Morpholine

Method no.:	PV2123
Control no.:	T-PV2123-01-0305-CH
Target concentration:	20 ppm (70 mg/m³)
OSHA PEL:	20 ppm (70 mg/m³)
ACGIH TLV:	20 ppm
Procedure:	Samples are collected by drawing workplace air through tubes containing 10% phosphoric acid coated XAD-7 tubes with personal sampling pumps. Samples are extracted with 1 mL of 20% deionized water in methanol for 0.5 h with shaking; then 0.5 mL of sample is removed and added to 0.5 mL 20% 1.0 N sodium hydroxide in methanol and analyzed by gas chromatography using a flame ionization detector.
Recommended air volume and sampling rate:	10 L at 0.1 L/min
Reliable quantitation limit:	45 ppb (160 µg/m³)
Status of method:	Partially evaluated method. This method has been subjected to established evaluation procedures of the Methods Development Team and is presented for information and trial use.

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1. General Discussion

1.1 Background

1.1.1 History

The fully validated NIOSH Method S-150 for morpholine suggests that morpholine can be collected on silica gel tubes[1]. Silica gel has a high affinity for water and the water may displace any morpholine collected from the silica gel. In PV2016 cyclohexylamine showed good retention and storage efficiency when collected on tubes containing 10% phosphoric acid coated XAD-7 tubes, which had 10 L of humid air (83%@ 23°C) drawn through them[2]. This evaluation uses tubes containing 10% phosphoric acid coated XAD-7 tubes. Morpholine collected on these tubes also indicate good extraction, retention and storage efficiency.

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

Morpholine causes visual disturbance, nose irritation, coughing respiratory irritation, liver and kidney damage. When guinea pigs and rats inhaled 12,000 ppm morpholine for 8 hours obvious ocular and upper respiratory tract irritation were recorded. Cloudy swelling of the renal tubular epithelium and of the interstitial hepatic parenchyma and cellular debris in the bronchi were noted at necropsy[3]. The single oral LD_{50} for morpholine is 1.05 g/kg body weight and the single dermal LD_{50} for 24 hour skin contact is 0.5 mL/kg[4]. Workers exposed for several hours at low concentrations complained of foggy vision with rings around lights, resulting from a transient corneal edema, which cleared within 2 to 4 hours after cessation of exposure[5].

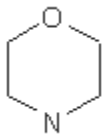
1.1.3 Workplace exposure

Morpholine is a cheap solvent for resins, waxes, casein and dyes. Morpholine fatty acid salts are used as surface agents and emulsifiers. Other morpholine compounds are used as corrosion inhibitors, antioxidants, plasticizers, viscosity improvers, insecticides, fungicides, herbicides, local anesthetics and antiseptics[6].

1.1.4 Physical properties and other descriptive information[7]

CAS number:	110-91-8	IMIS number[8]:	1797
Molecular weight:	87.12	Density:	0.994
Vapor density:	3	Odor:	weak ammonia like
Vapor pressure:	10 kPa (mmHg)	Flash point:	38°C
Molecular formula:	C_4H_9NO	Boiling point:	128.9°C
Melting point:	4.9°C	Corrosive material	
Hydroscopic		Flammable liquid	
Miscible in:	water; methanol; ethanol; ethyl acetate; acetone		
Synonyms:	tetrahydro-2H-1,4-oxazine; diethylene oximide; tetrahydro-1,4-oxazine diethylenimide oxide; tetrahydro-4H-1-4,oxazine; 1-oxa-4-azacyclohexane.		

Structure:



This method was evaluated according to the OSHA SLTC "Evaluation Guidelines for Air Sampling Methods Utilizing Chromatographic Analysis"[9]. The Guidelines define analytical parameters, specify required laboratory tests, statistical calculations and acceptance criteria. The analyte air concentrations throughout this method are based on the recommended sampling and analytical parameters. Air concentrations listed in ppm are referenced to 25°C and 101.3 kPa (760 mmHg).

1.2 Detection limit of the overall procedure (DLOP) and reliable quantitation limit (RQL)

The DLOP is measured as mass per sample and expressed as equivalent air concentrations, based on the recommended sampling parameters. Ten samplers were spiked with equal descending increments of analyte that the highest sampler loading was 4.55 µg/sample. This is the amount spiked on a sampler that would produce a peak approximately 10 times the response for a sample blank. These spiked samplers and the sample blank were analyzed with the recommended analytical parameters, and the data obtained used to calculate the required parameters (standard error of estimate and slope) for the calculation of the DLOP. Values of 446 and 68.95 were obtained for the slope and standard error of estimate, respectively. DLOP was calculated to be 0.464 µg/sample (13 ppb, 46 µg/m³).

Table 1.2
Detection Limit of the Overall Procedure

mass per sample (µg)	area counts (µV-s)
0	0
0.93	302
1.24	411
1.76	614
2.30	846
2.67	1016
3.05	1196
3.53	1440
4.07	1735
4.55	2012

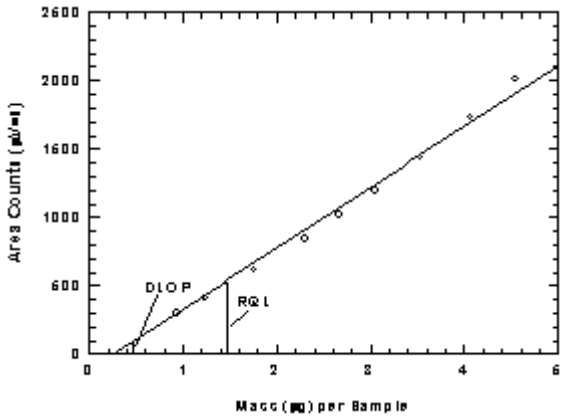


Figure 1.2.1 Plot of data to determine the DLOP/RQL. (Y=446X - 117)

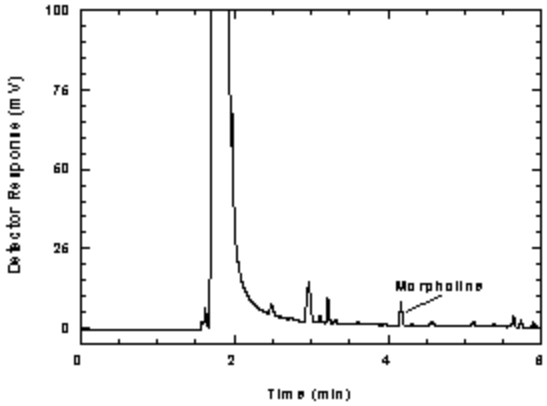


Figure 1.2.2 Chromatogram of the RQL

The RQL is considered the lower limit for precise quantitative measurements. It is determined from the regression line parameters obtained for the calculation of the DLOP, providing 75% to 125% of the analyte is recovered. The RQL is 1.55 µg per sample (45 ppb, 160 µg/m³). Recovery at this concentration is 90.0%.

2. Sampling Procedure

2.1 Apparatus

Samples are collected using a personal sampling pump calibrated, with the sampling device attached, to within ±5% of the recommended flow rate.

Samples are collected on 10% phosphoric acid coated XAD-7 tubes, lot 2409 containing 80 mg adsorbing section with a 40 mg backup section separated by a 2-mm portion of urethane foam, with a silanized glass wool plug before the adsorbing section and a 3-mm plug of urethane foam at the back of the backup section. The ends are flame sealed and the glass tube containing the adsorbent is 7-cm long, with a 6-mm o.d. For this evaluation, commercially prepared samplers were purchased from SKC, Inc. (Cat. No. 226-98).

2.2 Reagents

None required.

2.3 Technique

Immediately before sampling, break off the ends of the flame-sealed tube as to provide an opening approximately half the internal diameter of the tube. Wear eye protection when breaking ends. Use tube holders to minimize the hazard of broken glass. All tubes should be from the same lot.

The smaller section of the adsorbent tube is used as a back-up and is positioned nearest the sampling pump. Attach the tube holder to the sampling pump so that the adsorbent tube is in an approximately vertical position with the inlet facing down during sampling. Position the sampling pump, tube holder and tubing so they do not impede work performance or safety.

Draw the air to be sampled directly into the inlet of the tube holder. The air being sampled is not to be passed through any hose or tubing before entering the sampling tube.

After sampling for the appropriate time, remove the adsorbent tube and seal it with plastic end caps. Seal each sample end-to-end with an OSHA-21 form as soon as possible.

Submit at least one blank sample with each set of samples. Handle the blank sample in the same manner as the other samples except draw no air through it.

Record sample air volume (liters), sampling time (minutes) and sampling rate (mL/min) for each sample, along with any potential interferences on the OSHA-91A form.

Submit the samples to the laboratory for analyses as soon as possible after sampling. If delay is unavoidable, store the samples at refrigerator temperature. Ship any bulk samples separate from air samples.

All safety practices that apply to the work area being sampled should be followed. The sampling equipment should be attached to the worker in such a manner that it will not interfere with the work performance or safety.

2.4 Extraction efficiency

The extraction efficiencies of morpholine were determined by liquid-spiking media with the morpholine at 0.5 to 2 times the target concentration. These samples were stored overnight at ambient temperature and then extracted and analyzed. The mean extraction efficiency over the studied range was 102% for morpholine.

Table 2.4
% Extraction Efficiency of Morpholine

level		sample number				
× target concn	µg per sample	1	2	3	4	mean
0.1	69.6	102	104	104	105	104
0.5	398	101	100	100	103	101
1.0	696	101	104	106	102	103
2.0	392	104	97.4	97.8	103	101
Wet 1.0	696	98.8	100	98.4	100	99.3

2.5 Retention efficiency

Six sampling tubes were spiked with 696 µg (69.6 mg/m³) morpholine, allowed to equilibrate for 6 h, and then had 10 L humid air (absolute humidity of 15.9 mg/L of water, about 80% relative humidity at 22.2°C) pulled through them. The samples were extracted and analyzed. The mean retention efficiency is 94.0%. There was no morpholine found on the backup portion of the sampler.

Table 2.5
% Retention Efficiency of Morpholine

	sample number						
section	1	2	3	4	5	6	mean
front	95.0	93.4	95.0	95.0	93.3	92.0	94.0
rear	0	0	0	0	0	0	0
total	95.0	93.4	95.0	95.0	93.3	92.0	94.0

2.6 Sample storage

Fifteen sampling tubes were each spiked with 695.8 µg (19.6 ppm) of morpholine. They had 10 L of air with an absolute humidity of 15.7 milligrams of water per liter of air (about 80% relative humidity at 22.2°C) drawn through them. Six were sealed and stored at room temperature. Six were sealed and stored at 5 degrees centigrade. Immediately 3 were analyzed. After eight days, three at room temperature and three at refrigeration were analyzed and the remaining six after 14 days of storage. The amounts recovered, which are corrected for extraction efficiency, indicate good storage stability for the time period studied.

Table 2.6
Storage Test for Morpholine

	sample no.			
time (days)	1	2	3	mean
Immediate	101	97	97	98
8 ambient	104	99	102	102
refrigerated	107	97	102	102
14 ambient	95	89	87	91
refrigerated	87	91	lost	89

2.7 Recommended air volume and sampling rate

Based on the data collected in this evaluation, 10-L air samples should be collected at a sampling rate of 0.1L/min.

3. Analytical Procedure

Adhere to the rules set down in your Chemical Hygiene Plan[10]. Avoid skin contact and inhalation of all chemicals and review all MSDSs.

3.1 Apparatus

Gas chromatograph equipped with an FID. A Hewlett-Packard Model 6890 was used in this evaluation.

3.2 Reagents

Methanol, (CAS 67-56-1).The methanol used in this evaluation was HPLC grade (lot no. B0502782) purchased from Acros (New Jersey).

Morpholine, (CAS no.110-91-8). The morpholine used in this evaluation was 99.5+% (Lot No. 10131EO) purchased from Aldrich (Milwaukee, Wisconsin).

Water purifier. A Barnstead NANOpure Diamond system was used to produce 18.0 MΩ-cm DI water in this evaluation.

Sodium hydroxide (98%) (CAS no. 1310-73-2) (Lot no. X20944) purchased from J.T. Baker.

Extraction solution: 20% by volume DI water in methanol (20:80 v/v). Adjust the pH of the extraction solution to 7-8 with sodium hydroxide solution.

Sodium hydroxide in 20/80 DI water/methanol extraction solution: prepare a solution containing 1.0N NaOH by diluting 4.0 g of 98% sodium hydroxide to 100 mL with extraction solution.

3.3 Standard preparation:

Prepare concentrated stock solutions of morpholine in methanol. The PEL of morpholine is 70 mg/m³: 70 µg/L x 10 L = 700 µg and the density of morpholine is 994 µg/µL. Dilute this 994 µg/µL solution 0.1 to 99.4 µg/µL , 0.01 to 9.94 µg/L and 0.001 to 0.994 µg/µL. Prepare working analytical standards by injecting microliter amounts of concentrated stock solutions into 2-mL vials containing 1 mL of extracting solution. Prepare standards by injecting 14 µL, 7µL and 4µL of the 99.4 µg/µL solution ; 7 µL of the 9.94 µg/µL solution and 7µL of the 0.994 µg/uL solution. The concentrations are: 1391.6, 695.8, 397.6, 69.6 and 6.96µg/mL. To analyze compliance samples dilutions of 2 concentrated stock solutions at the 2X PEL could be made. Dilutions of these stock solutions to approximately 7µg/mL level could be made.

3.4 Sample preparation

Remove the plastic end caps from the sample tube and carefully transfer each section of the adsorbent to separate 2-mL vials. Include the glass wool plug in the front section of the sample media.

Add 1.0 mL of extracting solution to each vial and immediately seal the vials with polytrafluoethylene-lined caps.

Extract the samples on a rototurner for 0.5 hr.

Transfer 0.5 mL of sample to a 2 mL vial and add 0.5 mL of 1.0N NaOH in 20/80 DI water/methanol solution. Shake. The solid that forms doesn't interfere with the analysis. The samples are centrifuged before analysis.

3.5 Analysis

column:	MDN-1; 30-m; 0.32 mm i.d.; 1.0 µm df
GC conditions:	
temperature program:	50°C at 10°C per minute to 110°C

zone temperatures:	200°C (injector) 250°C (detector)
run time:	6 minutes
column gas flow:	2.0 mL/min
injection size:	1.0 µL, 10:1 split
retention times:	1.67 min methanol 4.45 min morpholine
FID conditions	
hydrogen flow:	40.0 mL/min
air flow:	450 mL/min
nitrogen makeup flow:	15 mL/min

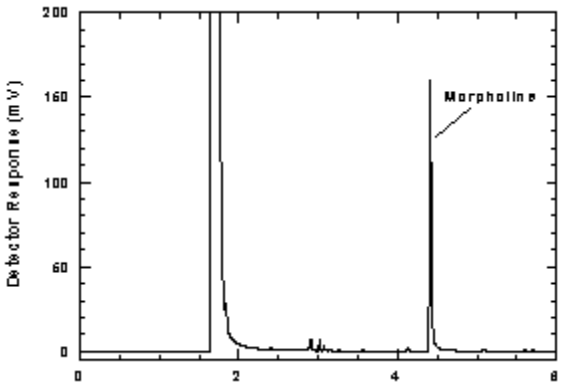


Figure 3.5 Chromatogram at the target concentration

3.6 Analytical Interferences

Any compound that produces a FID response and has a similar retention time as morpholine or internal standard is a potential interference. If any potential interferences were indicated by the industrial hygienist, they should be considered before samples are extracted. Generally, chromatographic conditions can be altered to separate an interference from morpholine.

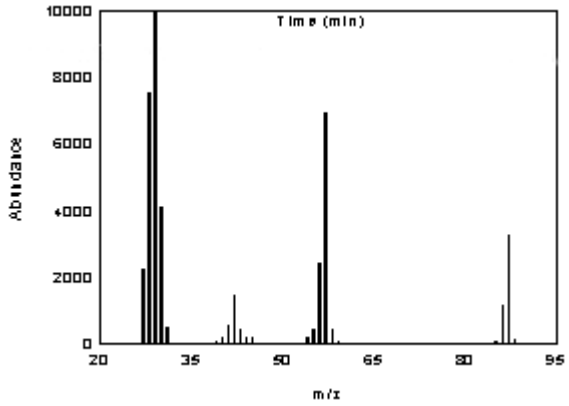


Figure 3.6 Mass spectrum of morpholine.

3.7 Calculations

The amount of morpholine per sampler is obtained from the appropriate calibration curve in terms of micrograms per sample, uncorrected for extraction efficiency. The back section is analyzed primarily to determine the extent of sampler saturation. If any morpholine is found on the back section, it is added to the amount on the front section. This total amount is then corrected by subtracting the total amount (if any) found on the blank. The air concentration is calculated using the following formulas.

$$C_M = \frac{M}{VE_E}$$

where

C_M is concentration by weight (mg/m³)
M is micrograms per sample
V is liters of air sampled
E_E is extraction efficiency, in decimal form

$$C_V = \frac{V_M C_M}{M_r}$$

where

C_V is concentration by volume (ppm)
V_M is molar volume at 25°C and 760 mmHg (NTP)
C_M is concentration by weight
M_r is molecular weight (87.12)

3.8 Safety precautions

Avoid skin contact and inhalation of all chemicals. Wear safety glasses, gloves and a laboratory coat at all times while in laboratory areas.

4. Recommendations for further study:

Collection studies need to be performed.

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10. Occupational Exposure to Hazardous Chemicals in Laboratories. Code of Federal Regulations, Part 1910,1450, Title 29, 1998.