Triclosan and Its Impurities

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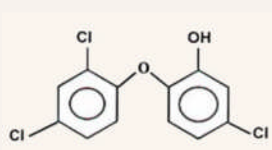
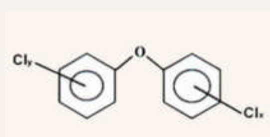
Triclosan is a broad-spectrum antibacterial/anti-microbial agent. It is manufactured in the by BASF (formerly Ciba Specialty Chemicals), under their trade name Irgasan and IrgaCare, and by several other manufacturers outside of the U.S.. As a result of its bacteriostatic activity against a wide range of both gram-negative and gram-positive bacteria it has found increasing and recent popular use in personal care products, i.e.- toothpaste, deodorant soaps, deodorants, antiperspirants and body washes, detergents, dish washing liquids, cosmetics and anti-microbial creams, lotions and hand soaps. It is also used as an additive in plastics, polymers and textiles to give these materials antibacterial properties.

Triclosan is a diphenyl ether (bis-phenyl) derivative, known as either 2,4,4'-Trichloro-2'-hydroxydiphenyl ether or 5-Chloro-2-(2,4-dichlorophenoxy) phenol. It is related in structure to a number of bis-phenyl polychlorinated and bis-phenyl chlorophenol compounds. Due principally to the synthesis chemistry of polychloro diphenyl ethers and phenoxy phenols there is the potential for the formation of small amounts of unwanted trace byproducts which are of concern. Beginning in the early 1970's and into the mid 1980's research revealed that phenoxy herbicides such as 2,4-D and 2,4,5-T (1,2,3), the major components of Agent Orange, the bactericide Hexachlorophene (4,5), various chlorophenols, i.e.-pentatchlorophenol, used in wood treatment (6), certain polychloro phenoxy phenols (7) and polychloro diphenyl ethers (8) and diphenyl ether herbicides (9) contained various low levels of polychlorinated dioxins and polychlorinated furans

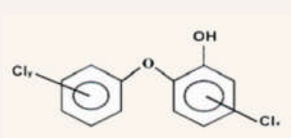
Triclosan



Polychloro Diphenyl Ether

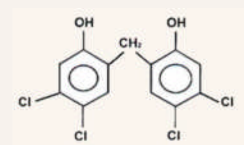


Polychloro Phenoxy Phenol



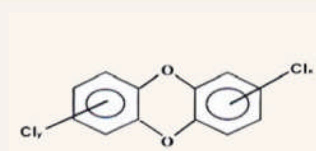
ethers (8) and diphenyl ether herbicides (9) contained various low levels of polychlorinated dioxins and polychlorinated furans.

Hexachlorophene

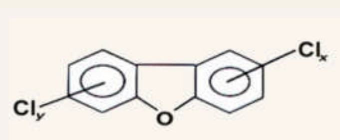


Consequently, since triclosan is by its chemical structure a polychloro phenoxy phenol it is possible that several polychlorodibenzo-p-dioxins (dioxins- and polychloro-dibenzofurans (dibenzofurans) can be found in varying low level amounts, as synthesis impurities in triclosan. Their presence or absences is dependent upon the type and purity of the starting materials used to synthesize triclosan as well as reaction conditions such as temperature, pressure and the like. If present, their relative concentrations as impurities can vary from batch to batch. This raises concerns because of the toxicity of dioxins and dibenzofurans.

Polychlorodibenzo-p-dioxins



Polychlorodibenzofurans



The toxicity of dioxins and dibenzofurans varies with the position and number of chlorine atoms attached to the aromatic rings. In general, their toxicity increases with increasing chlorine substitution. Those dioxins and dibenzofurans that have chlorine atoms at the 2,3 and 7 positions are particularly toxic. Tetrachlorodibenzo-pdioxin and tetrachlorodibenzofuran, which have chlorine

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atoms at the 2,3,7, and 8 positions, are considered the most toxic of the dioxins and dibenzofurans (4), with 2,3,7,8-tetrachlorodibenzo-p-dioxin referred to as one of the most toxic substances known.

As a result of the potential for the formation of dioxins and dibenzofurans as unwanted low level trace by-products the USP (10, 11), beginning in USP 24, issued a new monograph for the specific testing of triclosan. This monograph details the assay and testing of USP triclosan. In addition to setting product specification standards and procedures to assay the purity and physical identity of USP triclosan, it also defines the limits and methods of testing for unwanted trace by-products which may be present. The proposed tests for these unwanted byproducts are (1) Limit Test for Monochlorophenol and 2,4-Dichlorophenol, (2) Limit Test for 1,3,7-trichlorodibenzo-p-dioxin 2,8-dichlorodibenzo-pdioxin, 2,8-Dichlorodibenzofuran, and 2,4,8-Trichlorodibenzo-furan, and (3) Limit of 2,3,7,8- Tetra-chlorodibenzo-p-dioxin and 2,3,7,8-Tertrachloro-dibenzofuran.

Quantex Laboratories is currently the only commercial contract testing laboratory company in the U.S. capable of analyzing triclosan for dioxins and dibenzofurans employing isotope dilution high resolution gas chromatography/mass spectrometry (HRGC/MS), as required by the USP monograph. For those requiring the testing and certification of triclosan as meeting the proposed USP limits for unwanted trace by-products Quantex Laboratories can perform the three limit tests (1) Limit Test for Monochlorophenol and 2,4-Dichlorophenol, (2) Limit Test for 1,3,7-trichlorodibenzo-p-dioxin 2,8-dichlorodibenzo-pdioxin, 2,8-Dichlorodibenzofuran, and 2,4,8-Trichlorodibenzo-furan, and (3) Limit of 2,3,7,8-Tetra-chlorodibenzo-p-dioxin and 2,3,7,8-Tertrachloro-dibenzofuran. We can also provide the complete testing and assay of triclosan as proposed by the USP, for those requiring the certification of triclosan to USP, which includes the three limit tests, the assay of triclosan for purity, the testing for heavy metals, physical identification , melting range and residue on ignition. All analytical testing is conducted in conformance to cGMP (Good Manufacturing Practices).

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About the Authors

James Menoutis has over 34 years of experience as an analytical chemist, group leader and manager. His experience includes toxicology, methods development and analysis of botanicals, pharmaceuticals, analysis and methods development for the analysis of clinical pharmaceuticals, pesticide residue analyses, occupational health and toxicological analyses and environmental analytical methods. As a senior research analytical chemist with Givaudan he researched dioxin and dibenzofuran chemistry in hexachlorophene. He has an extensive analytical background which includes experience in isotope dilution HRGC/MS

Angela I. Parisi-Menoutis has over 36 years of experience in methods development and analysis of surfactants, quaternaries, amines, polyols, personal care products, specialty chemicals and intermediates. She spent 8 years as an R&D Group Leader with Lonza, Inc., and prior to that 7 years as an analytical chemist with Colgate Palmolive Company. Her background includes extensive expertise in mass spectral methods development and interpretation including analysis by isotope dilution HRGC/MS.

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