Editorial

Guest Editor:
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Dioxins

The contamination of food with certain polychlorinated dibenzo-*p*-dioxins (PCDD), polychlorinated dibenzofurans (PCDF), and related dioxin-like polychlorinated biphenyls (PCBs) is the major topic of this Issue. It covers the many facettes of this problem, including the sources, exposure, levels in breast milk, analysis, risk assessment, carcinogenicity and its molecular mechanisms.

The exposure estimates have been refined within the last decade and now provide a more precise picture of the contribution of food to the overall exposure. An example is given in this Issue by E. Fattore *et al.* for the situation in Italy. According to this analysis, fish and fishery products as well as milk and dairy products still are major contributors to the overall intake. The mean daily intake for all dioxin-like contaminants was estimated to be 5.34, 3.37, and 2.28 pg WHO-TEQ/kg body weight for the three age groups 0–6 (breastfeeding excluded), 7–12, and 13–94 years old, respectively. A substantial portion of the general population is assumed to still exceed the tolerable daily intake of 2 pg WHO-TEq/kg body weight adopted by the Scientific Committee on Food of the European Commission in 2001.

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In the recent discussion, findings of higher levels in eggs from free-range chicken of dioxin-like contaminants played a prominent role. G. Schoeters and R. Hoogenboom show that these eggs have a higher risk of being contaminated with increased levels of dioxins and PCBs than barn eggs. Soil particles from environmentally contaminated areas may contribute to this finding. Contamination levels in soil should be kept low and should be controlled in areas with free-range chickens, although the modifying factors which influence the uptake of dioxins and PCB from the environment and transfer into eggs are yet not well understood.

In a study by P. Fürst, more than 1000 human milk samples have been analyzed for dioxin-like contaminants over the last 30 years. It was found that the levels of most persistent organohalogen compounds in human milk have decreased significantly over the past three decades. Exceptions are the polybrominated diphenylethers (PBDEs) which have been and, in some cases, still are extensively used as flame retardants. PBDE levels in milk samples collected in the early 2000s are approximately 60% higher compared to samples taken 10 years earlier. In contrast to PCBs, PBDE levels are not correlated to PCDDs/PCDFs in human milk, indicating another mode of human exposure.

The toxicity of dioxins and dioxin-like contaminants is reviewed by J. C. Larsen in a risk assessment paper. The relative toxicity of a number of dioxin-like compounds is expressed in toxic equivalency factors (TEF) which express the combined toxicity of a sample as toxic equivalent (WHO-TEQ). The current risk assessment used the most sensitive adverse effects of tetrachlorodibenzodioxin (TCDD) in experimental animals, *i. e.* developmental and reproductive effects in the male offspring of rats administered TCDD during pregnancy. Because of the large difference between rats and humans in the biological half-life of TCDD, the assessment used a body burden approach to compare across species and derived a tolerable weekly intake (TWI) of 14 pg WHO-TEQ per kg body weight.

In a study by R. Hoogenboom the DR CALUX® assay was used in a survey in the Netherlands to control the dioxin levels in eel. Samples were analysed by GC/MS for dioxin-like contaminants and indicator PCBs, revealing a considerable number of samples exceeding the action limit of 30 pg/TEQ *per* g eel. A good correlation was found between the GC/MS method and the DR CALUX® assay which is based on the detection of arylhydrocarbon receptor-dependent gene transcription. The indicator PCBs also showed a good correlation with total TEQ levels, while the relation with PCDDs/PCDFs was very poor. Especially at high TEQ levels, dioxin-like PCBs contributed most of the total TEQ in wild eel.

The important issue of carcinogenicity of dioxins is covered in a paper by N. J. Walker *et al.* The study compares the design and results of two cancer bioassays carried out in rats with TCDD by the National Toxicology program (NTP) and the Dow Chemical company. Increased incidences of neoplasms were seen in both studies in the liver, lung and oral mucosa, while a significant increase in the incidence of cholangiocarcinomas of the liver was seen in the NTP study but not in the Dow study. Furthermore, differences in the shapes of the dose response curves for several neoplasms were noted.

The mechanisms of carcinogenicity of TCDD are the subject of a review by S. Knerr and D. Schrenk. From a variety of studies it is evident that TCDD acts as a potent tumor promoter in rodent liver, *i. e.* it enhances the growth of putative preneoplastic lesions, some of which eventually progress towards malignancy. The underlying mechanisms are complex, but seem to be related to a suppression of apoptosis (programmed cell death) which normally eliminates cells bearing critical genetic lesions. Furthermore, TCDD can lead to oxidative DNA lesions in the liver of female rats. This effect is estrogen-dependent and may be related to an extraordinary induction of drug metabolising enzymes of the cytochrome P450 family in combination with other still poorly defined factors.

Taken together, our understanding of the molecular mechanisms of the toxicity of dioxins is far from sufficient though enormous progress has been made over the last 30 years. A better understanding of the molecular processes is urgently required for the refinement of risk assessment including species extrapolation. In spite of a long-term trend towards lower levels of dioxin-like contaminants in human blood and breast milk, the current levels of intake still exceed the tolerable levels in a considerable portion of the population, in particular in children. The refinement of analytical methods, including the use of cell-based bioassays, allows the detection of food contaminations as shown for fish samples.

I sincerely hope that this compilation may serve as a source of information for scientists and foster future ideas and research activities. I would like to thank the editors of Molecular Nutrition & Food Research and all colleagues for their contributions and outstanding efforts which have made this Issue possible.

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Guest Editor

