

IV. ENVIRONMENTAL DATA AND BIOLOGIC EVALUATION

Engineering Controls

Engineering controls must be instituted in areas where the airborne concentration of organotin dusts and vapors exceeds the TWA concentration limit, to decrease the concentration of organotins to or below the prescribed limit. Industrial experience indicates that closed-system operations are commonly used in manufacturing processes. Such systems must be used whenever feasible to control dust and vapor wherever organotin compounds are manufactured or used. Closed systems should operate under negative pressure whenever possible so that, if leaks develop, the flow will be inward. Closed-system operations are effective only when the integrity of the system is maintained. This requires frequent inspection for, and prompt repair of, any leaks.

A ventilation system may be required if a closed system proves to be impractical and is desirable as a standby if the closed system should fail. The principles set forth in Industrial Ventilation - A Manual of Recommended Practice [112], published by the American Conference of Governmental Industrial Hygienists, and Fundamentals Governing the Design and Operation of Local Exhaust Systems, Z9.2-1971 [113], published by the American National Standards Institute, should be applied to control workplace atmospheric concentrations of organotins. Ventilation systems of this type will require regular inspection and maintenance to ensure effective operation, and a program of scheduled inspection should be established in which the ventilation systems are checked routinely. These routine checks should include face velocity measurements of the collecting

hood, inspection of the air mover and collector, and measurements of workroom airborne concentrations. Any changes which may affect the ventilation system or the operations being ventilated must be assessed promptly to ensure that engineering controls provide adequate protection of employees.

Sampling and Analytical Methods

The few sampling methods described for collecting organotins in air [JM Peters, written communication, December 1975, 114-116] either are not generally suitable for collection of all the organotin compounds or are not suitable for personal monitoring. Most of the organotins are either solids or liquids. In general, techniques are well defined for sampling air for particulates [117,118] and for gases and vapors [119,120].

For collection of low-volatility solids, the membrane filter method described in NIOSH Method No. P & CAM 173 [116] will provide sufficient collection efficiency. Although no report describing a suitable collecting medium for personal monitoring of organotin vapor in air was found in the literature, activated charcoal tubes as described in NIOSH Method No. P & CAM 127 [121] would be expected to provide sufficient collection efficiency. The recommended sampling method for the determination of organotins in air consists of drawing a known volume of air through a membrane filter followed by an activated charcoal sampling tube, as described in Appendix I. Although this sampling method has not been evaluated by NIOSH, it is recommended as an interim method pending planned research by NIOSH. If this research results in the development of a better

method, the new method will be forwarded.

The analytical methods appropriate for the determination of the greatest number of organotin compounds generally do not distinguish between different organotins which may be present in the sample. Total tin in all the organotin compounds in the sample is usually determined, although certain classes of organotins may be determined by use of specific techniques such as chromatography or solvent extraction to separate compounds or types of compounds.

Where determination of a specific organotin compound is required, separation techniques which may be useful include thin-layer chromatography [122-124], column chromatography [125], and paper chromatography [126-130]. Sample preparation techniques which have been applied to the analysis of various organometallic compounds include oxygen-flask or wet combustion [131] and use of hydrogen peroxide to destroy organic matter [132]. After separation and sample preparation, a quantitative determination of the organotins or of tin is performed. Personal monitoring to evaluate concentrations of organotin in air, to determine compliance with this recommended standard, requires an analytical method which will quantitatively determine amounts of tin in the range of 1 μg or less in the total sample.

Colorimetric methods have been most generally applied to the determination of organotins or of tin following breakdown of the organotins. Reagents used for analysis of organotins or of tin include dithizone (1,5-diphenylthiocarbazone) [133-136], dithiol (toluene-3,4-dithiol) [137-140], phenylfluorone [114], and pyrocatechol violet (catechol violet) [141-144], as well as quercetin [145,146], oxine (8-quinolinol)

[147,148], 4-(2-pyridylazo)resorcinol (PAR) [149], and diphenylcarbazone [150]. A molybdenum blue method also has been described [151]. Since colorimetric reagents usually lack specificity [137], efficient separation of organotins may be required prior to measurement.

Use of dithizone for the colorimetric determination of organotins has been described by Chapman et al [133], Aldridge and Cremer [134], Hardon et al [135], and Chromy and Uhacz [136]. Chapman et al [133] applied the dithizone method to the determination of dibutyltin and dioctyltin compounds in polyvinyl chloride, as well as diethyltin dichloride, dibutyltin dilaurate, and diphenyltin dichloride. Aldridge and Cremer [134] described a method for the separation of mixtures of diethyltin dichloride and triethyltin sulfate, with subsequent colorimetric determination with dithizone. Hardon et al [135] presented a method for the determination of triphenyltin acetate residue on celery. Chromy and Uhacz [136] discussed the use of dithizone for the determination of microgram amounts of bis(tri-n-butyltin) oxide and tri-n-butyltin acetate in aqueous solutions. No report describing the use of dithizone for the analysis of air samples has been found. About 5 μg of tin in a sample is the minimum amount which may be quantitatively determined by the dithizone method.

The dithiol colorimetric reagent has been used by Corbin [137] and by Trombetti and Maini [138] for the determination of trace amounts of tin present as organotin residues on fruit sprayed with Plictran, a miticide containing tricyclohexyltin hydroxide. Farnsworth and Pekola [139,140] used dithiol for the determination of small amounts of tin in several materials, including various methyltins, butyltins, phenyltins, and

lauryltins. Tin in organotins can be determined to a lower limit of about 2 μg by methods using the dithiol reagent [137].

Two of the more sensitive colorimetric reagents are phenylfluorone (2,3,7-trihydroxy-g-phenylfluorone) [114] and pyrocatechol violet (catechol violet) [141-145,152]. Selivokhin [114] reported the use of phenylfluorone for the determination of tetraethyltin and tetrabutyltin in factory air. The sensitivity was given as 0.1 μg of tin in the sample. Use of pyrocatechol violet for the determination of an organotin compound identified by the authors as dioctyltin S,S'-bis(isooctylmercaptoacetate), in the range of 0.2-1.6 μg of tin, was described by Adcock and Hope [141]. Thomas and Tann [142] described a method using pyrocatechol violet for the determination of triphenyltin hydroxide and triphenyltin acetate pesticide residues in potatoes. The limit of detection for tin as determined by this method was given as 0.5 μg . In a pyrocatechol violet method for the determination of tin presented by Corbin [143], a plot of absorbance against micrograms of tin was reported to deviate from linearity at quantities below 0.5 μg of tin in 50 ml of final solution.

In a report of work for the Metallic Impurities in Organic Matter Sub-Committee of the Analytical Methods Committee, Newman and Jones [153] presented a method for the selective extraction of tin(IV) iodide from a sulfuric acid solution into toluene. The tin(IV) was then determined by spectrophotometric measurement of the color of the complex formed between tin(IV) and pyrocatechol violet. No significant interference was found in tests made with a wide variety of anions and cations in which the ions under investigation were added to sulfuric acid solutions containing 20 μg of tin(IV). The ions which have shown no interference at the indicated

level are: Be, Ba, Cd, Hg(I), Hg(II), La(III), Ce(III), Ce(IV), Ti(IV), Th(IV), Ge(IV), Pb, As(III), As(V), Sb(III), Sb(V), Se(V), Bi, Cr(III), Cr(VI), Mo(VI), W(VI), U(VI), Mn(II), Co, Ni, Cu, Zn, and Fe(II) (100 μg); fluoride, chloride, nitrate, and pyrophosphate (1 mg); and Mg, Al, Fe(III), borate, orthophosphate, and citrate (5 mg). Since this method was found to be specific for tin in the presence of a wide variety of other metals and several anions, it should be applicable to the determination of tin in organic matter after wet decomposition in which a sulfate residue is produced. Recoveries of known amounts of tin analyzed by this procedure ranged from 96.0 to 101.0% with amounts of tin ranging from 5 to 30 μg . The calibration graph obtained by this pyrocatechol violet method was linear over the range of 0 to 1.2 μg of tin per ml.

The Metallic Impurities in Organic Matter Sub-Committee of the Analytical Methods Committee recommended the pyrocatechol violet colorimetric method for determination of amounts of tin up to 30 μg and suggested a dithiol colorimetric method for amounts of tin in the range of 30-150 μg [144]. No report on the use of pyrocatechol violet for the analysis of organotin compounds in air samples has been found. However, since quantities of tin collected in air samples may be in the vicinity of 1 μg or less, the pyrocatechol violet method offers sufficient sensitivity for evaluation of environmental samples to determine compliance with this standard. Although the color reaction between tin(IV) and pyrocatechol violet may not be completely selective [144], a separation of organotin compounds from interfering substances by chromatographic or solvent-extraction techniques would allow a specific determination.

Several analytical methods which have been used for the determination of tin do not possess the required sensitivity for the determination of organotins in the occupational environment, or the methods require tedious laboratory techniques or equipment not generally available. Chromatographic techniques used for separation of organotins have generally been followed by an appropriate sensitive colorimetric method such as pyrocatechol violet or phenylfluorone for quantitative determination of tin in the organotins identified.

Gas chromatography [115,126,145,154] has been used for the quantitative determination of various organotins. Only one report was found in which gas chromatography was applied to the analysis of air samples [115]. In this study, bis(tributyltin) oxide was collected on glass-fiber filters. A high-volume sampler was used to collect the tin compound from general workplace air. Following extraction with toluene, pyrolysis gas chromatography was used for analysis, since conventional gas chromatography of bis(tributyltin) oxide was unsuccessful. Gas chromatographic analysis has been applied to the determination of butyltin, octyltin, and phenyltin halides [154]. Under the analytical conditions used in this study, disproportionation did not occur, as shown by the absence of peaks associated with disproportionation products on the chromatogram. However, Franc et al [126] found that disproportionation was a problem which made gas chromatography unsuitable for the quantitative determination of some organotin mixtures.

Other chromatographic techniques have been used for the separation and identification of various organotins. Separation techniques have included thin-layer chromatography [122-124,145,155], paper chromatography

[126-130], and column chromatography [125].

Analytical methods, other than colorimetric or chromatographic techniques, which have been applied to the determination of tin include fluorimetric [156], polarographic [157,158], spectrographic [159,160], gravimetric [140,161], and atomic absorption [115,116,146,162,163] techniques. Generally, such techniques have not been applied to analysis of organotins in air; some have been applied predominantly to analysis of inorganic tin.

Vernon [156] presented a method for the determination of residues of triphenyltin compounds resulting from the treatment of potatoes with triphenyltin fungicides. The analytical method used the fluorimetric measurement of the triphenyltin moiety resulting from complex-formation with 3-hydroxyflavone. Recoveries averaging about 90% were obtained from potato samples to which 1 μg of tin as triphenyltin had been added. The limit of detection of this fluorimetric method was given as 0.16 μg of tin, with a standard deviation of $\pm 5.7\%$.

Atomic absorption spectrophotometric methods have been applied to the determination of tin in several types of samples. However, no study was found in which air samples obtained by personal monitoring were analyzed by atomic absorption. Jeltos [115] reported the determination of bis(tributyltin) oxide in high-volume air samples collected on glass-fiber filters. Following extraction of the filters with methylisobutyl ketone, the samples were analyzed by atomic absorption. To obtain a measure of filter efficiency for the collection of bis(tributyltin) oxide, sampling was done through two glass-fiber filters in series. More than 99% of the bis(tributyltin) oxide collected was obtained on the first filter. The

analytical sensitivity was not stated, but the determination of milligram quantities of bis(tributyltin) oxide was reported.

An atomic absorption analytical method for the determination of tin was applied to the analysis of several metallurgical samples by Capacho-Delgado and Manning [162]. The sensitivity for tin was about 1 ppm for 1% absorption, and the detection limit was about 0.1 ppm in a water solution.

Atomic absorption was found to be satisfactory for the determination of dibutyltin dilaurate in poultry feed formulations [163]. Essentially, theoretical recovery was obtained in formulations with dibutyltin dilaurate concentrations from 0.02 to 0.0375%. The authors stated that the method applies to feeds with dibutyltin dilaurate concentrations from 0.02 to 0.14%.

Engberg [146] reported that atomic absorption was satisfactory for the determination of tin in canned food, but the colorimetric method using quercetin (3,5,7,3',4'-pentahydroxyflavone) was preferred for very low tin concentrations, such as residues of organotin compounds. Amounts of tin as low as about 40 μg were quantitatively determined by atomic absorption.

In NIOSH Analytical Methods No. P & CAM 173 [116], a sensitivity of 5 $\mu\text{g}/\text{ml}$ is given for the determination of tin. While this may be sufficient for some general workplace air samples, a more sensitive method is needed for personal monitoring.

Few of the methods described in the literature possess the required accuracy and sensitivity to quantitatively determine amounts of tin of less than 1 μg in an air sample as required to determine compliance with this standard. The two methods found which possess the required sensitivity were colorimetric methods using phenylfluorone [114] and pyrocatechol

violet [143,153]. Tin(IV) produces a colloidal system with phenylfluorone rather than a water-soluble type of complex such as that produced by tin(IV) with pyrocatechol violet. The water-soluble property allows the use of simpler manipulative techniques [153].

The pyrocatechol violet method is generally available to industry, requires no highly specialized laboratory equipment, and has been shown to provide sufficient accuracy, sensitivity, and precision within the range required to determine compliance with this standard for all organotins. For analysis of specific organotins, any method shown to be equivalent or superior in accuracy, sensitivity, and precision may be used.

Because of its high sensitivity and the general availability of the required analytical reagents and equipment, the pyrocatechol violet method described in Appendix II is the recommended analytical technique for determination of organotins, measured as tin. If the determination of a specific organotin compound is required, it will be necessary to separate that compound from other components prior to analysis. NIOSH has not evaluated this method for the analysis of samples of organotins collected from air but believes that it should be satisfactory on the basis of published reports of its use in the analysis of solutions. If research now underway by NIOSH determines that a better method can be devised, the improved methodology will be provided.

Biologic Evaluation

Experimental techniques for analysis of animal urine and feces have been developed [86] and may have potential use in monitoring employee

exposure to organotin compounds.

Bridges et al [86] described a spectrophotometric method for the determination of organotins as tin in biologic samples. Total tin was determined by treating urine or homogenized feces with concentrated sulfuric acid followed by an excess of nitric acid. The solution was heated until sulfur trioxide fumes appeared, then it was cooled and reheated. Dithiol was then added, and the resulting red color was measured at 530 nm with a spectrophotometer. The limit of sensitivity of the test was reported to be 5 μg of tin/ml of sample.

A colorimetric method has been described by Aldridge and Cremer [134] for the separation and determination of diethyltin and triethyltin compounds. The test involved the formation of a dithizone complex with diethyltin or triethyltin. The dithizone-diethyltin complex had an absorption maximum at 510 nm in the presence of borate buffer. With triethyltin, maximum absorption was at 440 nm in the presence of borate buffer at pH 8.4, whereas maximum absorption occurred at the same wavelength (510 nm) for both the triethyltin-dithizone complex and dithizone alone in the presence of trichloroacetic acid. This method has been used successfully in the analysis of bile samples from rats for diethyltin by Bridges et al [86], who reported recovery of $96 \pm 5\%$. However, the method was found to be unreliable with urine samples. The applicability of this test to other organotin compounds needs to be determined.

The fluorimetric determination of monoethyltin in urine and bile samples has been used by Bridges et al [86]. The monoethyltin-(3-hydroxyflavone) complex is formed in the presence of sulfuric acid, and the

intensity of fluorescence at 445 nm is measured. The presence of phosphate ions interferes with the fluorescence, but this can be allowed for by the use of an internal standard.

V. DEVELOPMENT OF STANDARD

Basis for Previous Standards

Standards for organotin compounds have been established primarily to regulate the use of organotin additives in packaging materials for foods and beverages and to prevent occupational exposure of employees. As the first of many standards for the use of organotins in packaging materials, the Federal Food, Drug, and Cosmetic Act was amended in 1963 to allow the introduction of dibutyltin dilaurate in silicone polymer solids in amounts not to exceed 1 part of tin/100 parts of silicone polymer [Federal Register 28:7777, July 31, 1963]. Silicone polymers are used in the formulation of resinous and polymeric coatings in packaging materials which can be expected to come in contact with food products. A subsequent amendment to the Act allowed the use of di-n-octyltin S,S'-bis(isooctylmercaptoacetate) in vinyl chloride plastics. The amount of octyltin was limited to 15.1-16.4% by weight of tin and 8.1-8.9% by weight of mercapto sulfur. The amount of dioctyltin dichloride (if used in the synthesis of the mercaptoacetate derivative) was specified to be not less than 95% dichloride, not more than 5% trichloride derivative, not more than 0.2% isomers of dioctyltin, and not more than 0.1% for the higher and lower homologues of the octyltin. The Food and Agricultural Organization and World Health Organization have jointly recommended residue limits of 2 ppm for apples and pears, 0.2 ppm for meat, and 0.05 ppm for milk (fat bases) [164] and an acceptable daily intake for men of 0-0.0075 mg/kg body weight for the pesticide tricyclohexyltin hydroxide [165].

In 1965, the American Conference of Governmental Industrial

Hygienists (ACGIH) [166] established a threshold limit value (TLV) of 0.1 mg/cu m, measured as tin, for all organotin compounds in the occupational environment. The 1971 Documentation of the Threshold Limit Values for Substances in Workroom Air [167] by the ACGIH placed the TLV at 0.1 mg/cu m, measured as tin, by analogy with mercury, selenium, and thallium because of a lack of pertinent data. Only the TLV's for selenium and mercury were based on prolonged exposures of animals [167]. In 1973, the ACGIH [168] listed a proposed TLV for tricyclohexyltin hydroxide (Plictran) of 5 mg/cu m (1.2 mg/cu m, measured as tin). This standard was adopted in 1975.

The German Democratic Republic listed an NPK (maximum allowable concentration) for organotins of 0.1 mg/cu m [38]. No justification for this level was given. Rumania and Yugoslavia list maximum allowable concentrations of 0.1 mg/cu m, and these are based on the 1966 Documentation of TLV's of the ACGIH [169]. The level listed by Yugoslavia is measured as tin. Rumania does not state this qualification, but it is assumed that measurement is as tin.

The current federal standard, 29 CFR 1910.1000, is a TWA concentration limit of 0.1 mg/cu m, measured as tin. This is based on the ACGIH TLV established in 1965.

Basis for the Recommended Standard

Available reports on occupational exposure to the organotin compounds were descriptions of signs and symptoms of exposure. Only in the studies by Peters (written communication, December 1975) and Landa et al [38] were attempts made to relate the observed effects to the air concentration of

organotins. Landa et al [38] observed eye and upper respiratory tract irritation from bis(tributyltin) oxide (TBTO) at an average air concentration of 0.05 mg/cu m, measured as tin. However, since readings fluctuated at the limit of sensitivity of the analytical method (0.1 mg/cu m, as tin), the average concentration of 0.05 mg/cu m cannot be considered accurate. From data obtained by a questionnaire, Peters (written communication, December 1975) concluded that eye and upper respiratory tract irritation developed in employees exposed to TBTO at concentrations reported to be below the current TLV, but he did not provide any supportive information. Possible bias in the questionnaire was not accounted for in the report, nor was sufficient information on the sampling and analytical method provided to permit assessment of the accuracy of the reported air concentration. Because of its incompleteness, the report is of use only as an indicator of the irritative properties of the organotins at low concentrations.

Most of the animal data available was based on oral administration, and such studies are useful only in determining the type of effects that may occur from organotin exposure. Of the inhalation studies found, only one dealt with organotin air concentrations near the current TWA concentration limit of 0.1 mg/cu m, as tin; the only effect reported at this concentration was a "less than normal" weight gain in rats after a 4-hour exposure [53]. Other inhalation studies were performed at air concentrations well above the current standard and therefore do not provide information for assessing organotin toxicity at the current standard.

Human and animal toxicity data neither support nor negate the current federal standard, which was set by analogy with mercury, selenium, and

thallium. NIOSH therefore recommends that the current standard of 0.1 mg/cu m, as tin, as a TWA concentration limit be retained for all organotin compounds until more definitive information has been obtained. NIOSH recognizes that the organotins are of varied toxicity and hazard and that a single standard, as recommended, may be unnecessarily restrictive for many of the organotins. However, because of the lack of adequate data to evaluate the health hazard of the individual compounds to which employees may be exposed, and because of the absence of a sampling and analytical method which can quantitatively separate and identify the individual components of an organotin mixture in the working environments, there is no practical alternative.

Peters (written communication, December 1975) observed irritation of the eyes and of the respiratory tract in employees exposed to TBTO at concentrations reported to be at or near the recommended TWA concentration limit. Together with demonstrated systemic effects in humans with exposure to unknown concentrations of organotins [34-36], a need for a medical surveillance program is indicated. This program should include preemployment examinations and annual physical examinations to ensure adequate protection for the employee. An emergency medical examination should be required within 24 hours of overexposure to any organotin compound, with an appropriate followup examination. Personnel at risk must be warned of the adverse effects of overexposure and must be informed of the symptoms of these disorders. If eye contact occurs, the affected eye should be immediately flushed with water and examined by a physician.

Where triorganotins and tetraorganotins are present, a closed system of control must be used whenever feasible and should be used with

diorganotins and monoorganotins to control airborne concentrations of organotins within the TWA concentration limit. If a closed system is not feasible, other forms of engineering controls, such as local exhaust ventilation, must be used whenever feasible. Where engineering controls are not feasible, respirators and protective clothing must be used to prevent overexposure to organotins. During the time required to install adequate controls and equipment, to make process changes, to perform routine maintenance operations, or to make repairs, overexposure to organotins must be prevented by the use of respirators and protective clothing. Work practices must be designed to prevent skin and eye contact. Emergency showers and eyewash fountains must be available in case of accidental contact.

Because organotins are potent systemic poisons, it is recommended that medical records be maintained for the duration of employment plus a minimum of 5 years. Personnel records, which are of vital importance in assessing a worker's exposure, should be maintained for the same period.

Many employees handle only small amounts of the organotin compounds or work in situations where, regardless of the amount used, there is only negligible contact with these compounds. Under these conditions, it should not be necessary to conduct extensive monitoring and surveillance. However, because many of the organotins have proved to be highly irritating to the skin and eyes at low concentrations, care must be exercised to ensure adequate protection against these effects where the potential for exposure to organotin compounds exists. Concern for employee health requires that protective measures be instituted at concentrations at or below the workplace environmental limit to ensure that exposures stay below

that limit. For this reason, occupational environments with concentrations at or below the action level require environmental monitoring once every year. When concentrations are above the action level, more frequent environmental monitoring is required.