Guidance on analysis of polychlorinated dibenzodioxins and dibenzofurans in technical active constituents

Introduction

Polychlorinated dibenzodioxins and dibenzofurans (PCDDs and PCDFs) are microimpurities formed as byproducts during the manufacture of certain chlorinated aromatic compounds.

Figure 1: General structure of polychlorinated dibenzo-p-dioxins (PCDDs), showing numbering for chlorine atom substituents

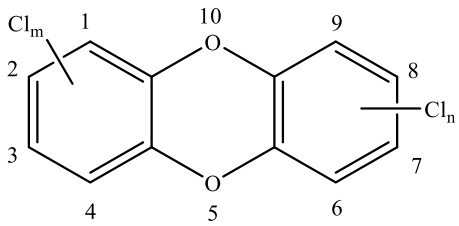
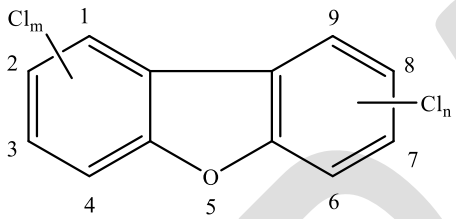
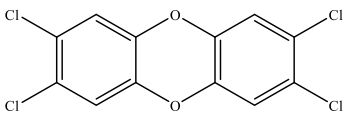
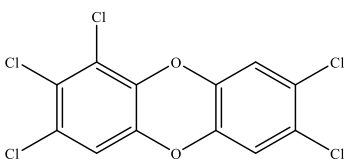


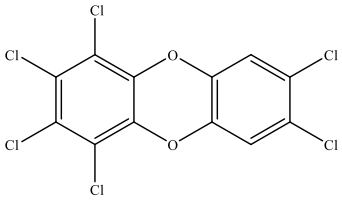
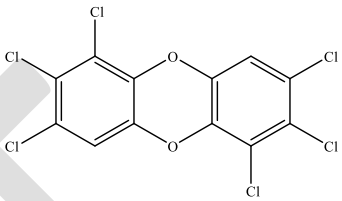
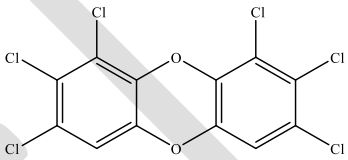
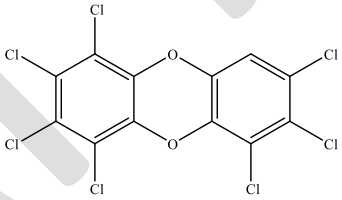
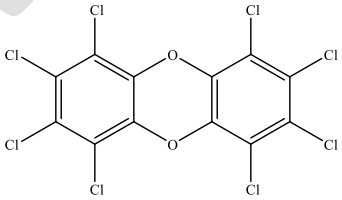
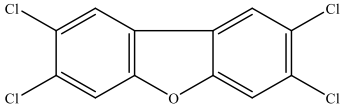
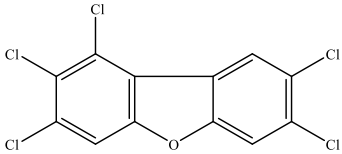
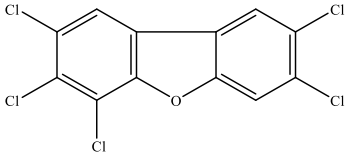
Figure 2: General structure of polychlorinated dibenzofurans (PCDFs), showing numbering for chlorine atom substituents

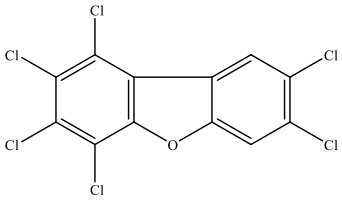
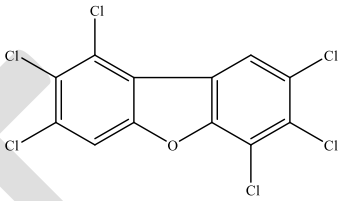
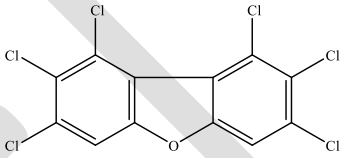
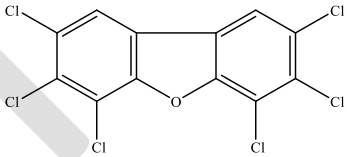
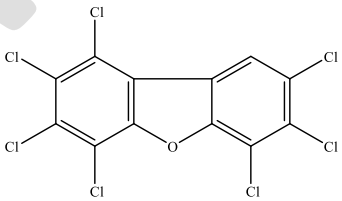
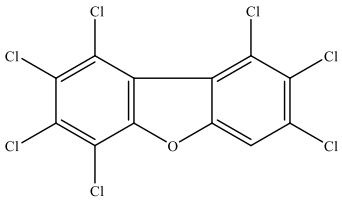
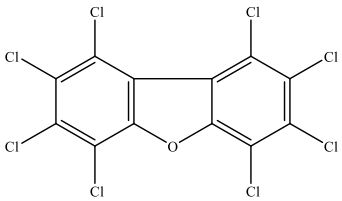


There are 75 possible congeners of PCDDs and 135 possible PCDF congeners. Only those with chlorine atoms in the 2, 3, 7, and 8 positions are of toxicological significance, giving a total of 17 congeners (seven of PCDDs and 10 of PCDFs) of interest. Their structures are tabulated in Table 1, along with their toxicological equivalence factors.

Table 1: The 17 toxicologically significant polychlorinated dibenzodioxin (PCDD) and polychlorinated dibenzofuran (PCDF) congeners

Name	Toxicological equivalence factor (TEF)—2005 WHO values	Structure
Polychlorinated dibenzodioxins (PCDDs)		
2,3,7,8-tetrachlorodibenzo-p-dioxin	1	
1,2,3,7,8-pentachlorodibenzo-p-dioxin	1	

Name	Toxicological equivalence factor (TEF)—2005 WHO values	Structure
1,2,3,4,7,8-hexachlorodibenzo-p-dioxin	0.1	
1,2,3,6,7,8-hexachlorodibenzo-p-dioxin	0.1	
1,2,3,7,8,9-hexachlorodibenzo-p-dioxin	0.1	
1,2,3,4,6,7,8-heptachlorodibenzo-p-dioxin	0.01	
Octachlorodibenzo-p-dioxin	0.0003	
Polychlorinated dibenzofurans (PCDFs)		
2,3,7,8-tetrachlorodibenzofuran	0.1	
1,2,3,7,8-pentachlorodibenzofuran	0.03	
2,3,4,7,8-pentachlorodibenzofuran	0.3	

Name	Toxicological equivalence factor (TEF)—2005 WHO values	Structure
1,2,3,4,7,8-hexachlorodibenzofuran	0.1	
1,2,3,6,7,8-hexachlorodibenzofuran	0.1	
1,2,3,7,8,9-hexachlorodibenzofuran	0.1	
2,3,4,6,7,8-hexachlorodibenzofuran	0.1	
1,2,3,4,6,7,8-heptachlorodibenzofuran	0.01	
1,2,3,4,7,8,9-heptachlorodibenzofuran	0.01	
Octachlorodibenzofuran	0.0003	

PCDDs and PCDFs are listed in Annex C of the Stockholm Convention on Persistent Organic Pollutants (Stockholm Convention 2017). Quantification of the toxicity of PCDD and PCDF congeners is achieved using Toxic Equivalence Factors (TEFs) to normalise the toxic effects

with those of 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) (WHO, 2006). Total concentrations of dioxins are thus reported as toxic equivalents (TEQs) of 2,3,7,8-TCDD.

Currently, the standards for 2,4-D, 2,4-D esters, 2,4-D sodium salt, and quintozene include maximum limits for PCDDs and PCDFs.

Analytical methods

For analysis of PCDDs and PCDFs, results must be generated by an analytical laboratory capable of determining PCDDs and PCDFs using a suitable method such as US EPA Method 1613, Revision B: Tetra – through Octa – Chlorinated Dioxins and Furans by Isotope Dilution HRGC/HRMS (US EPA, 1994).

Frequency of analysis

When seeking approval of a new source of an active constituent for which the standard specifies maximum limits for PCDDs and PCDFs, compliance of the new source with the standard should be demonstrated through analysis of batches of the technical active for PCDDs and PCDFs as part of the 5-batch analysis. In some circumstances, scientific argument may be used in conjunction with analytical results, for example through demonstrating that level of PCDDs and PCDFs are acceptable in the source of 2,4-D acid used to manufacture a 2,4-D ester.

As part of an application for registration of an agricultural chemical product where a chemistry package is provided, certificates of analysis demonstrating continued compliance of the active constituents with the APVMA standard are generally required.

The standard conditions of registration of agricultural chemical products also specify that registrants must not supply a chemical product unless they have in their possession batch analysis results that show that the active constituent contained in the chemical product comply with the relevant APVMA active constituent standard. This includes demonstrating that any impurity specified in the standard is below the relevant maximum limit.

It is recognised that the analytical methods used for determination of the low levels of PCDDs and PCDFs observed in technical active constituents require specialised equipment and skilled personnel, are available in comparatively few laboratories and are significantly more expensive than chemical analyses typically required routinely for analysis of active content and impurities in technical agricultural active constituents. It is therefore recognised by APVMA that requiring every batch of a technical active to be tested for the 17 relevant congeners of PCDDs and PCDFs would be an unreasonable burden on industry, noting the available data showing generally very low levels of these impurities in technical active constituents.

Therefore, for demonstration of compliance of a technical active constituent batch with the APVMA standard in respect of total PCDDs and PCDFs for the purpose of demonstrating compliance with the active standard for a technical active to be used in a proposed product or for complying with the conditions of product registration regarding possession of batch analysis results demonstrating compliance with the standard, there is an acceptable alternative to testing PCDDs and PCDFs for every batch of technical active constituent. The alternative is a quality control program involving periodic testing (at least every 3 months) of batches for compliance with the total PCDDs/PCDFs limit and reporting of batch testing results as a range

observed in the two years prior to manufacture of a particular batch of technical active constituent.

References

Stockholm Convention, 2017, *Stockholm Convention on persistent organic pollutions (POPs).* Text and Annexes, available at pops.int/TheConvention/Overview/TextoftheConvention/tabid/2232/Default.aspx.

US EPA, 1994, *Method 1613 – Tetra- through Octa-chlorinated Dioxins and Furans by Isotope Dilution HRGC/HRMS*, US Environmental Protection Agency (Office of Water), October 1994, available at https://well-labs.com/docs/epa_method_1613b_1994.pdf.

WHO, 2006, Van den Berg, M, Birnbaum, L, Denison, M, De Vito, M, Farland, W, Feeley, M, Fiedler, H, Hakansson, H, Hanberg, A, Haws, L, Rose, M, Safe, S, Schrenk, D, Tohyama, C, Tritscher, A, Tuomisto, J, Tysklind, M, Walker, N and Peterson, RE *Review: The 2005 World Health Organisation Re-evaluation of Human and Mammalian Toxic Equivalency Factors for Dioxins and Dioxin-like Compounds*. Toxicological Sciences 93(2): 223–241.