Ziram

Method number:	PV2073
Matrix:	Air
Target concentration:	0.4 mg/m^3 (arbitrary). No OSHA (PEL) or ACGIH (TLV)
Procedure:	Samples are collected by drawing known volumes of air through OSHA versatile sampler (OVS-2) tubes, each containing a glass fiber filter and two sections of XAD-2 adsorbent. Samples are desorbed with chloroform and analyzed by high performance liquid chromatography (HPLC) using an ultraviolet (UV) detector.
Recommended air volume and sampling rate:	180 Liters at 1.0 L/min (180 minutes)
Detection limit of the overall procedure:	0.01 mg/m^3 (based on the recommended air volume and the analytical detection limit)
Status of method:	Partially validated method. This method has been partially evaluated and is presented for information and trial use only.

June 1989 (final)

Duane Lee

Carcinogen and Pesticide Branch
OSHA Salt Lake Technical Center
Salt Lake City UT

1 General Discussion

1.1 Background

1.1.1 History of procedure

The OSHA Analytical Laboratory received a set of samples requesting the analysis of ziram. The samples had been collected on OVS-2 tubes. This report describes the analytical method developed for ziram.

1.1.2 Toxic effects (This section is for information only and should not be taken as the basis for OSHA policy.)

The oral LD_{50} of ziram is 150 mg/kg in guinea pigs, 480 mg/kg in mice, 1400 mg/kg in rats, and 400 mg/kg in rabbits. The intraperitoneal LD_{50} of ziram is 73 mg/kg in mice, 23 mg/kg in rats and 50 mg/kg in rabbits. Studies have been done on mice and rats to determine the carcinogenicity of ziram. The data available is inadequate to make a determination. (Ref. 5.1 and 5.2)

1.1.3 Potential workplace exposure

Ziram is used in various applications. One application found ziram to be useful as a fungicide in 1944. It is registered in the U.S. for use on 24 fruits, vegetable crops, and ornamental flowers. Another application of ziram is as an accelerator or promoter in the rubber-processing industry. In addition, small amounts of ziram are used in industrial fungicides in combination with 2-mercaptobenzothiazole. In 1973, ziram was produced in the U.S. by eight companies whose combined production amounted to 1 million kg. No estimate of worker exposure could be found. (Ref 5.1)

1.1.4 Physical properties (Ref. 5.1 to 5.4)

CAS number:	137-30-4
IMIS number:	D126
Molecular weight:	305.81
Melting point:	250 °C (crystals); 148 °C (dust)
Solubility:	Practically insoluble in water; soluble at 0.2 g or less per 100 mL for carbon tetrachloride, diethyl ether and ethanol; soluble at 0.5 g or less per 100 mL for benzene, acetone, naphtha and other non-polar solvents; soluble in chloroform
Chemical name:	Bis(dimethyldithiocarbamato)zinc
Chemical formula:	$C_6H_{12}N_2S_4Zn$
Synonyms:	Bis(dimethyldithiocarbamato-S,S')zinc; Antene; Carbazinc; Corset; Human; Drupina 90; Fuclasin; Ultra; Fuklasin; Fungostop; Hexazir; Mezene; Tricarbamix; Triscabol; Zerlate; Zincmate; Ziram Technical; Ziramvis; Zirasan 90; Zirberk; Zirex 90.
Description:	White powder or crystals

UV Scan: Figure 1

1.2 Limit defining parameters

The detection limit of the analytical procedure is 2.1 ng per injection. This is the amount of analyte which will give a peak whose height is approximately five times the baseline noise.

2 Sampling Procedure

2.1 Apparatus

2.1.1 A personal sampling pump that can be calibrated within ±5% of the recommended flow rate with the sampling device in line.

2.1.2 OVS-2 tubes, which are specially made 13-mm o.d. glass tubes that are tapered to 6-mm o.d., packed with a 140-mg backup section, a 270-mg sampling section of cleaned XAD-2 adsorbent, and a 13-mm diameter glass fiber-filter. The backup section is retained by two foam plugs and the sampling section is between one foam plug and the glass fiber filter. The glass fiber filter is held next to the sampling section by a polytetrafluoroethylene (PTFE) retainer. (Figure 2)

2.2 Reagents

No sampling reagents are required.

2.3 Sampling technique

2.3.1 Immediately before sampling, remove the plastic caps from the OVS-2 tube.

2.3.2 Attach the small end of the tube to the sampling pump with flexible tubing.

2.3.3 Attach the tube vertically in the employee's breathing zone in such a manner that it does not impede work performance or safety.

2.3.4 After sampling for the appropriate time, remove the tube and seal with plastic caps.

2.3.5 Wrap each sample end-to-end with a Form OSHA-21 seal.

2.3.6 Record the air volume for each sample, and list any possible interference.

2.3.7 Submit at least one blank for each set of samples. Handle the blank in the same manner as the samples, except no air is drawn through it.

2.3.8 Submit bulk samples for analysis in a separate container. Do not ship with air samples.

2.4 Desorption efficiency (glass fiber filter and XAD-2 adsorbent)

Six vials each containing a 13-mm glass fiber filter and 270-mg of XAD-2 adsorbent were each liquid spiked on the glass fiber filter with 18 µL of a 4.05 mg/mL solution of ziram. These samples were allowed to equilibrate overnight in a drawer at ambient temperature. The next day each sample was desorbed with 2.0 mL of chloroform, shaken for 30 min, and analyzed as in Section 3. The results are listed in Table 2.4.

Table 2.4.
Ziram Desorption Efficiency

sample #	µg spiked	µg found	% recovered
1	72.90	64.12	88.0
2	72.90	64.24	88.1
3	72.90	64.99	89.1
4	72.90	64.66	88.7
5	72.90	64.62	88.6
6	72.90	65.06	89.2

average = 88.6%

2.5 Retention efficiency

Eighteen OVS-2 tubes were each liquid spiked with 18 µL of a 4.05 mg/mL solution of ziram by spiking the glass fiber filter. These were allowed to equilibrate overnight in a drawer at ambient temperature. The next day 180 L of humid air (~80% RH) were drawn through each tube at 1.0 L/min. Six of the tubes were each desorbed with 2.0 mL of chloroform, shaken for 30 min and then analyzed as in Section 3. The results are listed in Table 2.5. No ziram was found on the backup sections of these tubes. The remaining samples were stored, six in a drawer at ambient temperature and six in a freezer, for use in the storage study below.

Table 2.5.
Ziram Retention Efficiency

sample #	µg spiked	µg found	% recovered
1	72.90	62.19	85.3
2	72.90	63.55	87.2
3	72.90	59.38	81.5
4	72.90	57.19	78.4
5	72.90	59.08	81.0
6	72.90	58.89	80.8

average = 82.4%

2.6 Sample storage

After nine days of storage, the 12 tubes were each desorbed with 2.0 mL of chloroform, shaken for 30 min and then analyzed as in Section 3. The results are given in Tables 2.6.1 and 2.6.2.

Table 2.6.1.
Ziram Storage Study

days stored	ambient storage		% recovered
	µg spiked	µg found	
9	72.90	67.03	91.9
9	72.90	60.26	82.7
9	72.90	58.48	80.2
9	72.90	57.96	79.5
9	72.90	58.62	80.4
9	72.90	60.55	83.1

average = 83.0%

Table 2.6.2.
Ziram Storage Study

days stored	freezer storage		% recovered
	µg spiked	µg found	
9	72.90	70.69	97.0
9	72.90	62.19	85.3
9	72.90	72.04	98.8
9	72.90	60.93	83.6
9	72.90	63.25	86.8
9	72.90	61.58	84.5

average = 89.3%

2.7 Recommended air volume and sampling rate

2.7.1 The recommended air volume is 180 L.

2.7.2 The recommended flow rate is 1.0 L/min.

2.8 Interferences (sampling)

It is not known if any compounds will interfere with the collection of ziram. Any suspected interferences should be reported to the laboratory.

2.9 Safety precautions (sampling)

2.9.1 Attach the sampling equipment in such a manner that it will not interfere with work performance or employee safety.

2.9.2 Follow all safety practices that apply to the work area being sampled.

3 Analytical Procedure

3.1 Apparatus

3.1.1 An analytical balance capable of weighing to the nearest tenth of a milligram. A Mettler HL52 balance was used in this evaluation.

3.1.2 A mechanical shaker.

3.1.3 A high performance liquid chromatograph (HPLC) equipped with an ultraviolet (UV) detector. A Hewlett Packard (HP) 1090M equipped with an autosampler and diode array detector was used in this evaluation.

3.1.9 An HPLC column capable of separating ziram from any interference. A 50-mm x 4.6- mm i.d. ECON C_8 (3 µm) liquid chromatography column was used in this evaluation.

3.1.5 An electronic integrator, or some other suitable means for measuring detector response. The Hewlett-Packard 1090M Data System was used in this evaluation.

3.1.6 Volumetric flasks and pipettes.

3.1.9 Vials, 2-mL and 4-mL with PTFE-lined caps.

3.2 Reagents

3.2.1 Chloroform, reagent grade. This was obtained from Burdick and Jackson for this evaluation.

3.2.2 Ziram, reagent grade. A standard obtained from EPA (EPA # 7100, 98% purity) was used in this evaluation.

3.2.3 Methanol, reagent grade. This was obtained from Burdick and Jackson for this evaluation.

3.2.4 Water, HPLC grade.

3.2.5 Zinc sulfate heptahydrate ($ZnSO_4 \cdot 7H_2O$) reagent grade. This was obtained from Mallinckrodt for this evaluation.

3.2.6 4-Dodecyldiethylenetriamine, reagent grade. This was obtained from Eastman Kodak for this evaluation.

3.2.7 Ammonium acetate, HPLC grade. This was obtained from Fisher Scientific for this evaluation.

3.2.8 Zinc chelate (10 mM) of the C_{12}-dien-Zn (II) metal chelate. This was prepared by placing 2.71 grams of 4-dodecyldiethylenetriamine and 2.87 grams of $ZnSO_4 \cdot 7H_2O$ in a liter flask and diluting to volume with water.

3.3 Standard preparation

3.3.1 Stock standard - Prepare ziram stock standards by weighing 10 to 15 mg of ziram. Transfer the ziram to separate 10-mL volumetric flasks, and add chloroform to the mark.

3.3.2 Working standards - Make working range standards from 1.0 to 105 µg/mL by pipette dilutions of the stock standards with chloroform. Store stock and dilute standards in a freezer.

3.4 Sample preparation

3.4.1 Transfer the 13-mm glass fiber filter and the 270-mg sampling section of the tube to a 4-mL vial. Place the first foam plug and the 140-mg section in a separate 4-mL vial. A small glass funnel can be used to facilitate the transfer of the adsorbent. Discard the rear foam plug. Do not discard the glass sampling tube; it can be reused.

3.4.2 Add 2.0 mL of chloroform to each vial and seal with a PTFE-lined cap.

3.4.3 Shake the vials for 30 minutes on a mechanical shaker.

3.4.4 Transfer, if necessary, the samples to 2-mL vials for use in an HP autosampler.

3.5 Analysis

3.5.1 Instrument conditions

Column: 50-mm x 4.6-mm ECON C_8 (3 µm)

Mobile phase: 86% methanol 14% water with 1mM Zinc chelate and 0.13M ammonium acetate. (Ref. 5.5)

Flow rate: 0.5 mL/min

Retention time: 2.54 min

3.5.2 Chromatogram (See Figure 3.)

3.6 Interferences (analytical)

3.6.1 Any collected compound having a similar retention time to that of the analyte is a potential interference.

3.6.2 HPLC conditions may generally be varied to circumvent interferences.

3.6.3 Retention time on a single column is not proof of chemical identity. Analysis on an alternate HPLC column and confirmation by mass spectrometry are additional means of identification.

3.7 Calculations

3.7.1 Construct a calibration curve (Figure 4.) by plotting detector response versus concentration (µg/mL) of ziram.

3.7.2 Determine the µg/mL of ziram in both sections of each sample and blank from the calibration curve.

3.7.3 Blank correct each sample section by subtracting the µg/mL found in the blank section from the µg/mL found in the sample section and then add the sample sections together.

3.7.4 Determine the air concentration by using the following formula.

$$mg/m^3 = \frac{(ug/mL, blank\ corrected)(desorption\ volume, mL)}{(air\ volume, L)(desorption\ efficiency, decimal)}$$

3.8 Safety precautions (analytical)

3.8.1 Avoid skin contact and air exposure to ziram.

3.8.2 Avoid skin contact with all solvents.

3.8.3 Wear safety glasses, disposable gloves, and a lab coat at all times in laboratory areas.

4 Recommendation for Further Study

This method should be fully validated.

5 References

5.1 IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans; International Agency for Research on Cancer: Lyon, 1983; Vol. 12, pp 259-271.

5.2 Registry of Toxic Effects of Chemical Substances 1985-86 Edition; DHHS (NIOSH) Publication No. 89-119, U.S. Department of Health and Human Services: Cincinnati, OH, 1989; pp 5137-8.

5.3 Farm Chemicals Handbook; Berg, Gordon L. Ed.; Meister: Willoughby, Ohio, 1986; pp C253-4.

5.4 The Merck Index, 10th ed.; Windholz, Martha ED.; Merck: Rahway, N.J., 1983; p 1459.

5.5 Karger, B.L., Wong, W.S., Viavattene, R.L., Lepage, J.N., Davies, G.; J. of Chrom; 1968; 167; 253-272.

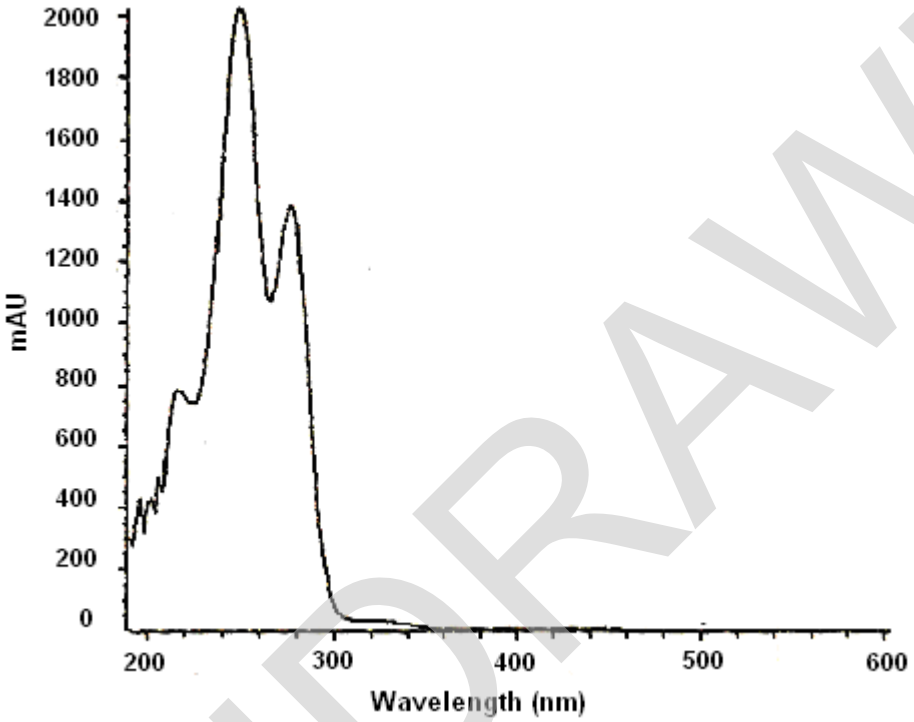

Figure I. UV Scan of Ziram in Mobile Phase

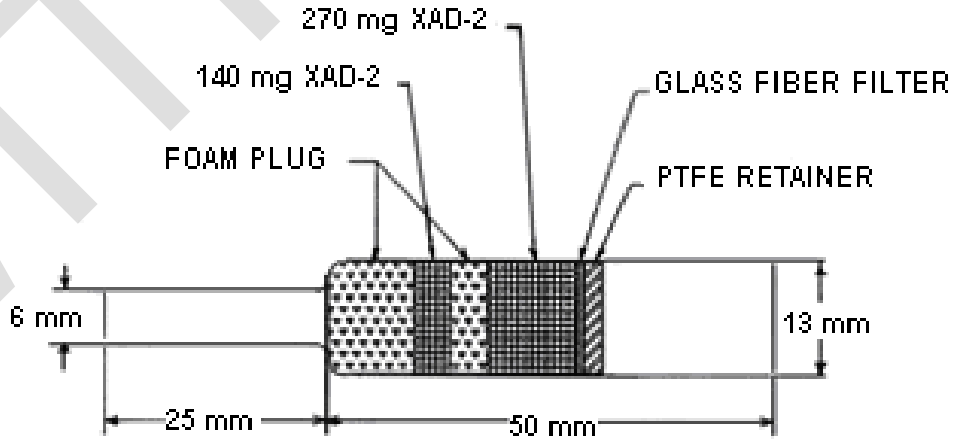

Figure 2. OVS-2 Sampling Tube

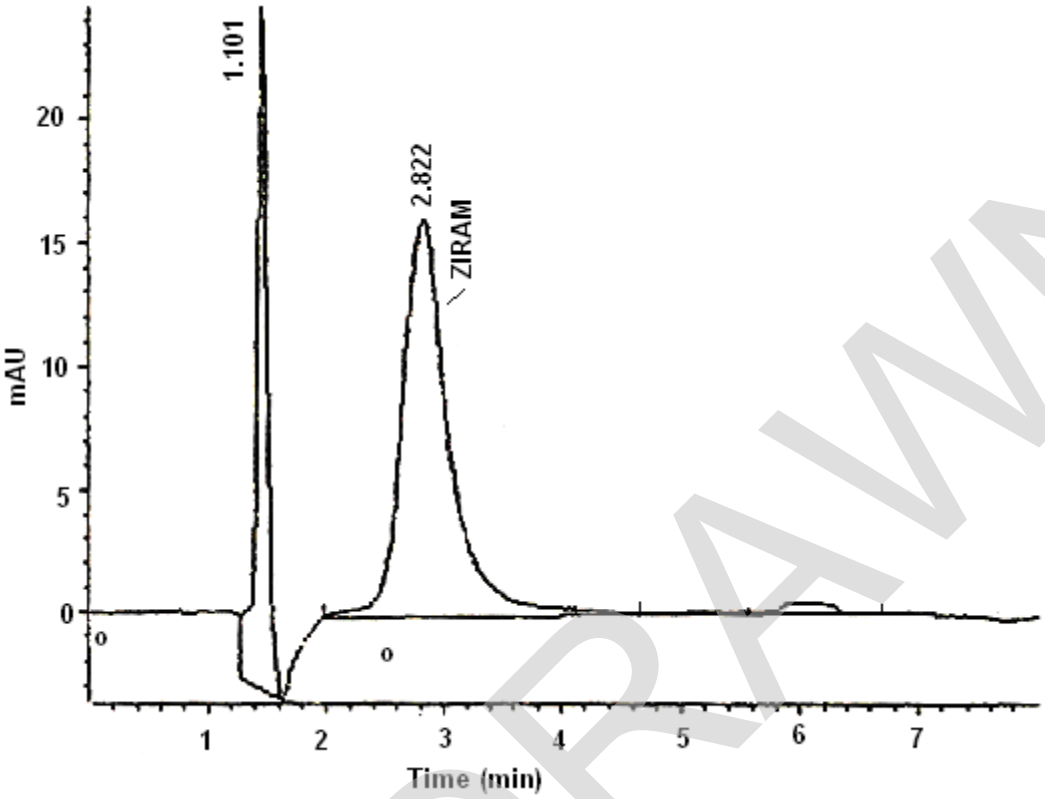

Figure 3. Chromatogram of Ziram

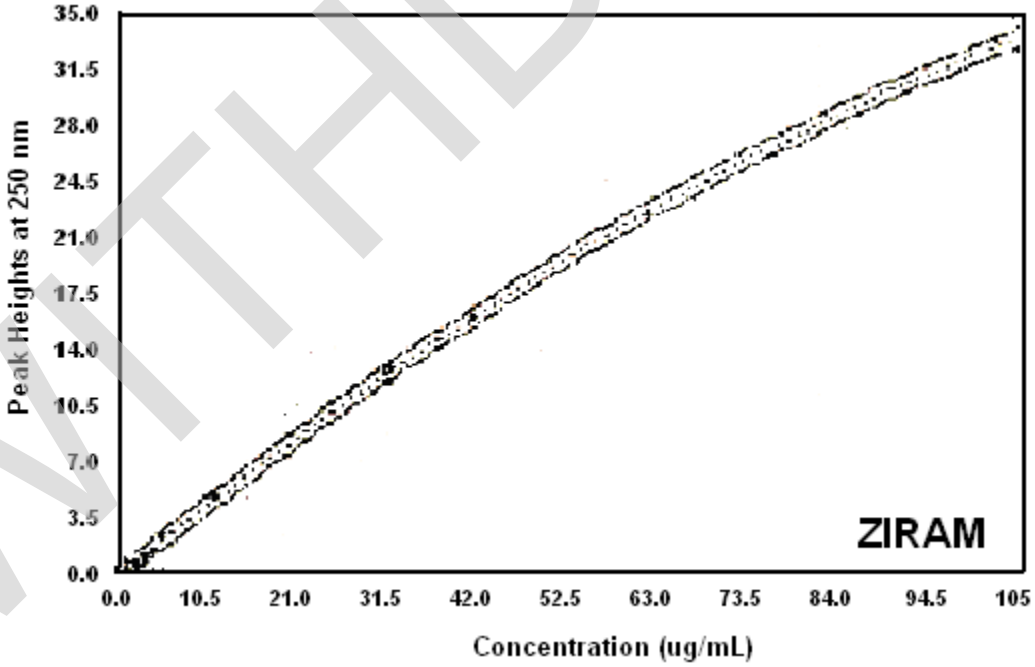

Figure 4. Calibration Curve