

## PREVENTING DISEASE THROUGH HEALTHY ENVIRONMENTS

### EXPOSURE TO DIOXINS AND DIOXIN-LIKE SUBSTANCES: A MAJOR PUBLIC HEALTH CONCERN

Human exposure to dioxins and dioxin-like substances has been associated with a range of toxic effects, including chloracne; reproductive, developmental and neurodevelopmental effects; immunotoxicity; and effects on thyroid hormones, liver and tooth development. Dioxins are also carcinogenic. Developmental effects in males are the most sensitive reproductive health end-point, making children – particularly breastfed infants – a population at elevated risk.<sup>1,2</sup> Dioxins and dioxin-like substances are persistent organic pollutants (POPs) covered by the Stockholm Convention on Persistent Organic Pollutants; they can travel long distances from the emission source and can bioaccumulate in food chains.<sup>3</sup> Human exposure occurs mainly through consumption of contaminated food.<sup>1,4</sup> but higher levels of exposure can occur in occupational settings. Public health and regulatory actions are needed to reduce emissions of these substances, as required by the Stockholm Convention, and to reduce human exposure, particularly for children.

#### What are dioxins and dioxin-like substances?

The term “dioxins and dioxin-like substances” commonly refers to polychlorinated dibenzodioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and polychlorinated biphenyls (PCBs). They are two- or three-ring structures that can be chlorinated to varying degrees. PCBs can have up to 10 chlorine atoms substituting for hydrogen atoms, and PCDDs and PCDFs can have up to eight. The compounds often have similar toxicity profiles and common mechanisms of action, and are generally considered together as a group to set guidelines.<sup>1,4</sup>

#### Sources of exposure to dioxins and dioxin-like substances<sup>1,4-7</sup>

PCDDs and PCDFs are widely present in the environment, occurring naturally, but mainly as unwanted byproducts of combustion and of various industrial processes. PCDFs were major contaminants of PCBs, but neither PCDDs nor PCDFs have ever been manufactured or used for commercial purposes other than for scientific research.

PCBs are not natural substances but were globally manufactured and used in the past. Although PCB manufacture is now prohibited under the Stockholm Convention, their release into the environment still occurs from the disposal of large-scale electrical equipment and waste, from metallurgical uses, and some chemical manufacture and processing.<sup>6</sup> The Stockholm Convention also requires the phase-out of the use of PCBs in equipment by 2025 and the final elimination of PCBs by 2028<sup>3</sup>; however, only 17% of the total amount of PCB has been eliminated thus far.<sup>8</sup>

Mixtures of the substances with different numbers and positions of chlorine substitution are found in the environment. The degree of chlorination of dioxin mixtures released into the environment through incineration is determined by the source material and the amount of chlorine available.

Remedial actions following regulation in the 1980s led to a significant decrease in levels of PCDDs and PCDFs in air by 2000 compared to levels seen in the 1970s; however, the relatively low measured values since 2000 have declined only slowly or do not show significant changes.<sup>9</sup> Based on a series of surveys of human breast milk in numerous countries, concentrations of PCDD/PCDF were found at relatively similar levels worldwide in both industrialized and less industrialized regions, with open burning processes and geophagy (consumption of clay by pregnant women) likely contributing to the measured levels in breast milk in some less industrialized countries.<sup>10</sup>

### ***Industrial processes and natural events***

PCDDs and PCDFs are byproducts of industrial processes, particularly waste incineration, cement kilns firing hazardous waste, chlorine bleaching of pulp, and thermal processes in the metallurgical industry, as well as the manufacture of chlorophenols and phenoxy herbicides. They can also be generated by natural events, such as volcanic eruptions and forest fires. PCBs were previously manufactured for use as dielectric insulating fluids (with low electrical conductivity) in larger-scale electrical products such as transformers and capacitors, in heat transfer and hydraulic systems, and in industrial oils and lubricants. PCDFs were common contaminants of commercial PCB mixtures.

### ***Environmental media and food***

Generally, levels of PCBs, PCDDs and PCDFs in air are very low, except in the vicinity of point sources such as inefficient incinerators. Concentrations of these compounds in drinking-water and surface water are also very low because they are poorly soluble in water. Releases into air from inadequate incineration and releases into air, water or soil from industrial and waste sites contaminate soil and aquatic sediments, leading to bioaccumulation and bioconcentration through food chains. The higher chlorinated components and components with specific positions of chlorination persist longer in the environment and show greater bioaccumulation. The substances have high fat solubility, which may lead to higher concentrations in fatty foods, such as dairy products, some fish, meat and shellfish. Most general population exposure is through ingestion of contaminated foods of animal origin.<sup>11</sup> These compounds persist in fatty tissue, with typical half-lives in humans in excess of seven years. Human breast milk can be a significant source of exposure to dioxins and dioxin-like compounds; however, longitudinal surveys suggest that levels in breast milk globally are on a downward trend.<sup>10</sup>

### ***Waste disposal***

Any source of organic materials in the presence of chlorine or other halogens will generate dioxins and furans during combustion. PCDDs and PCDFs are generated through the incineration of waste (domestic, industrial and health-care facilities) at low to moderate temperatures; guidance has been developed to identify and quantify releases from various incineration processes. The use of incineration technology operating at 850 to 1100 °C and fitted with special gas-cleaning equipment complies with international emission standards for dioxins and furans, whereas inadequate incineration creates them.<sup>12-14</sup>

Disposal of electrical equipment may release PCBs (and PCDF contaminants); guidance is available on equipment likely to contain PCBs.<sup>15</sup> Stockpiles of old industrial lubricants containing PCBs are also a potential source of emissions.

## Derivation of toxic equivalency factors (TEFs)

Some individual compounds with particular levels of chlorination and/or positions of the chlorine substitutions are much more toxic than others. Toxic equivalency factors (TEFs) have been established to compare the toxicities of individual PCDDs, PCDFs and PCBs relative to the most toxic of these compounds: 2,3,7,8-tetrachlorodibenzodioxin (TCDD), which is used as a reference and given a TEF of 1.<sup>16-17</sup> The common mechanism of action for these substances means that their effects are additive, and TEFs for individual compounds can be summed to establish a TEF for mixtures. This approach has proved robust as a method for establishing the relative toxicities of these compounds. Human exposure to all dioxins and dioxin-like substances combined is usually calculated in terms of a toxic equivalence quotient (TEQ), based on the TEFs.<sup>2,6</sup>

### World Health Organization (WHO) dioxin guidelines

#### Provisional tolerable monthly intake\*

In 2002, the Joint Food and Agriculture Organization of the United Nations (FAO)/WHO Expert Committee on Food Additives (JECFA) established a provisional tolerable intake of 70 pg/kg body weight per month for PCDDs, PCDFs and coplanar PCBs expressed as TEFs, based on reproductive end-points in male offspring of exposed pregnant rats.<sup>1</sup> The value is expressed per month to reflect that exposure is cumulative and chronic rather than acute.

#### Drinking-water

No water quality guidelines have been set for these substances because of their low water solubility.

#### Air

An air quality guideline for PCBs was not established because direct inhalation exposures constitute only a small proportion of the total exposure – in the order of 1–2% of the daily intake from food. Although this air concentration is only a minor contributor to direct human exposure, it is a major contributor to contamination of the food chain.<sup>18</sup>

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\* Since these substances induce tumours and likely other effects via a receptor-mediated mechanism, tolerable intake guidance based on non-cancer end-points observed at lower doses is considered protective for carcinogenicity.<sup>1</sup>

## Health effects

- Short-term exposure to high levels of dioxins and dioxin-like substances in occupational settings or following industrial accidents or poisonings may cause skin lesions known as chloracne, which is persistent; children may be particularly sensitive.<sup>1,2</sup>
- Based on the results of epidemiological studies and investigations in animals, longer-term exposure causes a range of toxicities, including reproductive, developmental and neurodevelopmental effects (especially impaired semen quality), altered male-to-female birth ratios, immunotoxicity, and effects on thyroid hormones, liver and tooth development. The most sensitive life stage is considered to be the fetus or neonate. Guidance values have been based on reproductive and developmental effects.<sup>1,2,4,5</sup>
- Dioxins and dioxin-like substances were carcinogenic in a range of experimental animal species, inducing tumours at multiple sites. Epidemiological studies in populations occupationally or accidentally exposed to TCDD also indicate human carcinogenicity at multiple sites combined. The International Agency for Research on Cancer (IARC) classified TCDD in Group 1 (*carcinogenic to humans*) based on sufficient evidence in humans and experimental animals. Likewise, 2,3,4,7,8-pentachlorodibenzofuran and 3,3',4,4',5-pentachlorobiphenyl (PCB 126) have been classified in Group 1, based on sufficient evidence in animals and strong evidence of a common mechanism of action as TCDD, involving initial binding to the aryl hydrocarbon receptor and subsequent events. In addition, IARC indicated that there is compelling evidence that the mechanism of action for TCDD-induced cancer in humans operates for numerous other dioxins and dioxin-like substances.<sup>6</sup> Dioxin-like PCBs with a TEF according to WHO (i.e. PCBs 77, 81, 105, 114, 118, 123, 126, 156, 157, 167, 169, 189) as a group were classified in Group 1 (*carcinogenic to humans*) in 2016.<sup>19</sup>
- Dioxins and dioxin-like substances were not directly genotoxic in a wide range of standard assays.<sup>2</sup>

## Risk mitigation recommendations

### ***Inventory and reduce emissions***

- Inventory emissions of dioxins and dioxin-like substances; guidance on inventory development and analysis of current inventories regionally and globally is available.<sup>12,15</sup> Countries should develop local inventories based on guidance for the identification and quantification of dioxin and furan releases.<sup>12</sup>
- Reduce emissions of dioxins and dioxin-like substances as required under the Stockholm Convention on Persistent Organic Pollutants,<sup>3</sup> following guidance on best available techniques and practices.<sup>20</sup>
- Incineration at high temperatures with long residence times and adequate mixing is required to reduce emissions of dioxins and dioxin-like substances. An inventory of suitable incineration facilities globally has been prepared.<sup>21</sup>

### **Disposal**

- Follow global guidelines for the identification of PCBs in materials and equipment to inform local actions.<sup>15</sup>
- Clean up and safely dispose of industrial waste containing PCBs and PCDFs (or likely to generate PCDDs). Routine rehabilitation of contaminated sediments is not recommended. The necessity for environmental cleanup should be decided through risk assessment on a case-by-case basis.
- Guidance is available on the disposal of health-care waste.<sup>13,14</sup>
- Further develop international programmes for disposal to aid countries without suitable waste management facilities.

### **Reduce contamination in food**

- Apply strategies developed by WHO/FAO to reduce contamination in food and feed. Countries should develop and implement local strategies.<sup>11</sup>

### **Monitoring**

- Monitor PCDDs, PCDFs and PCBs in food items and human milk. WHO has been involved in such monitoring since 1976, and this is properly done at the international level.<sup>10,22</sup> These more cost-effective international surveys should precede costly chemical analysis in individual developing countries.
- Monitor PCDDs, PCDFs and PCBs in air. The United Nations Environment Programme (UNEP) has published methodology to support the Global Monitoring Plan (GMP) on Persistent Organic Pollutants under the Stockholm Convention.<sup>23</sup>
- Monitor exposures to PCDDs, PCDFs and PCBs in representative groups of workers likely to be exposed at higher than background levels.

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