5 is of the general opinion that there is a need for regular monitoring of food contamination and dietary habits because both dietary habits and contaminant profiles in food change with time. It is now 10 years since the last national dietary survey. A re-calculation of the previously estimated dietary intake of dioxins and dl-PCBs with the revised TEFs would be based on possibly outdated consumption data. Panel 5 is therefore of the opinion that a new estimation of dietary intake of dioxins and dl-PCBs in Norway should await new consumption data. Furthermore, Panel 5 recommend that in the next national assessment of dietary exposure to dioxins and PCBs the exposure should be calculated with both the 1998 and the 2005 TEFs in order to better investigate the impact of the new TEFs on calculated exposure. This will also be important when documenting the exposure time-trends.

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