Toxicological and Health Aspects of Bisphenol A

Report of Joint FAO/WHO Expert Meeting

2–5 November 2010

and

Report of Stakeholder Meeting on **Bisphenol A**

1 November 2010

Ottawa, Canada

Food and Agriculture Organization of the United Nations

World Health Organization

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List of acronyms and abbreviations

AC_{50}	half-maximal activity concentration
BASC-2	Behavioural Assessment System for Children-2
BMD	benchmark dose
BMDL	95% lower limit on the benchmark dose
$BMDL_{10}$	95% lower limit on the benchmark dose for a 10% response
BMI	body mass index
BPA	bisphenol A
BRIEF-P	Behavior Rating Inventory of Executive Function (Preschool Version)
bw	body weight
CVD	cardiovascular disease
CYP	cytochrome P450
DES	diethylstilbestrol
DMBA	7,12-dimethylbenz[a]anthracene
DNA	deoxyribonucleic acid
ELISA	enzyme-linked immunosorbent assay
ESR1	estrogen receptor 1
F_1	first filial generation
FAO	Food and Agriculture Organization of the United Nations
GD	gestation day
HPG	hypothalamic–pituitary–gonadal
IUPAC	International Union of Pure and Applied Chemistry
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LOAEL	lowest-observed-adverse-effect level
LOEC	lowest-observed-effect concentration
MS	mass spectrometry
MS/MS	tandem mass spectrometry
NHANES	National Health and Nutrition Examination Survey (USA)
NOAEL	no-observed-adverse-effect level
NTP	National Toxicology Program (USA)
P_0	first parental generation
PBPK	physiologically based pharmacokinetic
PC	polycarbonate
PND	postnatal day
PVC	polyvinyl chloride
USA	United States of America
USEPA	United States Environmental Protection Agency
USFDA	United States Food and Drug Administration
WHO	World Health Organization

Executive summary

Bisphenol A (BPA) is an industrial chemical that is widely used in the production of polycarbonate (PC) plastics (used in food contact materials, such as baby bottles and food containers) and epoxy resins (used as protective linings for canned foods and beverages and as a coating on metal lids for glass jars and bottles). These uses result in consumer exposure to BPA via the diet.

Although a large number of studies on the toxicity and hormonal activity of BPA in laboratory animals have been published, there have been considerable discrepancies in outcome among these studies with respect to both the nature of the effects observed as well as the levels at which they occur. This has led to controversy within the scientific community about the safety of BPA, as well as considerable media attention.

In light of uncertainties about the possibility of adverse human health effects at low doses of BPA, especially on reproduction, the nervous system and behavioural development, and considering the relatively higher exposure of very young children compared with adults, the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) jointly organized an Expert Meeting to assess the safety of BPA.

Analytical methods for the determination of BPA in food and biological samples

Sensitive and reliable analytical methods are available for the determination of BPA in both food and biological samples. Solvent extraction and solid-phase extraction are the most commonly used and most effective methods for the extraction of BPA in food and biological samples. Although isotope dilution methods based on mass spectrometry and tandem mass spectrometry are the most reliable for the detection of BPA, many of the results of BPA determination in both food and biological samples have been generated by methods that are not based on mass spectrometry.

The majority of methods used to measure free and total BPA in food and biological samples have been validated for certain performance parameters, such as accuracy, precision, recovery and limit of detection. Most methods fulfil the requirements of single-laboratory validation. For biological samples, however, validation of methods for conjugated BPA is very limited. By the current standards of analytical science, findings of BPA in food samples and most biological samples are reliable. Nevertheless, care needs to be taken to avoid cross-contamination with trace levels of BPA during sample collection, storage and analysis.

Occurrence of BPA in food

The Expert Meeting considered BPA concentrations in food from food surveys and from migration studies from food contact materials. Free BPA levels were no more than 11 µg/l in canned liquid infant formula as consumed and no more than 1 µg/l in powdered infant formula

as consumed. In toddler food, BPA concentrations were approximately 1 µg/kg on average. Total BPA levels were below 8 µg/l in breast milk. For adult foods, 30 studies representing about 1000 samples from several countries were available, and the data were segregated according to food type. The occurrence data that were deemed to be valid for use in the exposure assessment were tabulated. For adult foods, average concentrations ranged from 10 to 70 µg/kg in solid canned food and from 1 to 23 µg/l in liquid canned food. For the migration of BPA from PC, worst-case realistic uses were defined, and a maximum migration of 15 µg/l was selected for use in the exposure assessment.

Exposure assessment

The Expert Meeting estimated exposure to BPA by reviewing published exposure estimates in seven countries and regions and by calculating international exposure from the available information on food consumption patterns and the occurrence of BPA in foods relevant to the population groups of interest.

On the basis of the most relevant national published estimates, the exposure of adults to BPA was <0.01–0.40 µg/kg body weight (bw) per day at the mean and 0.06–1.5 µg/kg bw per day at the 95th/97.5th percentile. For young children and teenagers, mean exposure was 0.1–0.5 µg/kg bw per day, and exposure at the 95th/97.5th percentile was 0.3–1.1 µg/kg bw per day.

To estimate international exposure to BPA, the Expert Meeting considered a variety of possible scenarios of model diets, combining daily consumption from the worst-case scenario (100% of consumption from packaged food) to the best-case scenario (25% of consumption from packaged food) with concentration data (average and maximum concentrations).

The mean exposure of exclusively breastfed babies (0–6 months) to BPA is estimated to be 0.3 µg/kg bw per day, and exposure at the 95th percentile is estimated to be 1.3 µg/kg bw per day. Once solid foods are introduced (at 6–36 months), exposure to BPA decreases relative to body weight. Exposure estimates are generally higher for infants fed with liquid compared with powdered formula and for infants fed using PC compared with non-PC bottles. The highest