U.S. Food and Drug Administration's Dioxin Monitoring Program

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Introduction

Dioxin-like compounds (DLCs) are a group of environmental contaminants whose primary route of human exposure occurs via the consumption of fatty foods of animal origin. Recent safety risk assessments conducted by national and international organizations broadly agree that risk management actions should be developed to decrease DLC exposure. Since the mid-1990s, the U.S. Food and Drug Administration (FDA) has tested specific foods with the goal of describing and reducing DLC exposure. In 2001, FDA developed a strategy for DLCs (http://vm.cfsan.fda.gov/~lrd/dioxstra.html) and substantially expanded its dioxin monitoring program to obtain more comprehensive data on background levels of DLCs in specific food and feed samples as well as to identify and reduce pathways of DLC contamination. FDA's dioxin monitoring program analyzes food collected under its Total Diet Study (TDS) and food and feed from targeted sampling. The TDS is FDA's ongoing market basket survey of approximately 280 core foods in the U.S. food supply. FDA targeted sampling collects and analyzes foods suspected of having both higher DLC levels and more variability in those levels than other foods. The contribution of dietary DLCs to overall exposure and the possible introduction of DLCs in animal-based food via the use of particular feed components was recently identified by the National Academy of Sciences Committee on the Implications of Dioxin in the Food Supply and confirmed FDA's approach articulated in its dioxin strategy.[1]

Methods and Materials

Size of the program. In 2001, FDA expanded its dioxin monitoring program to obtain more comprehensive data on background levels of DLCs as well as to identify opportunities to reduce DLC exposure (**Table 1**).

TABLE 1 - Sample Requests for FDA's Expanded Dioxin Monitoring Program

Year	Total Diet Study Samples	Targeted Samples	Total Samples
2001	270	500	770
2002	214	1,065	1,279
2003	232	1,438	1,670
2004[1]	232	1,500	1,750

[1]Planned samples

Analysis methods used. Three methods are currently used by FDA to identify and quantify DLCs in foods. The first is high resolution mass spectroscopy (HRMS), which is the preferred method for high consumption-rate foods with very low or no expected DLC levels. HRMS is also the preferred method for TDS samples, given that TDS is used for estimating DLC exposure and these estimates may depend on the level of detection of the analytical methodology. The second method FDA uses is ion trap mass spectroscopy (ITMS) which is the preferred method for lower consumption-rate foods with higher expected DLC levels. Both ITMS and HRMS provide congener-specific estimates of concentration. ITMS method detection levels are often 3 to 10 fold higher than HRMS method detection levels depending on the congener and/or given food. ITMS uses less expensive and more easily maintained equipment, resulting in lower cost per sample and a higher total sample throughput compared to HRMS. The third method FDA uses is CALUX (chemical-activated luciferase gene expression cell bioassay system). Currently FDA uses this cell-based assay as a screening method for feed and feed components. CALUX is less expensive than MS-based methods and it is possible to analyze a large number of samples. Unlike ITMS and HRMS, CALUX does not provide congener-specific information. The ability to analyze a large number of samples quickly and the low cost of CALUX compared to MS-based methods has prompted FDA to investigate the possibility of using this method more widely for food and feed samples.

Dietary exposure estimates. For dietary exposure estimation, FDA relies on information obtained from the FDA's TDS. The TDS is FDA's ongoing market basket survey of approximately 280 core foods in the U.S. food supply to determine levels of various pesticide residues, contaminants, and nutrients in foods and to estimate dietary intake of these substances. The TDS foods represent the major components of the average U.S. diet as determined from data collected in national food consumption surveys. Four times each year, samples of each TDS food are purchased in 3 different cities, prepared as they would be consumed (table-ready) and then composited for analysis. In 1999, FDA began analyzing selected TDS foods from one of the four sample collections for DLC's, specifically polychlorinated dibenzo-*p*-dioxin (PCDD) and polychlorinated dibenzofuran (PCDF) congeners. Beginning in 2003, three dioxin-like PCB congeners were also included in the analyses. FDA is planning to include additional dioxin-like PCBs to the program. Dietary exposure estimates for DLCs were calculated by multiplying PCDD/PCDF concentrations in these TDS food by average consumption amounts as reported in the USDA 1994-96, 1998 Continuing Survey of Intakes by Individuals (CSFII).[2]

Identification of DLC pathways in the diet. FDA targeted sampling collects and analyzes foods suspected of having both higher DLC levels and more variability in those levels than other foods. This additional sampling provides better estimates of the various distributions of DLC levels in specific foods than provided by the limited number of samples of a given food taken for the TDS. Targeted sampling also identifies foods with elevated DLC levels to allow investigation of potential sources and pathways for DLC contamination of the food supply.

Results and Discussion

Dietary Exposure Estimates. The monthly PCDD/PCDF exposure estimate for all age-sex groups from TDS data for 2001 and 2002 was 11.6 pg WHO-TEQ/kg body weight/month (ND=0) representing 16.6% of the Joint FAO/WHO Expert Committee on Food additives (JECFA)

Provisional Tolerable Monthly Intake (PTMI) (Table 2). The food category contributing greatest to exposure was "meat and mixtures" (43.7%) followed by "other foods and mixtures" and "dairy foods and mixtures" (14.8% and 14.5%, respectively) when ND=0. The relatively high contribution of "other foods and mixtures" and "fruits, vegetables and mixtures" to overall exposure came from foods in these categories containing animal-based ingredients (e.g., lasagna, pizza, scalloped potatoes, French fries, etc.). The age-sex groups with the highest PCDD/PCDF exposure from the total diet were males/females 10 years and younger (Table 3) though calculated estimates were well below JECFA's PTMI.

In 2001, JECFA established a PTMI of 70 pg WHO-TEQ/kg body weight/month.[3] Because of the long half-life of DLCs in humans, JECFA established a PTMI instead of a tolerable daily or weekly intake. FDA's dietary exposure estimates include only PCDDs and PCDFs and not dioxin-like PCBs and, therefore, may underestimate overall DLC exposure. Since 2003, three dioxin-like PCBs have been included in FDA's dioxin monitoring program. FDA is planning to include additional dioxin-like PCBs in the program.

Zinc oxide Investigation. In 2003, FDA's dioxin monitoring program found elevated levels of DLCs in both aquaculture catfish and catfish feed. The source of the DLC contamination was traced to a mineral component of the mineral feed premix. Zinc oxide, a component of the contaminated mineral feed premix, was estimated to contain elevated levels of dioxin (40-80 ng/g WHO-TEQ). The contaminated zinc oxide was produced as a by-product from industrial metal production. Manufacturers of the zinc oxide and mineral feed premix containing the contaminated zinc oxide voluntarily recalled these products. FDA expanded its dioxin monitoring to include additional sampling of feed and feed components as well as human dietary supplements.

Targeted Sampling Results. FDA is currently compiling data for targeted sampling results from 2001-2004. When complete, FDA will post targeted sampling results on FDA's website (http://www.cfsan.fda.gov/).

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References

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TABLE 2 - Dietary PCDD/PCDF Exposure Estimates (pg WHO-TEQ/kg body weight/month) for Different Food Categories for All Age-Sex Groups[1,2,3]

Food Categories	ND = 0[5]	ND = 0.5 LOD	ND = LOD
Dairy foods and mixtures	1.7 (14.5%)	2.6 (12.3%)	3.5 (11.5%)
Eggs and mixtures	0.3 (2.6%)	0.4 (1.8%)	0.5 (1.5%)
Fats, oils and mixtures	0.2 (1.6%)	0.2 (1.2%)	0.3 (1.0%)
Fish and mixtures	1.0 (8.6%)	1.1 (5.3%)	1.2 (4.1%)
Fruits, vegetables and mixtures	1.1 (9.5%)	2.9 (13.6%)	4.6 (15.1%)
Meat and mixtures	5.1 (43.7%)	5.9 (28.1%)	6.8 (22.2%)
Poultry and mixtures	0.5 (4.7%)	0.8 (3.9%)	1.1 (3.6%)
Other foods and mixtures[4]	1.7 (14.8%)	7.1 (33.8%)	12.6 (41.1%)
Total	11.6 (100.0%)	21.1 (100.0%)	30.6 (100.0%)

[1]PCDD/PCDF concentrations from U.S. Food and Drug Administration Total Diet Study (2001, 2002).
[2]Food Consumption based on the USDA 1994-1996, 1998 Continuing Survey of Food Intake by Individuals (CSFII).
[3]Abbreviations: ND, Nondetects; LOD, Limit of Detection; TEQ, Toxicity Equivalents; WHO, World Health Organization; PCDD, polychlorinated dibenzo-*p*-dioxin; PCDF, polychlorinated dibenzofuran.
[4]Grains and mixtures, legumes and mixtures, beverages (other than milk and juice), candy.
[5]Reflects treatment of samples for which no dioxin congener was detected.

TABLE 3 – Dietary PCDD/PCDF Exposure Estimates (pg WHO-TEQ/kg body weight/month) for Different Age-Sex Groups for the Total Diet[1,2,3,4]

Sex	Age	ND = 0[5]	% of PTMI	ND = 0.5 LOD	% of PTMI	ND = LOD	% of PTMI
Males/Females	6-11 months	12.0	17.1	35.9	51.3	59.8	85.5
Males/Females	2 years	27.1	38.7	45.2	64.6	63.4	90.6
Males/Females	6 years	21.1	30.1	35.8	51.1	50.5	72.1
Males/Females	10 years	14.9	21.3	26.3	37.6	37.7	53.9
Females	14-16 years	9.1	12.9	17.8	25.4	26.5	37.8
Males	14-16 years	12.0	17.1	22.4	32.0	32.8	46.9
Female	25-30 years	7.9	11.3	15.6	22.2	23.2	33.2
Male	25-30 years	9.9	14.2	18.7	26.8	27.5	39.3
Females	40-45 years	8.3	11.8	15.6	22.3	22.9	32.7
Males	40-45 years	9.7	13.9	17.5	25.0	25.2	36.0
Females	60-65 years	7.6	10.8	13.6	19.5	19.7	28.1
Males	60-65 years	9.4	13.5	15.6	22.2	21.7	31.0
Females	70+	7.5	10.7	13.6	19.4	19.6	28.1
Males	70+	9.7	13.9	16.2	23.2	22.7	32.4
All Age-Sex Groups		11.6	16.6	21.1	30.2	30.6	43.8

[1]PCDD/PCDF concentrations from U.S. Food and Drug Administration Total Diet Study (2001, 2002).
[2]Food Consumption based on the USDA 1994-1996, 1998 Continuing Survey of Food Intake by Individuals (CSFII).
[3]Abbreviations: ND, Nondetects; LOD, Limit of Detection; TEQ, Toxicity Equivalents; WHO, World Health Organization; PTMI, Provisional Tolerable Monthly Index; PCDD, polychlorinated dibenzo-*p*-dioxin; PCDF, polychlorinated dibenzofuran.
[4]Joint FAO/WHO Expert Committee on Food Additives (JECFA) Provisional Tolerable Monthly Intake (PTMI) is 70 pg WHO-TEQ/kg body weight/month.
[5]Reflects treatment of samples for which no dioxin congener was detected.