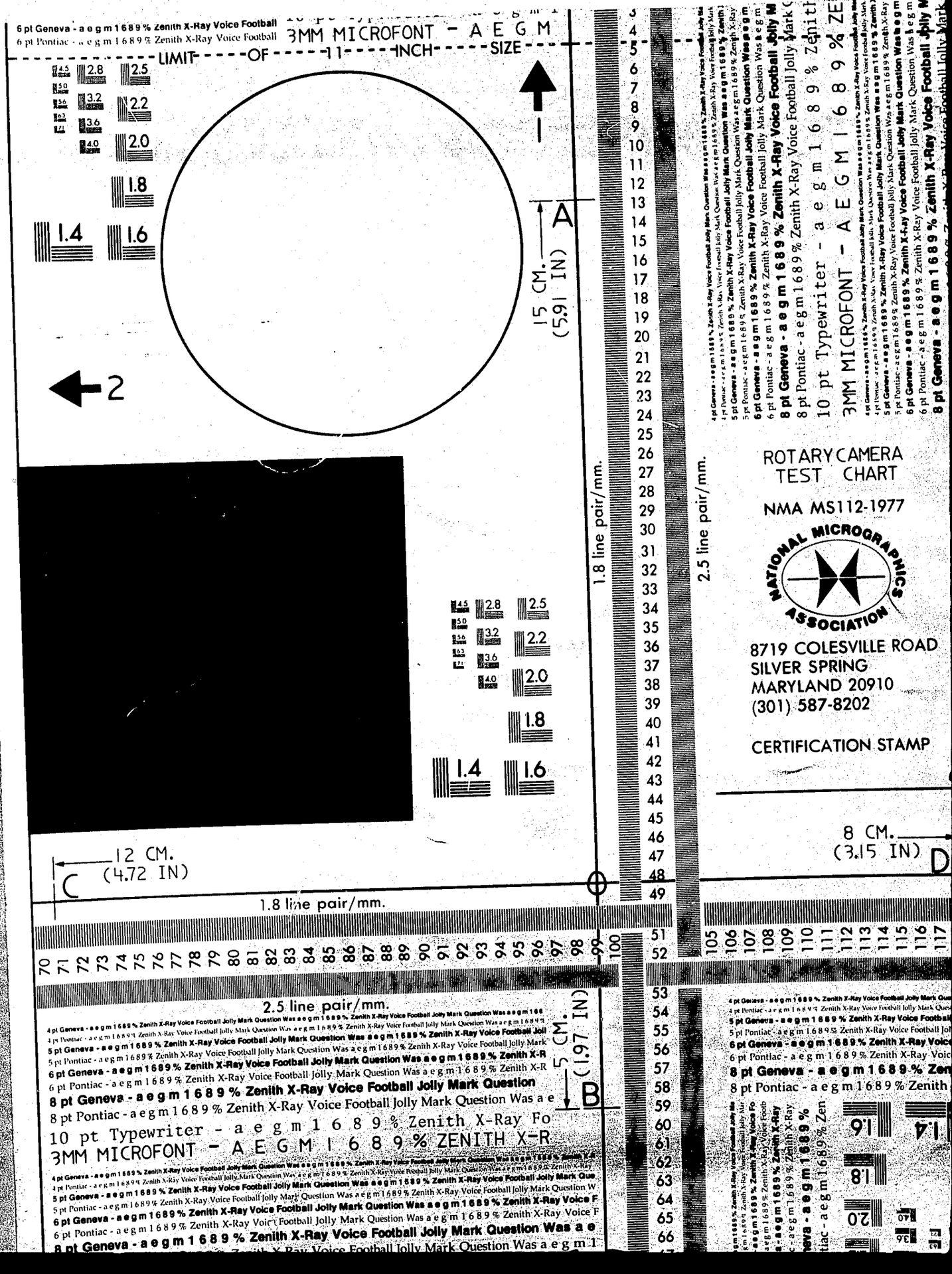
3MM MICROFONT - A E G M
LIMIT - OF - 11 - INCH - SIZE
15 CM. (5.91 IN)
A
2
1.8 line pair/mm.
2.5 line pair/mm.
12 CM. (4.72 IN)
C
1.8 line pair/mm.
8 CM. (3.15 IN)
D
5 CM. (1.97 IN)
B
2.5 line pair/mm.
ROTARY CAMERA TEST CHART
NMA MS112-1977
NATIONAL MICROGRAPHICS ASSOCIATION
8719 COLESVILLE ROAD
SILVER SPRING
MARYLAND 20910
(301) 587-8202
CERTIFICATION STAMP

Failure Report No. S180

April 13, 1979

Substance: Maleic Anhydride

OSHA Standard: 0.25 ppm (1 mg/cu m)

Chemicals Used: Maleic Anhydride, 99%, from Aldrich Chemical Company
Maleic Acid, 98%, from Matheson, Coleman, and Bell

Methods Attempted

The method studied included collection of maleic anhydride in a midget bubbler containing 15 mL of distilled water. Maleic anhydride is hydrolyzed to maleic acid in the bubbler, and the resulting sample is analyzed by high pressure liquid chromatography (HPLC).

Reason for Failure

Collected samples stored for one week were not stable. A loss of 13% was found when the results obtained from collected samples stored for one week before analysis were compared to those obtained when collected samples were analyzed immediately.

Discussion

All requirements for validation of a method were met as outlined in NIOSH Contract 210-76-0123 except for storage stability of collected samples. More work should be done to develop a procedure for stabilizing the collected samples. It was recommended that the method, although conditional, be submitted in the P&CAM format. Thus, complete details of the method developed and experimental work performed appear in NIOSH Method P&CAM 302, Sampling Data Sheet No. 302, and Backup Data Report No. 302.

Recommendations

It is recommended that the submitted method be used at the present time. Further work should be done to stabilize collected samples such as investigating the use of an acidic collecting medium.

It is also recommended that future work should be pursued to develop a solid sorbent coated with a suitable amine to derivatize maleic anhydride specifically.

Maleic Anhydride

Measurements Research Branch

Analytical Method

Analyte:	Maleic Acid	Method No.:	P&CAM 302
Matrix:	Air	Range:	0.50-2.14 mg/cu m
Procedure:	Bubbler collection, HPLC	Precision (RSD):	0.063
Date Issued:	5/1/79	Classification:	E (Proposed)
Date Revised:			

1. Synopsis

1.1 A known volume of air is drawn through a midget bubbler containing 15 mL of distilled water to collect maleic anhydride.

1.2 Maleic anhydride is hydrolyzed to maleic acid in the bubbler.

1.3 The resulting sample is analyzed by high pressure liquid chromatography (HPLC) with a uv detector at 254 nm.

2. Working Range, Sensitivity, and Detection Limit

2.1 This method was tested over the range of 0.50-2.14 mg/cu m at an atmospheric temperature of 20°C and pressure of 757 mm Hg, using a 360-liter sample.

2.2 The upper limit of the range of the method is dependent on the collection efficiency of the midget bubbler.

2.3 Under the instrumental conditions used in the study, a sensitivity of approximately 0.01 absorbance units/µg maleic anhydride was obtained. The HPLC flow cell path length was 0.8 cm.

2.4 The limit of detection is estimated to be 50 ng per injection or 15 µg maleic acid per sample.

3. Interferences

3.1 When interfering compounds are known or suspected to be present in the air, such information, including their suspected identities should be transmitted with the sample.

3.2 Any compound that has the same retention time as maleic acid at the operating conditions described in this method is an interference. Retention time data on a single column cannot be considered proof of chemical identity.

3.3 Maleic anhydride is immediately hydrolyzed to maleic acid upon collection. This method will not differentiate between maleic acid and maleic anhydride.

4. Precision and Accuracy

4.1 The Relative Standard Deviation (RSD) for the total analytical and sampling method in the range of 0.50-2.14 mg/cu m was 0.063. This value corresponds to a standard deviation of 0.063 mg/cu m at the OSHA standard level. Statistical information can be found in Reference 11.1. Details of the test procedures can be found in Reference 11.2.

4.2 In the experiments, this method was found to be capable of coming within ±25% of the "true" value on the average 95% of the time over the range tested. The concentrations obtained at 0.5, 1, and 2 mg/cu m were 6.7% lower than the dynamically generated test concentrations (n = 17). In these experiments the average analytical method recovery was 1.044 for a loading of 180.7-723 µg of maleic acid in the bubbler. No correction was applied for this recovery. In storage stability studies, the mean of samples analyzed after 7 days were 13% lower than the mean of samples analyzed immediately after collection. Collection efficiency was determined to be at least 0.978 within the range tested; therefore, no correction for collection efficiency is necessary. Experiments performed in the study are described in Reference 11.2.

5. Advantages and Disadvantages

5.1 Collected samples are analyzed by means of a quick, instrumental, method.

5.2 A disadvantage of the method is the awkwardness in using midget bubblers for collecting personal samples. If the worker's job performance requires much body movement, loss of the collection solution during sampling may occur. The use of spill-proof impingers is recommended.

5.3 The precision of the method is limited by the reproducibility of the pressure drop across the bubbler. This drop will affect the flow rate and cause the volume to be imprecise, because the pump is usually calibrated for one bubbler only.

5.4 The bubblers are more difficult to ship than adsorption tubes or filters because of possible breakage and leakage of the bubblers during shipping.

6. Apparatus

6.1 Glass midget bubblers with fritted glass stems.

6.2 Personal Sampling Pump. A calibrated personal sampling pump whose flow rate can be determined to an accuracy of 5%. Each personal sampling pump must be calibrated with a bubbler and trap in the line to minimize errors associated with uncertainties in the volume sampled. The sampling pump is protected from splashover or solvent condensation by a trap. The trap is a midget bubbler or impinger with the stem broken off which is used to collect spillage. The trap is attached to the pump with a metal holder. The outlet of the trap is connected to the pump by flexible tubing.

6.3 Manometer.

6.4 Thermometer.

6.5 HPLC equipped with a uv detector at 254 nm and a sample injection valve with a 50-microliter sample loop.

6.6 HPLC column (300 mm x 3-mm I.D. stainless steel) packed with μ-Bondapak C-18*, or equivalent.

6.7 An electronic integrator or some other suitable method for measuring peak areas.

6.8 Volumetric Flasks: Convenient sizes for preparing standard solutions.

6.9 Pipets: Convenient sizes for preparing standard solutions and 15-mL pipets for measuring the collection medium.

6.10 Teflon tubing (15 cm long x 7-mm I.D.) or Teflon plugs for sealing the inlet and outlet of the bubbler stem before shipping.

7. Reagents

Whenever possible, all reagents used must be ACS reagent grade or better.

7.1 Maleic anhydride, 99+%. Note: Maleic anhydride will slowly hydrolyze in the presence of humid air. Care should be taken to protect it from humid conditions.

7.2 Water, deionized and distilled.

7.3 Dicyclohexylamine.

7.4 Formic acid.

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* This column is available from Waters Associates, Milford, Mass.

7.5 Methanol, HPLC grade.

7.6 HPLC Mobile Phase

7.6.1 Add 10 mL of dicyclohexylamine and 10 mL of formic acid to a 100-mL volumetric flask. Bring to volume with distilled water.

7.6.2 Add 10 mL of the solution prepared in Section 7.6.1 and 250 mL of methanol to a 1-liter volumetric flask. Bring this solution to volume with distilled water. Filter and degas prior to use.

7.7 Acetone.

7.8 Stock Maleic Anhydride Standard Solution. Prepare a 1.08 mg/mL stock solution of maleic anhydride in acetone.

8. Procedure

8.1 Cleaning of Equipment. All glassware used for the laboratory analysis should be detergent washed, thoroughly rinsed with tap water and distilled water, and dried.

8.2 Collection and Shipping of Samples

8.2.1 Pipet 15 mL of distilled water into a midget bubbler, and mark the liquid level before inserting the bubbler frit. Be sure that the bubbler frit is completely immersed in the water. If the water does not cover the frit, do not use the bubbler. Maleic anhydride will not be collected efficiently unless the bubbler frit is completely immersed in the water.

8.2.2 Connect the outlet of the midget bubbler to the trap's inlet. When a trap is used, it is attached to the pump by tape or a metal holder. The outlet of the trap is connected by tubing to the pump's inlet. Material collected in the trap must never be returned to the midget bubbler. If more than 1 mL of material is collected in the trap after sampling, the sample should be considered invalid, otherwise, the trap material can be discarded. The bubbler must be maintained in a vertical position during sampling.

8.2.3 Air being sampled should not pass through any hose or tubing before entering the bubbler.

8.2.4 A sample size of 360 liters is recommended. Sample at a flow rate of 1.5 liters per minute. The flow rate should be known with an accuracy of 5%.

8.2.5 Turn the pump on and begin sample collection. The pump rotameter should be observed frequently, and the sampling should be terminated at any evidence of a problem.

8.2.6 It may be necessary to replace some of the water in the bubbler during sampling because of evaporation. If the liquid level drops more than 5 mL, add water to the 15-mL mark.

8.2.7 Terminate sampling at the predetermined time and record sample flow rate, collection time and ambient temperature and pressure. If pressure reading is not available, record the elevation. Also record the type of sampling pump used.

8.2.8 After sampling, disconnect the bubbler. The inlet and outlet of the bubbler stem should be sealed by connecting a piece of Teflon tubing between them or inserting Teflon plugs in the inlet and outlet. Do not seal with rubber. The standard taper joint of the bubbler should be taped securely to prevent leakage during shipping.

8.2.9 With each batch or partial batch of ten samples submit one bubbler containing water from the same lot of bubblers used for sample collection. This bubbler must be subjected to exactly the same handling as the samples except that no air is drawn through it. Label this bubbler as the blank.

8.2.10 The bubblers should be shipped in a suitable container, designed to prevent damage in transit. The samples should be shipped to the laboratory as soon as possible.

8.3 Analysis of Samples

8.3.1 Remove the bubbler stem from the bubbler. Allow water to drain from the frit into the bubbler. If the sample volume is less than 15 mL, add water until the volume reaches the 15-mL mark.

8.3.2 HPLC Conditions. The typical operating conditions for the HPLC are:

Column Temperature: Ambient
Flow Rate: 1.7 mL/minute
Mobile Phase: 1% PIC reagent (Section 7.6.1) / 25% methanol / 74% distilled water
Detector: uv photometer at 254 nm
Retention Time: 6 minutes

During the experimental study, all samples and blanks contained a peak eluting after maleic acid (at about 8 minutes) which was believed to be phthalic acid.

8.3.3 Injection. The first step in the analysis is to inject the sample into the HPLC. The chromatograph is fitted with a sample injection valve and a 50-microliter sample loop. Flush this loop thoroughly with the sample (500 microliters), and inject the sample.

8.3.4 The area of the sample peak is measured by an electronic integrator or some other suitable form of area measurement, and results are read from a standard curve prepared as discussed below.

9. Calibration and Standardization

9.1 A series of standards, varying in concentration over the range corresponding to approximately 0.1-3 mg/cu m for the sample under study, is prepared and analyzed under the same HPLC conditions and during the same time period as the unknown samples. Curves are established by plotting concentration in micrograms/15 mL versus peak area. Note: Since no internal standard is used in this method, standard solutions must be analyzed at the same time as the samples. This will minimize the effect of known day-to-day variations and variations during the same day of the uv detector response.

9.2 From the stock solution (Section 7.8), appropriate aliquots are withdrawn and diluted with distilled water. Prepare at least 5 working standards to cover the range of 36-1080 micrograms/15 mL. This range is based on a 360-liter sample. Analyze samples as described in Section 8.3.

9.3 Prepare a standard calibration curve by plotting concentration of maleic anhydride in micrograms/15 mL versus peak area. Although maleic acid is the actual specie analyzed, all concentrations should be expressed as maleic anhydride.

10. Calculations

10.1 Read the weight, in micrograms, corresponding to each peak area from the appropriate standard curve. No volume correction is needed, because the standard curve is based on micrograms/15 mL of distilled water and the volume of sample injected is identical to the volume of the standards injected.

10.2 A correction for the blank must be made for each sample.

$$\mu g = \mu g \text{ sample} - \mu g \text{ blank}$$

where:

μg sample = μg found in sample bubbler

μg blank = μg found in blank bubbler

10.3 For personal sampling pumps with rotameters only, the following volume correction should be made.

$$\text{Corrected Volume} = f \times t\left(\sqrt{\frac{P_1}{P_2} \times \frac{T_2}{T_1}}\right)$$

where:

f = flow rate sampled
t = sampling time
P_1 = pressure during calibration of sampling pump (mm Hg)
P_2 = pressure of air sampled (mm Hg)
T_1 = temperature during calibration of sampling pump (°K)
T_2 = temperature of air sampled (°K)

10.4 The concentration of maleic anhydride in the air sample can be expressed in mg/cu m.

$$\text{mg/cu m} = \mu\text{g/liter} = \frac{\mu\text{g (Section 10.2)}}{\text{Corr. Air Volume Sampled (L) (Section 10.3)}}$$

11. References

11.1 Documentation of NIOSH Validation Tests, National Institute for Occupational Safety and Health, Cincinnati, Ohio (DHEW-NIOSH Publication #77-185), 1977. Available from Superintendent of Documents, U.S. Government Printing Office, Washington, D.C., Order No. 017-033-00231-2.

11.2 Backup Data Report No. 302 for Maleic Anhydride prepared under NIOSH Contract No. 210-76-0123

Ellen L. Fernandez
SRI International
NIOSH Contract No. 210-76-0123

Sampling Data Sheet No. 302

May 1, 1979

Substance

Maleic Anhydride

Standard

8-hour time-weighted average: 0.25 ppm (1 mg/cu m)

Analytical Method

A known volume of air is drawn through a midget bubbler containing 15 mL of distilled water to collect maleic anhydride. Maleic anhydride is hydrolyzed to maleic acid and the sample is analyzed by high pressure liquid chromatography. The method has been tested over the range of 0.50--2.14 mg/cu m for a 360-liter sample at 20°C and 757 mm Hg atmospheric temperature and pressure. Details of the sampling and analytical method are given in the method referenced below.

Sampling Equipment

Sampling equipment includes a calibrated personal sampling pump whose flow rate can be determined accurately (±5%) at 1.5 liters/minute and a midget bubbler containing 15 mL of distilled water. The pump should be protected from spillage or splashover by using a trap which is a second bubbler or impinger downstream of the midget bubbler. Teflon tubing (15 cm long x 7-mm I.D.) or Teflon plugs are needed for sealing the inlet and outlet of the bubbler stem before shipping.

Sample Size

A sample size of 360 liters is recommended. Sample at a flow rate of 1.5 liters/minute.

Sampling Procedure

1. Pipet 15 mL of distilled water into each bubbler. Mark the liquid level with a china marker before inserting the bubbler frit. Be sure that the frit is completely immersed in the liquid. If the liquid level does not cover the frit, do not use the bubbler. Maleic anhydride will not be collected efficiently unless the bubbler frit is completely immersed in the distilled water.

2. Connect the outlet of the midget bubbler to the trap's inlet. The stem of the trap should be broken off. When a trap is used, it is attached to the pump by tape or a metal holder. The outlet of the trap is connected by tubing to the pump's inlet. If more than

1 mL of material is collected in the trap after sampling, the sample should be considered invalid, otherwise the trap material can be discarded. The bubbler must be maintained in a vertical position during sampling.

3. Air being sampled should not pass through any hose or tubing before entering the bubbler.

4. Set the flow rate as accurately as possible using the manufacturer's directions. Record the temperature and pressure of the atmosphere being sampled. If the pressure reading is not available, record the elevation. Also report the type of sampling pump used. The pump rotameter should be observed frequently, and readjusted as needed. If the rotameter cannot be adjusted to correct a problem, terminate the sampling. If the liquid level in the bubbler drops more than 5 mL add water up to the 15-mL mark before resuming sampling.

5. After sampling, the inlet and outlet of the bubbler stem should be sealed by connecting a piece of Teflon tubing between them or inserting Teflon plugs in the inlet and outlet. Do not seal with rubber. The standard taper joint of the bubbler should be taped securely to prevent leakage during shipping.

6. Carefully record the sample identity and all relevant sampling data such as sample flow rate and collection time.

7. With each batch of ten samples submit one midget bubbler containing 15 mL of distilled water. This bubbler must be of the same type as that used for sample collection and be subjected to exactly the same handling as the samples except that no air is drawn through it. Label this bubbler as the blank.

Special Consideration

When other compounds are known or suspected to be present in the air, such information, including their suspected identities, should be transmitted with the sample.

Shipping Instructions

The bubblers should be shipped in a suitable container, designed to prevent damage in transit. The samples should be shipped to the laboratory as soon as possible.

Bulk Sample

A sample of the bulk material should be submitted in a glass container with a Teflon-lined cap or equivalent. This sample must not be transported in the same container as the bubblers.

Reference

Maleic Anhydride, NIOSH Method P&CAM 302.

Backup Data Report No. 302

May 1, 1979

Substance: Maleic Anhydride

OSHA Standard: 0.25 ppm (1 mg/cu m)

Chemical Used for Validation: Maleic Anhydride, 99%, from Aldrich
Maleic Acid, 97%, from Matheson, Coleman, and Bell

General

The procedure for collection and analysis of air samples of maleic anhydride is described in NIOSH Method P&CAM 302. This method consists of collection of the sample in a midget bubbler containing 15 mL of distilled water. The resulting solution is analyzed as maleic acid by high pressure liquid chromatography (HPLC).

This method has been tested for a 360-liter air sample, using the criteria outlined in Reference 1.

The protocol for testing this method was to:

Analyze 18 samples (6 each at 0.5X, 1X, and 2X the OSHA standard) spiked with the appropriate amounts of maleic anhydride to represent 360-liter air samples.

Analyze 18 samples collected from dynamically generated test atmospheres (6 samples collected at each of 0.5X, 1X, and 2X the OSHA standard).

Determine the collection efficiency of the midget bubbler containing 15 mL of distilled water.

Test the storage stability of six collected samples.

Assess the precision and accuracy of the method.

Details of these procedures are discussed below.

Analysis

A description of the method of analysis is given in NIOSH Method P&CAM 302. Spiked samples were prepared at 0.5X, 1X, and 2X the OSHA standard to represent 360-liter air samples. Known amounts of a solution of maleic anhydride in acetone were spiked into midget bubblers containing 15 mL of distilled water. The bubblers were allowed to stand overnight before analysis. The samples were analyzed by HPLC and compared to standards prepared by using a stock solution of maleic acid in acetone. The results of the analytical method recoveries are presented in Table 302-6.

Experiments showed that hydrolysis of maleic anhydride in a water solution is immediate, although the crystalline maleic anhydride dissolved slowly when placed in water.

Under the instrumental conditions used in the study, a sensitivity of approximately 0.01 absorbance units/µg maleic anhydride was obtained. The HPLC flow cell path length was 0.8 cm.

The limit of detection is estimated to be 50 ng per injection or 15 µg maleic acid per sample.

Sampling and Analysis

Test atmospheres of maleic anhydride in air were generated with the vapor generation apparatus described in Attachment A. Solid crystalline maleic anhydride was placed in the vapor generator. The generator was immersed in a constant temperature water bath and a flow of nitrogen passed through a dessicant trap and then through the maleic anhydride. The amount of vapor generated is dependent upon the vapor pressure of the material, the bath temperature, and the flow of nitrogen. The required levels of maleic anhydride were generated at a water bath temperature of 38°C. Dilution air was added downstream to obtain samples at 2X the OSHA standard. Dilutions to 1X and 0.5X the OSHA standard were made as described in Attachment B.

Six samples at each level were collected as described in NIOSH Method P&CAM 302. The sampling time was 240 minutes, and the average volume was 345 liters. The midget bubblers were recharged with distilled water once after 2 hours of sampling. The results of the analysis of these samples are presented in Table 302-7.

In addition, backup bubblers at 2X the OSHA standard were found to contain less than the limit of detection, estimated at 15 µg maleic acid per sample.

Storage Stability

A storage stability test was conducted to assess whether maleic anhydride could be successfully stored in solution as maleic acid for one week after collection. Six samples were collected at 1X the OSHA standard at a concentration of 1.091 mg/cu m (as determined by the independent method).

The samples were collected for 240 minutes at an average flow rate of approximately 1.4 liters/minute.

The samples were analyzed immediately after collection, and then capped and stored on the laboratory bench for 7 days. The samples were then reanalyzed. The results of the storage stability test are presented in Table 302-1.

Table 302-1

Storage Stability

	Samples Analyzed Immediately (mg/cu m)	Samples Analyzed After Seven Days (mg/cu m)
	0.964	0.925
	1.020	0.877
	1.054	0.957
	1.047	0.795
	0.971	0.883
	0.997	0.840
mean	1.009	0.880
std dev	0.038	0.058
CV	0.038	0.066

The two means compare within 13%. There were no previous indications that maleic acid would not be stable in a water solution. Standards prepared in water and stored under ambient conditions exhibited no noticeable deterioration. It is possible that refrigeration may retard deterioration, or that addition of acid may stabilize the solution. Lack of time prevented further investigation.

Collection Efficiency

Collection efficiency tests were conducted by sampling test atmospheres containing 2.14 mg/cu m with midget bubblers connected in series. Each bubbler contained 15 mL of distilled water. The test atmosphere was generated as described in the Sampling and Analysis Section. Six samples were collected for 240 minutes at an average flow rate of 1.4 liters/min. The results of the collection efficiency tests are presented in Table 302-2.

The results of the collection efficiency test demonstrate that maleic anhydride is collected efficiently using a single midget bubbler. No correction for collection efficiency is necessary.

Table 302-2

Collection Efficiency

micrograms found in first bubbler	micrograms found in backup bubbler	Collection Efficiency
684	N.D.*	$\geq$ 0.978
665	N.D.	$\geq$ 0.978
673	N.D.	$\geq$ 0.978
686	N.D.	$\geq$ 0.978
727	N.D.	$\geq$ 0.978
657	N.D.	$\geq$ 0.978

* N.D. = Not detected at a detection limit of 15 micrograms per sample.

Discussion

The failure report for maleic anhydride, prepared under NIOSH Contract CDC-99-74-45, recommended collection in 0.1 N HCl or by solid sorbent and analysis by HPLC. The intent of our research was to develop a method capable of differentiating between maleic anhydride and maleic acid. Problems were anticipated, because of the low levels to be sampled and the inherent instability of maleic anhydride. Three separate channels of investigation were conducted, none of which resulted in a validated procedure.

Solid Sorbent Investigations

Solid sorbent investigations were undertaken based on a paper by Qazi, Vincent, and Ketcham delivered to the American Industrial Hygiene Association in May 1978 (Reference 2). This paper described a method for sampling and analysis of acetic anhydride in industrial atmospheres. Acetic anhydride was collected on Porapak N, desorbed with acetone, and analyzed by gas chromatography. Porapak N was chosen from several porous polymers which were investigated for possible use.

Storage stability tests were performed, and it was determined that refrigeration was necessary to obtain a 90% recovery after 5 days (unrefrigerated samples gave a 53% recovery).

GC conditions were established for the analysis of maleic anhydride in acetone based on this paper:

Column: Tenax GC, 80/100 mesh, 6 ft x 1/8 in (nickel)
Column Temperature: 160°C
Detector: FID
He carrier gas at 30 mL/min

The OSHA standard for acetic anhydride is twenty times that for maleic anhydride. For a sample size of 50 liters the sensitivity of maleic anhydride was poor. Peak shape was also poor. It was later discovered that at column or injector temperatures above 100°C, maleic acid

dehydrates, and the acid and anhydride coelute. More attention to column selection may improve the problems of peak shape and selectivity.

The sorbents tested were Porapak Q, Porapak N, Chromosorb 102, XAD-2, and Tenax GC. Each sorbent was washed with 2-25 mL aliquots each of water, acetone, and diethyl ether. Chromosorb 102 required 6-25 mL washings of acetone to obtain a clear supernatant. The sorbents were dried overnight in a vacuum oven at 40°C.

Fifty-microgram aliquots of maleic anhydride in acetone, representing a 50-liter sample at 1X the OSHA standard, were spiked onto each sorbent. Each vial was capped and set aside until analysis.

For analysis, 1.0 mL of desorbing solvent (acetone, chloroform, or diethyl ether) was added to each vial, and the solution was analyzed by GC. The results are presented in Table 302-3.

Table 302-3

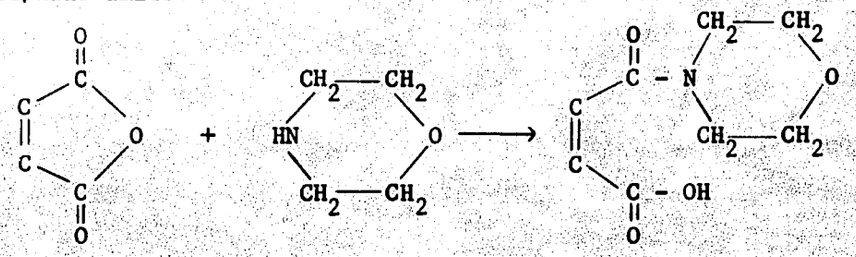
Sample	Recovery	
	One Day	Seven Days
Porapak Q/acetone	85%	-0-
Porapak N/acetone	97%	-0-
Tenax GC/acetone	96%	-0-

In addition, Tenax GC/chloroform gave 95% recovery after 1 day. All of the other sorbent/solvent combinations gave recoveries less than 60% after 1 day.

The low recoveries were probably caused by the instability of maleic anhydride. It will hydrolyze if water is present, and may react irreversibly with any residual monomers on the porous polymers. It was felt that maleic anhydride could not be successfully collected or meet the criteria for storage stability using a solid sorbent; therefore, the work was abandoned.

Derivatization, Analysis by HPLC

To overcome the problems associated with storage stability, it was decided to investigate the possibility of derivatizing maleic anhydride during collection. Johnson and Funk reported a method for the determination of carboxylic acid anhydrides in the presence of and to the exclusion of the corresponding acids (Reference 3). They reported a rapid and quantitative reaction of anhydrides with morpholine to form the half acid/half amide:



Several anhydrides were measured by back titration of excess morpholine. Johnson and Funk could not measure maleic anhydride because its acidity interfered with the indicator, but later measured it by potentiometric titration (Reference 4). It has been reported that morpholine may add across the double bond of maleic anhydride (Reference 5).

Addition of morpholine to a solution of maleic anhydride in ether resulted in immediate formation of a precipitate. The following procedure was used to isolate the precipitate:

> One milliliter of morpholine in 50 mL of ether was added slowly to 1.07 g of maleic anhydride in 75 mL of ether. The ether was decanted, and the beaker was rinsed with ether. The residue was rather oily, and stuck to the walls of the beaker. The precipitate was dissolved in 50 mL of acetone, and 10 mL of ether was added. A precipitate formed immediately. The material was filtered and rinsed with ether and then dried in a vacuum oven at 25°C. The product was white and flocculant.

HPLC conditions were established as follows:

> Column - Waters μBondapak C-18
> Eluant - 20% methylene chloride/30% ethanol/50% hexane
> Detector - uv at 254 nm
> Flow Rate - 1.5 mL/minute

Under these conditions maleic anhydride eluted in 2.9 minutes, maleic acid in 6.2 minutes, and the maleic anhydride/morpholine derivative in 9.2 minutes.

It was determined that the reaction between maleic anhydride and morpholine proceeded rapidly. The reaction occurred exclusively with the anhydride, and the acid was not affected by the presence of morpholine. The retention time of the isolated product and the solution reaction product were identical. In addition, the detection limit of the derivative using a HPLC was vastly improved over that of the anhydride underivatized.

The reaction proceeds in alcohols, acetonitrile, chlorinated hydrocarbons, acetone, and ethyl acetate. All of these solvents are unacceptable for use as a collection medium in a bubbler. Shipping regulations prohibit their being shipped because of high volatility and low flash points. No suitable bubbler medium was found.

It is felt that morpholine or another amine such as aniline, could be coated on a solid sorbent to simultaneously collect and derivatize anhydrides. This would stabilize otherwise reactive compounds, eliminate the awkwardness associated with the use of bubblers, and increase uv detectability for HPLC analysis. There was insufficient time in this study to pursue this method of approach.

Hydrolysis/Analysis by HPLC

The failure report prepared under NIOSH Contract CDC-99-74-45 recommended collection of maleic anhydride in 0.1 N HCl or by solid sorbent and analysis of the hydrolysis product by HPLC. Although this method does not differentiate between the anhydride and the acid, it was believed that a successful method could be developed in the remaining time.

Collection efficiency tests were conducted to determine if it was necessary to use HCl to collect and hydrolyze maleic anhydride. Six sets of bubblers, each containing 15 mL of distilled water or 0.01 N HCl, were used to collect 320-liter samples from a test atmosphere of approximately 2 mg/cu m. The front and backup bubbler of each set was analyzed separately. The results are presented below:

Table 302-4

Collection Efficiency

Collection Medium	µg Found (Front)	µg Found (Back)
Distilled water	611	N.D.*
	656	N.D.
	656	N.D.
0.01 N HCl	653	N.D.
	639	N.D.
	691	N.D.

* Not detected at a detection limit of 15 micrograms/sample.

Based upon these results water was considered to be an adequate collection medium and was used in the study.

Independent Method

It was desired to collect and analyze maleic anhydride as the anhydride to independently measure the concentration in each generation chamber. HPLC conditions for analyzing maleic anhydride were as follows:

Column - Waters µPorasil
Flow Rate - 1.6 mL/minute
Mobile Phase - 0.02% acetic acid/2% isopropanol/8% methylene chloride/90% hexane
Detector - uv at 254 nm
Injection Volume - 50 microliters
Retention Time - 6.5 minutes

Samples were collected with midget bubblers containing 15 mL ethyl acetate placed in an ice bath. At the 2X level, a backup bubbler was added. Three samples at each level were collected at 1.5 liters/minute for 240 minutes. It was necessary to recharge the bubblers at 30-minute

intervals to maintain the liquid level. Each sample was analyzed separately and the concentrations obtained are presented in Table 302-5.

Table 302-5

Independent Method

Level		Taken Concentration (mg/cu m)
0.5X		0.517
		0.528
		0.464
	mean	0.503
	std dev	0.034
	CV	0.068
1X		1.025
		1.109
		1.139
	mean	1.091
	std dev	0.059
	CV	0.054
2X		2.206
		2.076
		2.141
	mean	2.141
	std dev	0.065
	CV	0.030

The backup bubblers for the 2X level were found to contain less than the limit of detection which was 50 micrograms/sample.

Precision and Accuracy

The statistical procedures and a definition of the terms used are described in Reference 6.

Bartlett's test for homogeneity of variances was applied to the coefficients of variation of 0.5X, 1X, and 2X the OSHA standard for generated samples. The data (Table 302-7) gave a chi squared value of 0.057. Thus, Bartlett's test is passed and it is feasible to pool the coefficients of variation to calculate $\overline{CV}_T$.

The precision of the analytical method was assessed using the data in Table 302-6. The pooled Coefficient of Variation ($\overline{CV}_1$) for three sets of analytical samples was found to be 0.032.

Precision and accuracy of the total sampling and analytical method was evaluated using the data in Tables 302-6 and 302-7 and the results obtained from collection efficiency tests and storage stability tests. The pooled Coefficient of Variation ($\overline{CV}_p$) for the three sets of samples collected from test atmospheres is 0.036. To obtain a measure of the accuracy of the method, the mean value of the concentration found by analysis at each level was compared with the value for the concentration taken.

The average recovery (concentration found divided by concentration taken) for all three test levels was 93.3%. The value for the taken concentration was obtained as described under the Independent Method Section. The difference between the taken and found concentrations is considered to result from experimental uncertainties in the value for the taken concentration and does not represent a bias in the method. Further confidence in the accuracy of the tested method is established by the results of the collection efficiency test, described above.

The total Coefficient of Variation ($\overline{CV}_T$) is 0.063.

Table 302-6

Data Sheet: Maleic Anhydride

Analysis

Level	0.5X			1X			2X	
µg taken	µg found	A.M.R.*	µg taken	µg found	A.M.R.	µg taken	µg found	A.M.R.
180.7	183.4	1.015	361	389	1.078	723	761	1.053
180.7	190.9	1.056	361	386	1.069	723	761	1.053
180.7	185.0	1.024	361	382	1.058	723	763	1.055
180.7	187.1	1.035	361	381	1.055	723	749	1.036
180.7	190.4	1.054	361	400	1.108	723	752	1.040
180.7	188.0	1.040	361	341	0.945	723	745	1.030
n =		6			6			6
mean		1.037			1.052			1.044
std dev		0.016			0.056			0.011
CV_1		0.015			0.053			0.011

$\overline{CV}_1$ 0.032

$\overline{CV}_{A+\overline{AMR}}$ 0.035

*A.M.R. = Analytical Method Recovery = $\frac{\text{µg found}}{\text{µg taken}}$

No analytical method recovery corrections were made.

Table 302-7

Data Sheet: Maleic Anhydride

Sampling and Analysis

Test Level	Found			Taken	Percent Recovery
	µg	Liters	mg/cu m	mg/cu m	
0.5X	156.9	349	0.450	0.503	
	157.3	347	0.453	0.503	
	169.1	352	0.480	0.503	
	158.2	348	0.455	0.503	
	170.0	353	0.482	0.503	
	130.7	354	0.369*	0.503	
		n = 5			
		mean	0.464		92.2
		std dev	0.016		
		CV_2	0.034		
1X	323	335	0.964	1.091	
	358	351	1.020	1.091	
	369	350	1.054	1.091	
	377	360	1.047	1.091	
	340	350	0.971	1.091	
	348	349	0.997	1.091	
		n = 6			
		mean	1.009		92.5
		std dev	0.038		
		CV_2	0.038		
2X	684	330	2.073	2.141	
	665	334	1.991	2.141	
	673	335	2.009	2.141	
	686	339	2.024	2.141	
	727	335	2.170	2.141	
	657	333	1.973	2.141	
		n = 6			
		mean	2.040		95.3
		std dev	0.072		
$\overline{CV}_2$	0.036	CV_2	0.035		

* This value did not pass the Grubbs' outlier test the 1% significance level as described in Reference 6.

References

1. Contract 210-76-0123, National Institute for Occupational Safety and Health, Division of the Department of Health, Education and Welfare, U. S. Government.

2. Qazi, A. H., W. J. Vincent, and N. H. Ketcham, "Sampling and Analysis of Acetic Anhydride in Air," presented at the American Industrial Hygiene Association in May 1978. The authors are employed by Union Carbide Corporation, P. O. Box 8361, South Charleston, West Virginia 25303.

3. Johnson, James B. and G. L. Funk, "Determination of Carboxylic Acid Anhydrides by Reaction with Morpholine," Anal. Chem., 27(9), September 1955, 1464.

4. Critchfield, Frank E. and James B. Johnson, "Reaction of Carbon Disulfide with Primary and Secondary Aliphatic Amines as an Analytical Tool," Anal. Chem., 28(4), April 1956, 430.

5. Critchfield, Frank E., Gregory L. Funk, and James B. Johnson, "Determination of Alpha, Beta-Unsaturated Compounds by Reaction with Morpholine," Anal. Chem., 28(1), January 1956, 76.

6. Documentation of NIOSH Validation Tests, National Institute for Occupational Safety and Health, Cincinnati, Ohio (DHEW-NIOSH Publication #77-185), 1977. Available from Superintendent of Documents, U. S. Government Printing Office, Washington, DC, Order No. 017-033-00231-2.

Attachment A

Vapor Generation System

Test atmospheres of organic vapors can be generated with an apparatus described in Reference 1, which describes a method for measuring liquid vapor pressure.

The vapor generator was adapted from the apparatus described in Reference 1. A schematic diagram of this vapor generator is shown in Figures 302-A1 and 302-A2. The vapor generator consists of two sections--a generating section (Figure 302-A1) and a diluting section (Figure 302-A2) which are connected by a ground glass joint.

The generating section (Figure 302-A1) consists of a pyrex glass tube which is 2.4 cm in diameter and 19.5 cm long. A coarse glass frit is sealed in the bottom of the tube. The bottom of this tube is connected to a 7-mm O.D. glass tube which is bent 180° and extends up until it is nearly as high as the larger tube. The sample, which may be either a liquid, low melting solid, or a solid with a high vapor pressure, is introduced into the large tube. This part of the apparatus is immersed in a thermostated bath with the analyte level below the bath level. Nitrogen is introduced through the small tube and passes through the frit. The small bubbles, which form at the frit, rise through the liquid or solid and become saturated or nearly saturated with the vapor. The bath temperature and the flow of nitrogen determine the actual amount of vapor generated. Increasing either the nitrogen flow or the bath temperature, increases the amount of vapor generated.

The diluting section (Figure 302-A2) of the vapor generator consists of a pyrex glass tube which is 2.4 cm in diameter and 13 cm high. The dilution air is introduced through a 7-mm O.D. glass tube connected to the side of the diluting tube. Sufficient air is added to dilute the vapor in nitrogen to the desired concentration.

The equations given in Reference 1 can be used to determine the approximate vapor concentration in the saturated nitrogen stream.

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1. Physical Methods of Chemistry, Part V, A. Weissberger and B. W. Rossiter, eds., (John Wiley & Sons, 1971), 61-66.

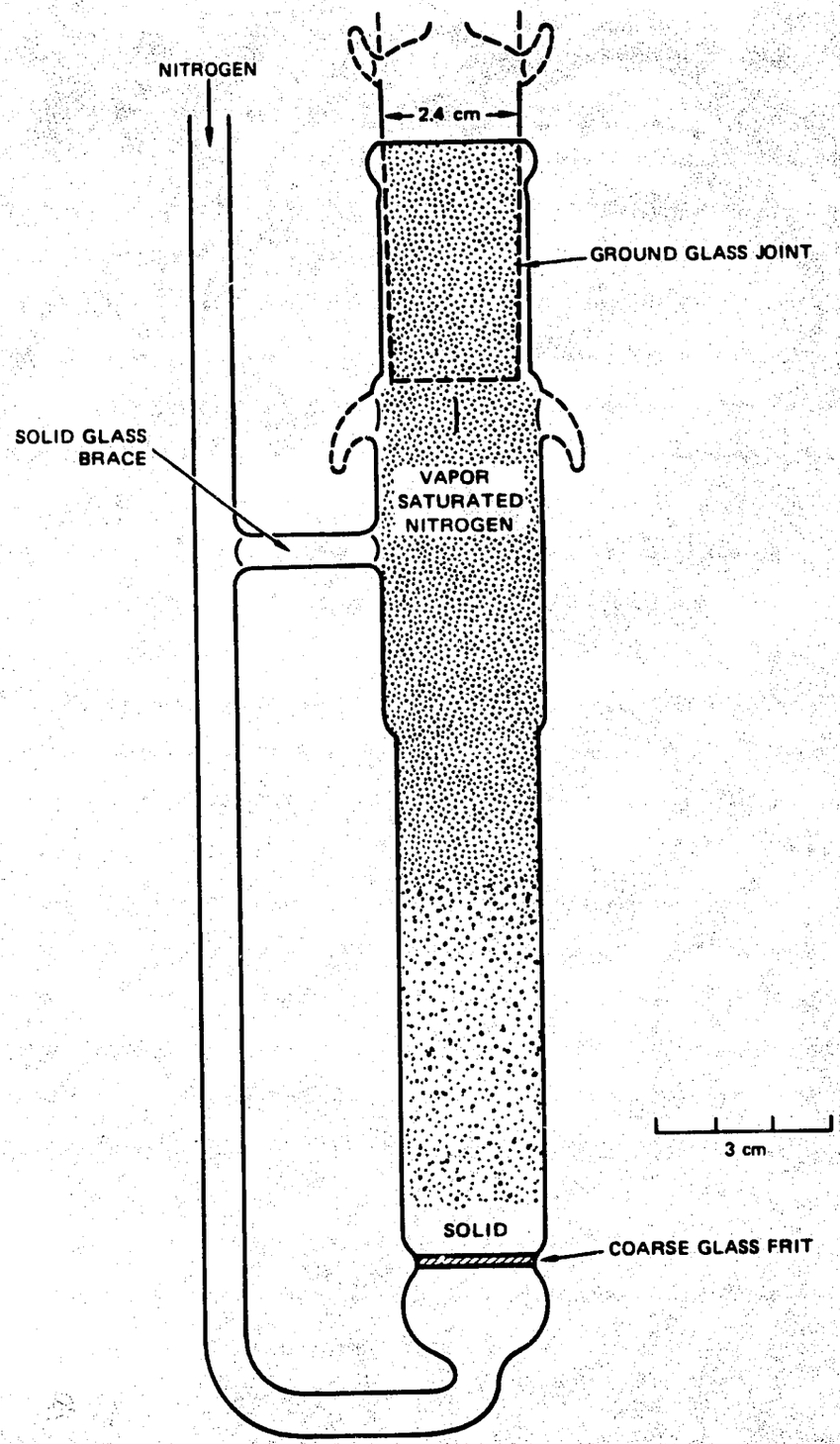

FIGURE 302-A1 VAPOR GENERATOR (GENERATING SECTION)

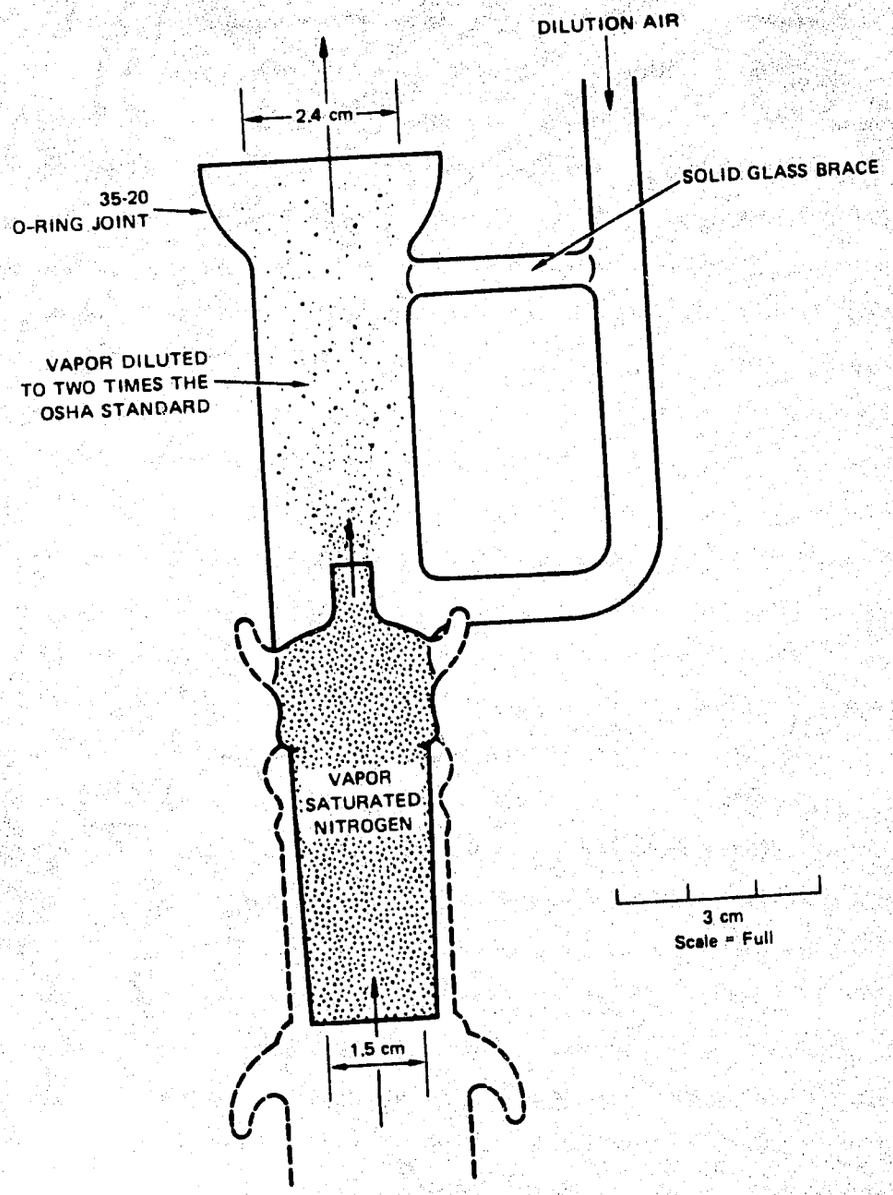

FIGURE 302-A2 VAPOR GENERATOR (DILUTING SECTION)

Attachment B

Generation of Test Atmospheres

The system for generating and collecting samples of vapor, inorganic/organic particulate, dusts, and fumes consists basically of a sample generator, a mixing and dilution section, and three sampling chambers. Samples are generated at a concentration 2X the OSHA standard, serial dilutions are made to 1X and 0.5X the standard, and samples are collected simultaneously at the three concentrations. A schematic of the generation system and associated components is presented in Figure 1.

The generation system is large enough to be used for polydispersed aerosols as well as for gases and vapors. The primary dilution chamber is 48 inches by 4 inches and may handle air flows up to 400 liters/minute. The large volume dilution chamber is important for several reasons. Even at high air flow rates, the velocity of particles is low to allow complete solvent evaporation in the generation of aerosols. The air velocity is also low enough to avoid impaction on the walls while great enough to prevent particle diffusion to the walls. For these same reasons, the sample rationing system is only 1 inch in diameter and handles a flow of only 52 liters/minute. Gravitational settling is avoided by maintaining a sufficient air velocity.

The sampling cones for the three chambers are 6-inch I.D. at the base (point of sample collection) and narrow to 1-inch I.D. at the point of attachment to the sample rationing system. A constant total air flow of 26 liters/minute through each cone causes a gradual reduction in aerosol velocity toward the point of sample collection. The air velocity at the collection point is 2.4 cm/second.

All portions of the generation system that come in contact with the test atmosphere are constructed of stainless steel or Teflon to avoid any contamination problems. Sections of the generation system at which dilution air is added are constructed such that the incoming air forms a "high-velocity sheath" around the air/analyte mixture that is to be diluted. This sheath serves two functions. The dilution air sheath becomes increasingly less coherent and stable as it moves downstream of its point of entrance and hence is turbulently mixed with air/analyte test atmosphere. At the point of entrance of the dilution air stream, a Venturi effect accelerates the air/analyte mixture to a high velocity. The dilution air sheath also prevents interaction of the accelerated air/analyte stream with the walls of the chamber, thus eliminating a large source of aerosol loss by impaction.

The system being used to generate the initial concentrations of vapor, gas, or particulate is interfaced with the dilution apparatus at the primary dilution chamber. The output of the generator is diluted with the appropriate amount of air to obtain a concentration 2X the OSHA standard. Of the total amount of material generated at the 2X level, a flow of 52 liters/minute enters the rationing system. Under control of a vacuum exhaust orifice, material at the 2X level enters the first sampling chamber at a rate of 26 liters/minute. Downstream of the entrance to the first sampling chamber, dilution air is added (via a critical orifice) at a rate of 26 liters/minute. Thus the flow of material at the 2X level that did not enter the first sampling chamber

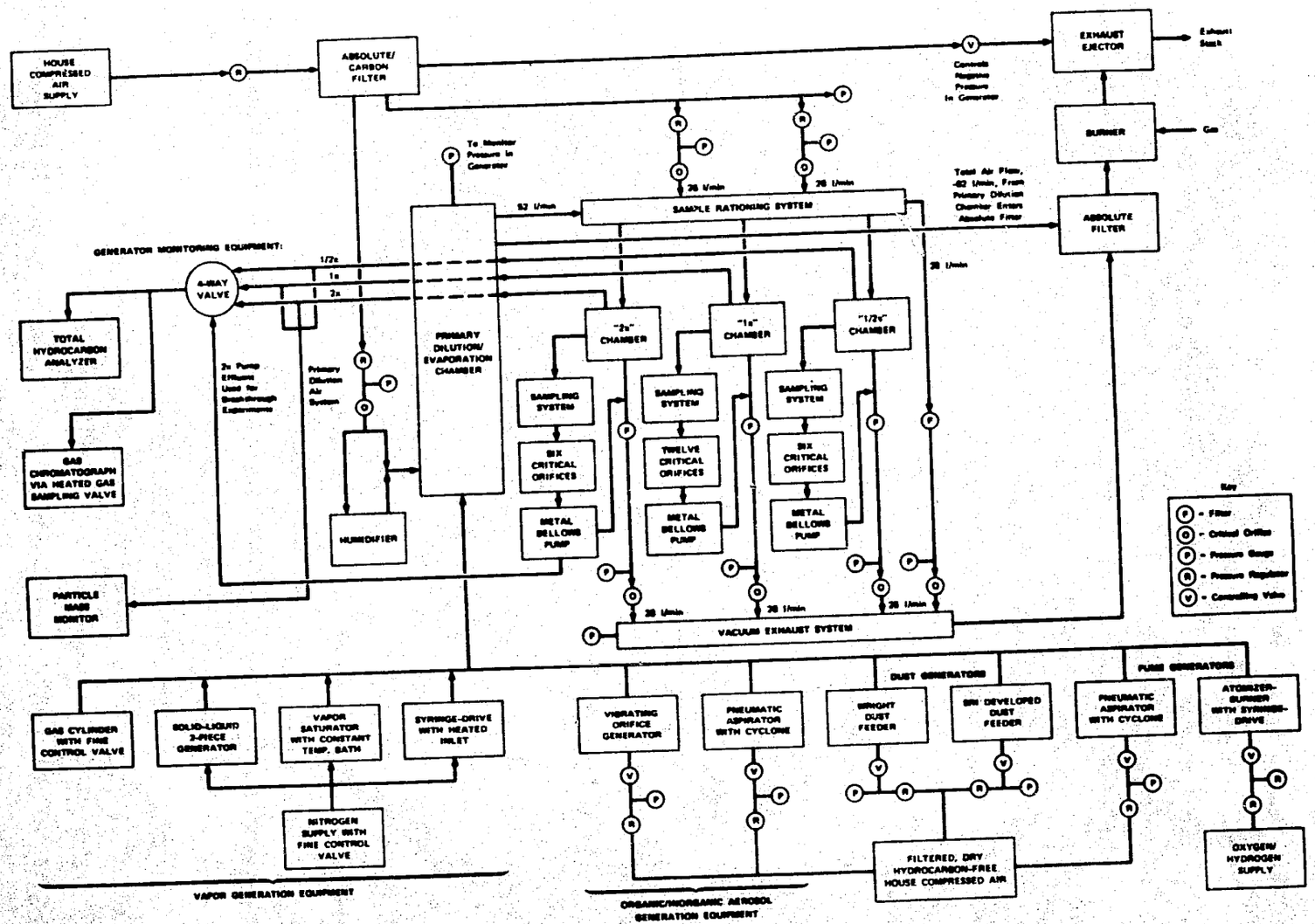

FIGURE 302-B1 SCHEMATIC OF SAMPLE GENERATION FACILITIES

(26 liters/minute) is diluted with air at a flow rate of 26 liters/minute to a final concentration of 1X the OSHA standard level. Analyte at the 1X level then enters the second sampling chamber at a rate of 26 liters/minute. The remaining flow, 26 liters/minute is diluted again with air at 26 liters/minute to achieve 0.5X the OSHA standard level. The analyte/air mixture at the 0.5X level is drawn into the third sampling chamber at 26 liters/minute. The remaining material in the rationing system not drawn into the sampling chambers is removed at a rate of 26 liters/minute by the fourth critical orifice in the vacuum exhaust system. This removal of test atmosphere volumes and addition of measured volumes of air thus achieves serial dilutions to 1X and 0.5X the OSHA standard level.

The dilution ratios from chamber to chamber can also be varied by simply changing the amount of dilution air that is added. This is particularly advantageous in generating aerosols, where wall deposition of particles in the rationing system can be offset by changing the rate of addition of dilution air.

The cylindrical section at the base of each sampling chamber contains the fittings necessary to collect samples, using any of a variety of sampling media--solid sorbent tubes, filters, liquid scrubbers, or a combination of these. Six to twelve samples each at three concentration levels can be collected simultaneously. A metal bellows vacuum pump is used for sampling from each chamber. Separate critical flow orifices are used for each sample. Air taken from the chamber during sampling is returned via the sampling pump exhaust line to the chamber outlet line, thus preserving the proper air flows during the time of sampling. The sampling rate therefore does not affect the concentration of material in any of the chambers.

The entire system is maintained at 1-inch water vacuum to prevent toxic materials from escaping into the laboratory. All exhaust air streams (from the vacuum exhaust system and excess from the primary dilution chamber) are fed into a combustion chamber where all toxic materials present are burned before entering the atmosphere.