External and Internal Human Exposure

Takumi Takasuga[a] and Donald G. Patterson Jr[b]

[a]Shimadzu Techno Research Inc., Kyoto, Japan

[b]Organic Analytical Toxicology Branch, DLS/NCEH/ATSDR/CDC, Georgia USA

Exposure of toxic contaminants occurs to general human populations by various pathways and cause serious health concern. Enormous literature has been documented the continuing public concern over the health risks posed by exposures to toxic contaminants such as organochlorine pesticides (OCPs), polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), polychlorinated biphenyls (PCBs), polybrominated diphenylethers (PBDEs) etc. For example, increasing rates of cancer in humans have prompted questions about the potential link to residues from OCPs, PCDDs, PCDFs, PCBs, PBDEs etc., either by external or internal exposures. Historically, estimates of human exposure to toxic contaminants have been based on the concentration of these chemicals in environmental media such as air, water, and food along with assumptions about how people are exposed.

In this meeting, importance of human exposure has taken in to an account and thus special session was proposed. Totally eighteen short papers submitted among them, fifteen are considered to be suitable since these studies comprise human exposure of toxic organic contaminants through, -waste incineration, -contaminated food, -polluted indoor air, -Yusho PCB Oil Accident -impurities from agrochemicals, -wood treatment plant, -fire accident, -contaminated site, and -hydroxylated metabolites of PCBs from human cerebro spinal fluid (CSF) samples. Particularly, work of this session represents efforts by authors from Brazil, Germany, Japan, Norway, Russia, Spain and the USA. Some of the highlights of the papers presented in this session have been summarized as follows;

A study from Spain by Agramunt et al. reported that plasma and urine of Hazardous Waste Incineration (HWI) workers decreased maximum of hexachlorobenzene (HCB), PCBs, PCDD/DFs, I-TEQ and chlorophenols in between 1999 to 2003. Particularly they report significant levels in plant workers than laboratory of administration workers. According to the results of their survey performed 4 years after of regular operations in the HWI facility, no evidence of significant exposure to the organic substances has been found. Finally they concluded that under the present occupational conditions, no additional health risks for the workers at the HWI.

Hirai and his co-workers from Japan reported two papers on PBDEs and PCBs, respectively from maternal blood, cord plasma, placenta and breast milk from 4 pregnant women from Japan. Greater PBDE, PCBs were noticed in breast milk than other samples. Finally they concluded that cross-placental behavior of PBDE and PCBs were minimized since placenta blocked most of analyzed congeners.

Based on 77% reduction of dioxins and PCBs in between 1997 to 2001, Mato and his co-workers from Japan estimated human exposure for the year 2001 using inhalation, soil ingestion and foodstuff data. Total exposure was estimated 1.68 pg-TEQ/kg-bw/day with foodstuff account >90% to the total exposure than inhalation and soil ingestion. Furthermore fish and shellfish accounted 45-70% total intake depending upon age. Finally they conclude, average and 95th percentile of dioxins and PCBs exposure in Japan (4 pg-TEQ/kg-bw/day) were below the WHO-proposed tolerable daily intake (TDI) levels.

Miyata et al. from Japan reported time course difference of dioxins, furans and PCBs concentrations in between breast milk, blood and their impact to transfer to the infants. They showed considerable difference of ratio of concentrations in between time. They concluded that meal play a vital role in dioxin concentrations in mothers and the suckling babies. Furthermore, ingestion of contaminants by babies differed in morning, afternoon, evening and night zones. Finally, they concluded that contaminants ingested by infants reflect the amount in meal that intake by mother at particular time during breast-feeding rather than historically deposit amount.

Indoor air contamination by dioxin-like with various sources of PCBs (PCB containing

Thiokol sealant and PCB containing flame retardant) has been reported by Heinzow et al. from Germany. According to their results the room with flame retardant source had 3 to 15-times higher TEQ when compare to Thiokol source rooms. Further, they recommend to uses algorithms to calculate the expected PCB TEQ in indoor air in highly contaminated rooms.

Current POPs levels in human breast milk (n=46) was reported by Polder et al. from four Norway counties Rogaland, Telemark, Troms and Østfold. Concentration OCPs such as HCB, β-HCH and DDTs declined in Norway. PCB levels in Norway also similar to findings from Sweden, Finland. Based on assumptions of 30% contribution by mono-ortho PCBs, the total TEQ could be calculated to 14.6 pg TEQ/g milk fat. The estimated daily intake of a 5-kg infant receiving 800 mL of a 3% fat breast milk/day would be 70 pg TEQ/kg bw/day or 490 pg TEQ/kg bw/week this exceeds the tolerable life-long weekly intake (TWI) established by EU. The mean sum PBDE level were close agreement with the level reported in Norwegian breast milk in 2001 with 3.04 ng/g milk fat.

D'Amato and co-workers presented DDT and its metabolites in fish from Brazilian Amazon during 1990's in order to assess potential health impacts by fish consumers (mothers) and breast-feeding infants. With their results 1990's DDT concentrations in fish considered to dangerous for infants in Tapajos and Madeira River Basin and Itaituba, Alta Floresta from Amazonas States. Daily intake (DI) estimation for mothers was less than FAO/WHO TDI of 0.01 mg/kg. Infant daily intake (IDI) results show less than guideline values (5.0×10^{-3} mg/kg/day) with a range of 0.52×10^{-3} mg/kg/day to 3.5×10^{-3} mg/kg/day.

Recent trend of Yusho PCB Accident victims was studied by Iida and his co-workers. They analyze blood samples collected from Yusho victims (n=279) and Yusho-suspected victims (n=92) as well as normal subjects (n=152) in 2002. WHO-TEQ was 137, 43 and 25, respectively for Yusho victims, Yusho-suspected victims and normal subjects on pg-TEQ/g lipid basis. The mean concentration ratio of 123478-HxCDF and 123678-HxCDF was 1.1 for normal and Yusho-suspect victims while, 1.9 for Yusho victims. According to these findings authors concluded that ratio of these two congeners is used as an indicators for exposure of Yusho oil and provide diagnostic tool for Yusho victims.

Michigan dioxin exposure; planning phase and protocol development for 2004-2006 was established by Adriaens et al. from USA based on serum concentrations from 700 local residents. Purpose of this model establishment is based on the response to concerns among the population in Midland and Saginaw Counties that dioxins from the Dow Chemical Company facilities in Midland have resulted in the contamination of areas. The model classified as study population selection, population sampling, bloods sampling, house dust sampling, soil sampling, analytical methods and statistical analysis. The samples has TEQ more than 8 ppt subjected into further in-vitro bioassay analysis and samples shows highest TEQ further subjected in to HRGC-HRMS analysis.

Dahlgren and his co-workers reported PAHs, PCDDs, PCDFs, dioxin-like PCBs, HCB, PBDE and pentachlorophenol in blood of residents living near wood treatment plant as well as control subjects who live away from plant. PAHs and DNA adduct in affected residents were 4.7 times greater than controls. Based on their conclusions, higher PAH-DNA adduct levels are believed to predict a high risk of cancer.

Chernyak and his colleagues from Russia reported PCDDs, PCDFs and PCBs in blood from firefighters after Shelekhov "Irkutskcable" factory fire incident during December 1992. Out of 20 firefighters, 11 have total TEQ exceed 100 pg/g lipid of these 5 have total TEQs exceed 200 pg/g lipid and 2 exceed 400 pg/g lipid. Controls (non-firefighters) had significantly less contamination levels. There was no pronounced difference in fighter work for 1 day and 2 day. Officers in "Irkutskcable" factory had lower levels when compare to non-officers. The Shelekhov fire appeared to result in greater exposures of PCDDs.

Monitoring of PCDD and PCDF levels in blood of employees who involved with road construction and controls were conducted by Rottler and colleagues from Germany. Three employees had > 20 pg I-TEQ/ g lipid while, 12 on-site employees showed 90 percentile 15.4 pg I-TEQ/g lipid. These levels are generally in good agreement with other German and European data and thus no extra PCDD/DF were loaded to employees. These levels were also decreased with in a year.

Joas and his co-workers reviewed current human exposure of PCDDs/PCDFs and PCBs in Candidate Countries launched by the European Commission by collecting information in Accession and Candidate Countries (AC/CC) in comparison to Member States (MS). According to review conclusions, the average contamination levels in AC/CC do not exceed MS. PCDDs/PCDFs contamination does not seem to present a problem in comparison to MS, there exist extremely high-contaminated “hot spots” for PCBs (e.g., Sloval Republic, Slovenia) that urgently needed remediation measures to present further dissemination and exposure of the local population. With respect to PCDDs/PCDFs emission, industrial facilities without abatement devices as well as uncontrolled burning on waste disposal sites or agricultural fields and domestic heating seems to be the major sources for pollution in AC/CC. Contamination trends from a number of time series show a constant decline over the last decade in food and tissue levels even if slowing down during the last years whereas the environmental contamination seems to be quiet stable and in part even slightly increases since 1997. With respect to legislation, administrative structure and capacity major progress has been made in the last years. However, further effort is needed in some cases with respect to implementation and enforcement, training and capacity for PCDDs/PCDFs analysis.

Takasuga and his co-workers reported established analytical methodology development for hydroxylated metabolites of PCBs (OH-PCBs) and total PCBs in human serum, human cerebro spinal fluid (CSF) and monkey plasma samples using isotope dilution technique with HRGC-HRMS for the first time. The ethyl derivative seems to better than trimethylsilylation “TMS” during cleanup. Approximately 28% of OH-PCBs were contributed to the PCBs burden in human serum. In biological samples metabolism of HpCB-187/183 to 4-OH HpCB-187 seem to have specific protein binding activity. Concentrations of OH-PCBs were greater than total PCBs in CSF. Specific protein binding in CSF seems to plausible reason for the results. Occurrence of OH-PCBs in CSF results their entro-CSF activity. Elevated OH-PCBs were noticed in monkey plasma than in human samples. Hydroxylated metabolites of TeCB-77 have marked structural resemblance to thyroxine, the natural ligand for TTR and, therefore, competitively bind to TTR and can cause reductions in plasma tetraidothyroxine (T4) levels and serum transport of Vitamin-A in rodents. Hydroxylated metabolites of PCBs have been shown in vitro to have binding affinities that are 10 times greater than TTR than for T4. These results in persistent retention of these metabolites in blood of both humans exposed environmentally to PCBs. In addition, occurrence of OH-PCBs in CSF is of major concern as it can alter and modulate any signal that originated from brain.