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Analytical Methods for the Determination of Pollutants in Pharmaceutical Manufacturing Industry Wastewater

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Disclaimer

This methods compendium has been reviewed by the Engineering and Analysis Division, U.S. Environmental Protection Agency, and approved for publication. Mention of trade names or commercial products does not constitute and endorsement or recommendation for use.

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Introduction

The U.S. Environmental Protection Agency (EPA) has promulgated effluent limitations guidelines and standards at 40 CFR part 439 for the Pharmaceutical Manufacturing Industry to control the discharge of pollutants into surface waters of the United States. This compendium of test procedures (methods) supports the final rule. These methods and methods promulgated at 40 CFR part 136 are used for filing permit applications and for compliance monitoring under the National Pollutant Discharge Elimination System (NPDES) program.

This compendium includes only those methods unique to the Pharmaceutical Manufacturing Industry. Other methods allowed under the proposed rule have been promulgated at 40 CFR part 136.

Questions concerning the methods in this compendium should be directed to:

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Method 1666

Volatile Organic Compounds Specific to the Pharmaceutical Manufacturing Industry by Isotope Dilution GC/MS

Revision A, July 1998

Method 1666, Revision A

Volatile Organic Compounds Specific to the Pharmaceutical Manufacturing Industry by Isotope Dilution GC/MS

1.0 Scope and Application

1.1 This method is for surveying and monitoring under the Clean Water Act. It is used to determine certain volatile organic pollutants specific to the pharmaceutical manufacturing industry (PMI) that are amenable to purge-and-trap gas chromatography/mass spectrometry (GC/MS) or direct aqueous injection GC/MS.

1.2 The PMI analytes listed in Tables 1 and 2 may be determined in waters, soils, and municipal sludges by this method or the method referenced at the end of that table.

1.3 The detection limits of the method are usually dependent on the level of interferences rather than instrumental limitations. The minimum levels (MLs) in Tables 3 and 4 are the level that can be attained with no interferences present.

1.4 The GC/MS portions of this method are for use only by analysts experienced with GC/MS or under the close supervision of such qualified persons. Laboratories unfamiliar with analysis of environmental samples by GC/MS should run the performance tests in Reference 1 before beginning.

1.5 This method is performance-based. The analyst is permitted to modify the method to overcome interferences or to lower the cost of measurements, provided that all performance criteria in this method are met. The requirements for establishing method equivalency are given in Section 9.1.2.

2.0 Summary of Method

2.1 Purge-and-trap GC/MS.

Stable, isotopically labeled analogs of the compounds of interest are added to the sample and the sample is purged with an inert gas at 45°C in a chamber designed for soil or water samples, as appropriate. In the purging process, the volatile compounds are transferred from the aqueous phase into the vapor phase, where they are passed into a sorbent column and trapped. After purging is completed, the trap is backflushed and heated rapidly to desorb the compounds into a gas chromatograph (GC). The compounds are separated by the GC and detected by a mass spectrometer (MS) (References 2 and 3).

2.2 Direct aqueous injection.

Certain volatile, water-soluble organic compounds do not purge well from water and are analyzed by direct aqueous injection.

2.2.1 The percent solids content of the sample is determined. If the solids content is known or determined to be less than 1%, stable, isotopically labeled analogs of the compounds of interest are added to a 5-mL sample. If the solids content of the sample is greater than 1%, 5 mL of reagent water and the labeled compounds are added to a 5-g aliquot of sample. The mixture is sonicated in a centrifuge vial with little or no headspace for 5 minutes. During this period the native analytes and labeled analogs will equilibrate between the solid and aqueous phases. In some cases, additional sonication will be necessary to establish equilibrium. The resulting suspension is centrifuged and the supernatant liquid analyzed.

2.2.2 One µL or more of the aqueous solution (or supernate) is injected into the GC/MS. The compounds are separated by the GC and detected by the MS (References 2 and 3). The labeled compounds serve to correct the variability of the analytical technique.

2.3 Identification of a pollutant (qualitative analysis) is performed by calibrating the GC/MS with authentic standards and storing a mass spectrum and retention time for each compound in a user-created library. A compound is identified when its retention time and mass spectrum agree with the library retention time and spectrum.

2.4 Quantitative analysis is performed in one of two ways by using extracted-ion current profile (EICP) areas. (1) For those compounds listed in Table 1 and Table 2, and for other compounds for which labeled analogs are available, the GC/MS system is calibrated and the compound concentration is determined using an isotope dilution technique. (2) For those compounds listed in Table 1 and Table 2, and for other compounds for which authentic standards but no labeled compounds are available, the GC/MS system is calibrated and the compound concentration is determined using an internal standard technique.

2.5 The quality of the analysis is assured through reproducible calibration of the GC/MS system.

3.0 Definitions

There are no definitions unique to this method.

4.0 Interferences

4.1 Impurities in the purge gas, organic compounds outgassing from the plumbing upstream of the trap, and solvent vapors in the laboratory account for the majority of contamination problems encountered with this method. The analytical system is demonstrated to be free from interferences under conditions of the analysis by analyzing reagent water blanks initially and with each sample batch (samples analyzed on the same 12-hour shift), as described in Section 9.5.

4.2 Samples can be contaminated by diffusion of volatile organic compounds (particularly methylene chloride) through the bottle seal during shipment and storage. A field blank prepared from reagent water and carried through the sampling and handling protocol may serve as a check on such contamination.

4.3 Contamination by carryover can occur when high-level and low-level samples are analyzed sequentially. To reduce carryover, the purging device (Figure 1 for samples containing less than 1% solids; Figure 2 for samples containing 1% solids or greater) in purge-and-trap analysis or the syringe in direct aqueous injection analysis is cleaned or replaced with a clean purging device or syringe after each sample is analyzed. When an unusually concentrated sample is encountered, it is followed by analysis of a reagent water blank to check for carryover. Purging devices and syringes are cleaned by washing with soap solution, rinsing with tap and distilled water, and drying in an oven at 100-125°C. The trap and other parts of the system are also subject to contamination; therefore, frequent bakeout and purging of the entire system may be required.

4.4 Interferences resulting from samples will vary considerably from source to source, depending on the diversity of the site being sampled.

5.0 Safety

5.1 The toxicity or carcinogenicity of each compound or reagent used in this method has not been precisely determined; however, each chemical compound should be treated as a potential health hazard. Exposure to these compounds should be reduced to the lowest possible level. The laboratory is responsible for maintaining a current awareness file of OSHA regulations regarding the safe handling of the chemicals specified in this method. A reference file of material safety data sheets should also be made available to all personnel involved in these analyses. Additional information on laboratory safety can be found in References 5 through 7.

6.0 Equipment and Supplies

Disclaimer: The mention of trade names or commercial products in this Method is for illustrative purposes only and does not constitute endorsement or recommendation for use by the Environmental Protection Agency. Equivalent performance may be achievable using apparatus, materials, or cleaning procedures other than those suggested here. The laboratory is responsible for demonstrating equivalent performance.

6.1 Sample bottles and septa.

6.1.1 Bottle—25- to 40-mL with screw-cap (Pierce 13075, or equivalent). Detergent wash, rinse with tap and distilled water, and dry at >105 °C for a minimum of 1 hour before use.

6.1.2 Septum-Polytetrafluoroethylene (PTFE)-faced silicone (Pierce 12722, or equivalent), cleaned as above and baked at 100-200°C for a minimum of 1 hour.

6.2 Purge-and-trap device-Consists of purging device, trap, and desorber.

6.2.1 Purging devices for water and soil samples.

6.2.1.1 Purging device for water samples-Designed to accept 5-mL samples with water column at least 3 cm deep. The volume of the gaseous headspace between the

water and trap shall be less than 15 mL. The purge gas shall be introduced less than 5 mm from the base of the water column and shall pass through the water as bubbles with a diameter less than 3 mm. The purging device shown in Figure 1 meets these criteria.

6.2.1.2 Purging device for solid samples-Designed to accept 5 g of solids plus 5 mL of water. The volume of the gaseous head space between the water and trap shall be less than 25 mL. The purge gas shall be introduced less than 5 mm from the base of the sample and shall pass through the water as bubbles with a diameter less than 3 mm. The purging device shall be capable of being controlled at a temperature of 45±2 °C while the sample is being purged. The purging device shown in Figure 2 meets these criteria.

6.2.2 Trap-25-30 cm long × 2.5 mm i.d. minimum, containing the following:

6.2.2.1 Methyl silicone packing-1±0.2 cm, 3% OV-1 on 60/80 mesh Chromosorb W, or equivalent.

6.2.2.2 Porous polymer-15±1.0 cm, Tenax GC (2,6-diphenylene oxide polymer), 60/80 mesh, chromatographic grade, or equivalent.

6.2.2.3 Silica gel-8±1.0 cm, Davison Chemical, 35/60 mesh, grade 15, or equivalent. The trap shown in Figure 3 meets these specifications.

6.2.3 Desorber-Shall heat the trap to 175±5 °C in 45 seconds or less. The polymer section of the trap shall not exceed a temperature of 180°C and the remaining sections shall not exceed 220°C during desorb, and no portion of the trap shall exceed 225°C during bakeout. The desorber shown in Figure 3 meets these specifications.

6.2.4 The purge-and-trap device may be a separate unit or coupled to a GC, as shown in Figures 4 and 5.

6.3 Gas chromatograph-Shall be linearly temperature programmable with initial and final holds, and shall produce results that meet the calibration (Section 10), quality assurance (Section 9), and performance tests (Section 15) of this method.

6.3.1 Column for purge-and-trap analyses-60 m long × 0.32 mm i.d., fused-silica microbore column coated with 1.5 µm of phenylmethyl polysiloxane (Restek RTX-Volatiles, or equivalent).

6.3.2 Column for direct aqueous injection analyses-30 m long × 0.32 mm i.d. fused-silica microbore column coated with 1.5 µm of 95% dimethyl- 5% diphenyl polysiloxane specially passivated for chromatography of amines (Restek RTX-5 Amine, or equivalent).

6.3.3 GC operating conditions.

6.3.3.1 Purge-and-trap-4 minutes at 0°C, 8°C per minute to 170°C. Helium carrier gas at 1.5 mL per minute.

6.3.3.2 Direct aqueous injection-4 minutes at 40°C, 8°C per minute to 100°C, then 25°C to 220°C with a 3-minute hold at 220°C. Helium carrier gas at 1.5 mL per minute. A pre-column split may be used to achieve acceptable peak shape.

6.4 Mass spectrometer-70 electron volt (eV) electron-impact ionization; shall repetitively scan from 20 to 250 Dalton every 2 to 3 seconds, and produce a unit resolution (valleys between m/z 174 to 176 less than 10% of the height of the m/z 175 peak), background-corrected mass spectrum from 50 ng 4-bromofluorobenzene (BFB) injected into the GC. The BFB spectrum shall meet the mass-intensity criteria in Table 5. All portions of the GC column, transfer lines, and separator that connect the GC column to the ion source shall remain at or above the column temperature during analysis to preclude condensation of less volatile compounds.

6.5 Data system-Shall collect and record MS data, store mass-intensity data in spectral libraries, process GC/MS data and generate reports, and calculate and record response factors.

6.5.1 Data acquisition-Mass spectra shall be collected continuously throughout the analysis and stored on a mass-storage device.

6.5.2 Mass spectral libraries-User-created libraries containing mass spectra obtained from analysis of authentic standards shall be employed to reverse search GC/MS runs for the compounds of interest (Section 10.2).

6.5.3 Data processing-The data system shall be used to search, locate, identify, and quantify the compounds of interest in each GC/MS analysis. Software routines shall be employed to compute retention times and EICP areas. Displays of spectra, mass chromatograms, and library comparisons are required to verify results.

6.5.4 Response factors and multipoint calibrations-The data system shall be used to record and maintain lists of response factors (response ratios for isotope dilution) and generate multi-point calibration curves (Section 10.4). Computations of relative standard deviation (coefficient of variation) are useful for testing calibration linearity. Statistics on initial and ongoing performance shall be maintained (Sections 9 and 10).

6.6 Syringes-5-mL glass hypodermic, with Luer-lok tips.

6.7 Micro syringes-10-, 25-, and 100-µL.

6.8 Syringe valves-2-way, with Luer ends (PTFE).

6.9 Syringe-5-mL, gas-tight, with shut-off valve.

6.10 Bottles-15-mL, screw-cap with PTFE liner.

6.11 Balances.

6.11.1 Analytical, capable of weighing 0.1 mg.

6.11.2 Top-loading, capable of weighing 10 mg.

6.12 Equipment for determining percent moisture.

6.12.1 Oven, capable of temperature control at 110±5 °C.

6.12.2 Desiccator.

6.12.3 Beakers-50- to 100-mL.

6.13 Centrifuge apparatus.

6.13.1 Centrifuge capable of rotating 10-mL centrifuge tubes at 5000 rpm.

6.13.2 Centrifuge tubes, 10-mL, with screw-caps to fit centrifuge.

6.14 Sonication apparatus capable of sonicating 10 mL centrifuge tubes and thoroughly agitating contents.

7.0 Reagents and Standards

7.1 Reagent water-Water in which the compounds of interest and interfering compounds are not detected by this method. It may be generated by any of the following methods.

7.1.1 Activated carbon-Pass tap water through a carbon bed (Calgon Filtrasorb-300, or equivalent).

7.1.2 Water purifier-Pass tap water through a purifier (Millipore Super Q, or equivalent).

7.1.3 Boil and purge-Heat tap water to 90-100 °C and bubble contaminant-free inert gas through it for approximately 1 hour. While still hot, transfer the water to screw-cap bottles and seal with a PTFE-lined cap.

7.2 Sodium thiosulfate-ACS granular.

7.3 Methanol-Pesticide-quality or equivalent.

7.4 Standard solutions-Purchased as solutions or mixtures with certification to their purity, concentration, and authenticity, or prepared from materials of known purity and composition. If compound purity is 96% or greater, the weight may be used without correction to calculate the concentration of the standard.

7.5 Preparation of stock solutions for purge-and-trap analysis.

7.5.1 Place approximately 9.5 mL of methanol in a 10-mL ground-glass-stoppered volumetric flask. Allow the flask to stand unstoppered for approximately 10 minutes or until all methanol-wetted surfaces have dried. In each case, weigh the stoppered flask, add the compound, restopper, then immediately reweigh to prevent evaporation losses from affecting the measurement.

7.5.2 Using a 100-µL syringe, permit two drops of liquid to fall into the methanol without contacting the neck of the flask. Alternatively, inject a known volume of the compound into the methanol in the flask using a microsyringe.

7.5.3 Fill the flask to volume, stopper, then mix by inverting several times. Calculate the concentration in milligrams per milliliter (mg/mL; equivalent to micrograms per microliter [µg/µL]) from the weight gain.

7.5.4 Transfer the stock solution to a PTFE-sealed screw-cap bottle. Store, with minimal headspace, in the dark at -20 to -10°C.

7.5.5 Replace standards after one month, or sooner if comparison with check standards indicate a change in concentration. Quality control check standards that can be used to determine the accuracy of calibration standards may be available from the National Institute of Standards and Technology, Gaithersburg, Maryland.

7.6 Preparation of stock solutions for direct aqueous injection analysis.

7.6.1 Place approximately 9.0 mL of reagent water in a 10-mL ground-glass-stoppered volumetric flask. Allow the flask to stand unstoppered for approximately 10 minutes or until all wetted surfaces have dried. In each case, weigh the stoppered flask, add the compound, restopper, then immediately reweigh to prevent evaporation losses from affecting the measurement.

7.6.2 Using a microsyringe, add sufficient liquid (about 100 mg) so that the final solution will have a concentration of about 10 mg/mL.

7.6.3 Fill the flask to volume, stopper, then mix by inverting several times. Calculate the concentration in milligrams per milliliter (mg/mL; equivalent to micrograms per microliter [µg/µL]) from the weight gain.

7.6.4 Transfer the stock solution to a PTFE-sealed screw-cap bottle. Store, with minimal headspace, in the dark at approximately 4°C. Do not freeze.

7.6.5 Replace standards after one month, or sooner if comparison with check standards indicate a change in concentration. Quality control check standards that can be used to determine

the accuracy of calibration standards may be available from the National Institute of Standards and Technology, Gaithersburg, Maryland.

7.7 Labeled compound spiking solutions.

7.7.1 Purge-and-trap analysis-From stock standard solutions (Section 7.5), or from mixtures, prepare the spiking solution to contain a concentration of labeled compound such that a 5- to 10-µL spike into each 5-mL sample, blank, or aqueous standard analyzed will result in a concentration of 50 µg/L of each compound with a minimum level (ML) of 20 µg/L or less, a concentration of 500 µg/L for each compound with an ML of 100 or 200 µg/L, and a concentration of 1 mg/L for each compound with an ML of 500 µg/L (see Table 3). Include the internal standards (Section 10.4.2) in this solution, if appropriate, so that a concentration of 50 µg/L in each sample, blank, or aqueous standard will be produced.

7.7.2 For direct aqueous injection-From stock standard solutions (Section 7.6), or from mixtures, prepare the spiking solution to contain a concentration such that a 50- to 100-µL spike into each sample, blank, or aqueous standard analyzed will result in a concentration of 1 mg/mL of each labeled compound. Include the internal standard in this solution so that a concentration of 1 mg/mL will be produced.

7.8 Secondary standards-Using stock solutions, prepare a secondary standard in methanol or water, as appropriate, to contain each pollutant at a concentration of 1 mg/mL, or 2.5 mg/mL for compounds with higher MLs.

7.8.1 Aqueous calibration standards-Using a microsyringe, add sufficient secondary standard (Section 7.8) to five reagent water aliquots to produce concentrations in the range of interest.

7.8.2 Aqueous performance standard-An aqueous standard containing all pollutants, internal standards, labeled compounds, and BFB is prepared daily, and analyzed each shift to demonstrate performance (Section 15). This standard shall contain concentrations of pollutants, labeled compounds, BFB, and internal standards, as appropriate, within a factor of 1-5 times the MLs of the pollutants listed in Table 3 or 4. It may be one of the aqueous calibration standards described in Section 7.8.1.

7.8.3 A methanolic standard containing all pollutants specific to this method (Table 1) and internal standards is prepared to demonstrate recovery of these compounds when syringe injection and purge-and-trap analyses are compared. This standard shall contain either 100 µg/mL or 500 µg/mL of the PMI analytes, and 100 µg/mL of the internal standards (consistent with the amounts in the aqueous performance standard in Section 7.8.2).

7.8.4 Other standards that may be needed are those for test of BFB performance (Section 10.1) and for collection of mass spectra for storage in spectral libraries (Section 10.1.1).

8.0 Sample Collection, Preservation, and Storage

8.1 Grab samples are collected in glass containers having a total volume greater than 20 mL. For aqueous samples that pour freely, fill sample bottles so that no air bubbles pass through the sample as the bottle is filled and seal each bottle so that no air bubbles are entrapped. Maintain the hermetic seal on the sample bottle until time of analysis.

8.2 Samples are maintained at 0-4 °C from the time of collection until analysis. If an aqueous sample contains residual chlorine, add sodium thiosulfate preservative (10 mg/40 mL) to the empty sample bottles just prior to shipment to the sample site. EPA Methods 330.4 and 330.5 may be used for measurement of residual chlorine (Reference 8). If preservative has been added, shake the bottle vigorously for 1 minute immediately after filling.

8.3 For aqueous samples, experimental evidence indicates that some PMI analytes are susceptible to rapid biological degradation under certain environmental conditions. Refrigeration alone may not be adequate to preserve these compounds in wastewaters for more than seven days. For this reason, a separate sample should be collected, acidified, and analyzed when compounds susceptible to rapid biological degradation are to be determined. Collect about 500 mL of sample in a clean container. Adjust the pH of the sample to about 2 by adding hydrochloric acid (1:1) while stirring. Check pH with narrow range (1.4-2.8) pH paper. Fill a sample bottle as described in Section 8.1. If residual chlorine is present, add sodium thiosulfate to a separate sample bottle and fill as in Section 8.1.

8.4 All samples shall be analyzed within 14 days of collection.

9.0 Quality Assurance/Quality Control

9.1 Each laboratory that uses this method is required to operate a formal quality assurance program (Reference 9). The minimum requirements of this program consist of an initial demonstration of laboratory capability, analysis of samples spiked with labeled compounds to evaluate and document data quality, and analysis of standards and blanks as tests of continued performance. Laboratory performance is compared to established performance criteria to determine if the results of analyses meet the performance characteristics of the method.

9.1.1 The analyst shall make an initial demonstration of the ability to generate acceptable accuracy and precision with this method. This ability is established as described in Section 9.2.

9.1.2 In recognition of advances that are occurring in analytical technology, and to allow the analyst to overcome sample matrix interferences, the analyst is permitted certain options to improve separations or lower the costs of measurements. These options include alternative concentration and cleanup procedures, and changes in columns and detectors. Alternative techniques, such as the substitution of spectroscopy or immunoassay, and changes that degrade method performance, are not allowed. If an analytical technique other than the

techniques specified in this method is used, that technique must have a specificity equal to or better than the specificity of the techniques in this method for the analytes of interest.

9.1.2.1 Each time a modification is made to this method, the analyst is required to repeat the procedure in Section 9.2. If the detection limit of the method will be affected by the change, the laboratory is required to demonstrate that the MDL (40 CFR part 136, Appendix B) is lower than one-third the regulatory compliance level. If calibration will be affected by the change, the analyst must recalibrate the instrument per Section 10.

9.1.2.2 The laboratory is required to maintain records of modifications made to this method. These records include the information below, at a minimum.

9.1.2.2.1 The names, titles, addresses, and telephone numbers of the analyst(s) who performed the analyses and modification, and of the quality control officer who witnessed and will verify the analyses and modification.

9.1.2.2.2 A listing of pollutant(s) measured, by name and CAS Registry Number.

9.1.2.2.3 A narrative stating the reason(s) for the modification.

9.1.2.2.4 Results from all quality control (QC) tests comparing the modified method to this method, including:

(a) Calibration (Section 10)
(b) Calibration verification (Section 15)
(c) Initial precision and accuracy (Section 9.2)
(d) Labeled compound recovery (Section 9.3)
(e) Analysis of blanks (Section 9.5)
(f) Accuracy assessment (Section 9.4)

9.1.2.3 Data that will allow an independent reviewer to validate each determination by tracing the instrument output (peak height, area, or other signal) to the final result, including:

(a) Sample numbers and other identifiers
(b) Analysis dates and times
(c) Analysis sequence/run chronology
(d) Injection logs
(e) Sample weight or volume
(f) Sample volume prior to each cleanup step, if applicable
(g) Sample volume after each cleanup step, if applicable

(h) Final sample volume prior to injection (Sections 11 and 12)
(i) Injection volume (Sections 11 and 12)
(j) Dilution data, differentiating between dilution of a sample or an extract (Section 16.4)
(k) Instrument and operating conditions
(l) Column (dimensions, liquid phase, solid support, film thickness, etc.)
(m) Operating conditions (temperature, temperature program, flow rates, etc.)
(n) Detector (type, operating condition, etc.)
(o) Chromatograms, printer tapes, and other recording of raw data
(p) Quantitation reports, data system outputs, and other data necessary to link raw data to the results reported.

9.1.3 Analyses of blanks are required to demonstrate freedom from contamination and that the compounds of interest and interfering compounds have not been carried over from a previous analysis (Section 4.3). The procedures and criteria for analysis of a blank are given in Section 9.5.

9.1.4 The laboratory shall spike all samples with labeled compounds to monitor method performance. This test is described in Section 9.3. When results of these spikes indicate atypical method performance for samples, the samples are diluted to bring method performance within acceptable limits (Section 16).

9.1.5 The laboratory shall, on an ongoing basis, demonstrate through the analysis of the aqueous performance standard (Section 7.8.2) that the analysis system is in control. This procedure is described in Sections 15.1 and 15.5.

9.1.6 The laboratory shall maintain records to define the quality of data that is generated. Development of accuracy statements is described in Sections 9.4 and 15.5.2.

9.2 Initial precision and accuracy—To establish the ability to generate acceptable precision and accuracy, the analyst shall perform the following operations for compounds to be calibrated:

9.2.1 Analyze two sets of four 5-mL aliquots (eight aliquots total) of the aqueous performance standard (Section 7.8.2) containing Table 1 PMI analytes by purge-and-trap. Or, for Table 2 PMI analytes, analyze two sets of four aliquots (eight aliquots total) by direct aqueous injection.

9.2.2 Using results of the first set of four analyses in Section 9.2.1, compute the average recovery (X) in percent of spike level and the standard deviation of the recovery (s) in percent of spike level, for each compound, by isotope dilution for pollutants with a labeled

analog, and by internal standard for labeled compounds and pollutants with no labeled analog.

9.2.3 For each compound, compare s and X with the corresponding limits for initial precision and accuracy found in Table 6. If s and X for all compounds meet the acceptance criteria, system performance is acceptable and analysis of blanks and samples may begin. If, however, any individual s exceeds the precision limit or any individual X falls outside the range for accuracy, system performance is unacceptable for that compound

Note: *The large number of compounds in Table 6 presents a substantial probability that one or more will fail one of the acceptance criteria when all compounds are analyzed. To determine if the analytical system is out of control, or if the failure can be attributed to probability, proceed as follows.*

9.2.4 Using the results of the second set of four analyses, compute s and X for only those compounds that failed the test of the first set of four analyses (Section 9.2.3). If these compounds now pass, system performance is acceptable for all compounds, and analysis of blanks and samples may begin. If, however, any of the same compounds fail again, the analysis system is not performing properly for the compound(s) in question. In this event, correct the problem and repeat the entire test (Section 9.2.1).

9.3 The laboratory shall spike all samples with labeled compounds to assess method performance on the sample matrix.

9.3.1 Spike and analyze each sample according to the appropriate method in Section 11 or 12.

9.3.2 Compute the percent recovery (P) of the labeled compounds using the internal standard method (Section 10.4.2).

9.3.3 Compare the percent recovery for each compound with the corresponding labeled compound recovery limit in Table 6. If the recovery of any compound falls outside its warning limit, method performance is unacceptable for that compound in that sample. Therefore, the sample matrix is complex and the sample is to be diluted and reanalyzed, per Section 16.

9.4 As part of the QA program for the laboratory, it is suggested but not required that method accuracy for wastewater samples be assessed and records maintained. After the analysis of five wastewater samples for which the labeled compounds pass the tests in Section 9.3.3, compute the average percent recovery (P) and the standard deviation of the percent recovery (sp) for the labeled compounds only. Express the accuracy assessment as a percent recovery interval from P - 2sp to P + 2sp. For example, if P = 90% and sp = 10%, the accuracy interval is expressed as 70-110%. Update the accuracy assessment for each compound on a regular basis (e.g., after each five to ten new accuracy measurements).

9.5 Blanks-Reagent water blanks are analyzed to demonstrate freedom from carryover and contamination (Section 4).

9.5.1 The level at which the purge-and-trap system will carry greater than the ML of a pollutant of interest (Table 1) into a succeeding blank shall be determined by analyzing successively larger concentrations of these compounds. When a sample contains this concentration or more, a blank shall be analyzed immediately following this sample to demonstrate no carryover at the ML.

9.5.2 With each sample batch (samples analyzed on the same 12-hour shift), a blank shall be analyzed immediately after analysis of the aqueous performance standard (Section 15.1) to demonstrate freedom from contamination. If any of the compounds of interest (Table 1 or 2) or any potentially interfering compound is found in a blank at greater than the ML (assuming a response factor of 1 relative to the nearest-eluted internal standard for compounds not listed in Tables 1 and 2), analysis of samples is halted until the source of contamination is eliminated and a blank shows no evidence of contamination at this level. All results must be associated with an uncontaminated method blank.

9.6 The specifications contained in this method can be met if the apparatus used is calibrated properly, then maintained in a calibrated state. The standards used for calibration (Section 7), calibration verification (Section 15.5), and initial (Section 9.2) and ongoing (Section 15.5) precision and accuracy should be identical, so that the most precise results will be obtained. The GC/MS instrument in particular will provide the most reproducible results if dedicated to the settings and conditions required for the analyses of volatiles by this method.

9.7 Depending on specific program requirements, field replicates may be collected to determine the precision of the sampling technique, and spiked samples may be required to determine the accuracy of the analysis when the internal-standard method is used.

10.0 Calibration and Standardization

Calibration of the GC/MS system is performed by direct aqueous injection (Section 10.3) or purging the compounds of interest and their labeled analogs from reagent water at the temperature to be used for analysis of samples (Section 10.2).

10.1 Assemble the GC/MS apparatus and establish the operating conditions to be used for sample analysis (Section 6.3.3.1 or Section 6.3.3.2). By injecting standards into the GC, demonstrate that the analytical system meets the minimum levels in Tables 3 or 4 for the compounds for which calibration is to be performed, and the mass-intensity criteria in Table 5 for 50 ng BFB.

10.1.1 Mass-spectral libraries-Detection and identification of the compounds of interest are dependent upon the spectra stored in user-created libraries.

10.1.1.1 For the compounds in Tables 1 and 2, and other compounds for which the GC/MS is to be calibrated, obtain a mass spectrum of each pollutant and

labeled compound and each internal standard by analyzing an authentic standard either singly or as part of a mixture in which there is no interference between closely eluted components. Examine the spectrum to determine that only a single compound is present. Fragments not attributable to the compound under study indicate the presence of an interfering compound. Adjust the analytical conditions and scan rate (for this test only) to produce an undistorted spectrum at the GC peak maximum. An undistorted spectrum will usually be obtained if five complete spectra are collected across the upper half of the GC peak. Software algorithms designed to "enhance" the spectrum may eliminate distortion, but may also eliminate authentic m/z's or introduce other distortion.

10.1.1.2 The authentic reference spectrum is obtained under BFB tuning conditions (Section 10.1 and Table 5) to normalize it to spectra from other instruments.

10.1.1.3 The spectrum is edited by saving the five most intense mass-spectral peaks and all other mass-spectral peaks greater than 10% of the base peak. The spectrum may be further edited to remove common interfering masses. If five mass-spectral peaks cannot be obtained under the scan conditions given in Section 6.4, the mass spectrometer may be scanned to an m/z lower than 20 to gain additional spectral information. The spectrum obtained is stored for reverse search and for compound confirmation.

10.2 Assemble the GC/MS apparatus and establish operating conditions given in Section 6.3.3.1. By injecting standards into the GC, demonstrate that the analytical system meets the minimum levels in Table 3 for the compounds for which calibration is to be performed, and the mass-intensity criteria in Table 5 for 50 ng BFB.

10.2.1 Assemble the purge-and-trap device. Pack the trap as shown in Figure 3 and condition overnight at 170-180°C by backflushing with an inert gas at a flow rate of 20-30 mL/min. Condition traps daily for a minimum of 10 minutes prior to use.

10.2.1.1 Analyze the aqueous performance standard (Section 7.8.2) according to the purge-and-trap procedure in Section 11. Compute the area at the primary m/z (Table 7) for each compound. Compare these areas to those obtained by injecting 1 µL of the methanolic standard (Section 7.5.1) to determine compound recovery. The recovery shall be greater than 50% for the PMI analytes. Maximum allowable recovery for the PMI analytes found in Table 1 are shown in Table 8. This recovery is demonstrated initially for each purge-and-trap GC/MS system.

The test is repeated only if the purge-and-trap or GC/MS systems are modified in any way that might result in a change in recovery.

10.2.1.2 Demonstrate that a reliable calibration point can be established at the ML for each compound (Table 2). If the MLs cannot be met, adjust the analytical system until this performance is achieved.

10.3 Assemble the GC/MS system for direct aqueous injection and establish the operating conditions to be used for sample analysis (Section 6.3.3.2). By injecting standards into the GC, demonstrate that the analytical system meets the minimum levels in Table 4 for the compounds for which calibration is to be performed, and the mass-intensity criteria in Table 5 for 50 ng BFB.

Demonstrate that 100 ng o-xylene (or o-xylene-d_{10}) produces an area at m/z 106 (or 116) approximately one-tenth that required to exceed the linear range of the system. The exact value must be determined by experience for each instrument. It is used to match the calibration range of the instrument to the analytical range and detection limits required.

10.4 The following calibration steps are to be performed for both the purge-and-trap PMI analytes found in Table 1 and the direct aqueous injection PMI analytes found in Table 2, as appropriate.

10.4.1 Calibration by isotope dilution-The isotope dilution approach is used for the PMI analytes when appropriate labeled compounds are available and when interferences do not preclude the analysis. If labeled compounds are not available, or interferences are present, the internal standard method (Section 10.4.2) is used. A calibration curve encompassing the concentration range of interest is prepared for each compound determined. The relative response (RR) vs. concentration in micrograms per liter is plotted or computed using a linear regression. An example of a calibration curve for o-xylene using o-xylene-d_{10} is given in Figure 6. Also shown are the ±10% error limits (dotted lines). Relative response is determined according to the procedures described below. A minimum of five data points are required for calibration.

10.4.1.1 The relative response (RR) of pollutant to labeled compound is determined from isotope ratio values calculated from acquired data. Three isotope ratios are used in this process:

R_x = *The isotope ratio measured in the pure pollutant (Figure 7A)*

R_y = *The isotope ratio of pure labeled compound (Figure 7B)*

R_m = *The isotope ratio measured in the analytical mixture of the pollutant and labeled compounds (Figure 7C)*

The correct way to calculate RR is:

$$RR = \frac{(R_y - R_m)(R_x + 1)}{(R_m - R_x)(R_y + 1)}$$

If R_m is not between $2R_y$ and $0.5R_x$, the method does not apply and the sample is analyzed by the internal standard method (Section 10.4.2).

10.4.1.2 In most cases, the retention times of the pollutant and labeled compound are similar, and isotope ratios (R's) can be calculated from the EICP areas, where:

$$R = \frac{(area\ at\ m_1/z)}{(area\ at\ m_2/z)}$$

If either of the areas is zero, it is assigned a value of 1 in the calculations; that is, if area of $m_1/z = 50721$, and area of $m_2/z = 0$, then $R = 50721/1 = 50720$.

The data from these analyses are reported to three significant figures (see Section 14.6). In order to prevent rounding errors from affecting the values to be reported, all calculations performed prior to the final determination of concentrations should be carried out using at least four significant figures. Therefore, the calculation of R above is rounded to four significant figures.

The m/z's are always selected such that Rx > Ry. When there is a difference in retention times (RT) between the pollutant and labeled compounds, special precautions are required to determine the isotope ratios.

R_x, R_y, and R_m are defined as follows:

$$R_x = \frac{[area\ m_1/z\ (at\ RT_1)]}{1}$$

$$R_y = \frac{1}{[area\ m_2/z\ (at\ RT_2)]}$$

$$R_m = \frac{[area\ m_1/z\ (at\ RT_1)]}{[area\ m_2/z\ (at\ RT_2)]}$$

10.4.1.3 An example of the above calculations can be taken from the data plotted in Figure 7 for o-xylene and o-xylene-d_{10}. For these data:

$$R_x = \frac{168920}{1} = 168900$$

$$R_y = \frac{1}{60960} = 0.00001640$$

$$R_m = \frac{96868}{82508} = 1.174$$

10.4.1.4 The RR for the above data is then calculated using the equation given in Section 10.4.1.1. For the example, rounded to four significant figures, RR = 1.174. Not all labeled compounds elute before their pollutant analogs.

To calibrate the analytical system by isotope dilution, analyze an aliquot of each of the aqueous calibration standards (Section 7.8.1) spiked with an appropriate constant amount of the labeled compound spiking solution (Section 7.7), using the appropriate procedure in Section 10. Compute the RR at each concentration.

10.4.1.5 Linearity-If the ratio of relative response to concentration for any compound is constant (less than 20% coefficient of variation) over the five-point calibration range, an averaged relative response/concentration ratio may be used for that compound; otherwise, the complete calibration curve for that compound shall be used over the five-point calibration range.

10.4.2 Calibration by internal standard-Used when criteria for isotope dilution (Section 10.4.1) cannot be met. The method is applied to pollutants having no labeled analog and to the labeled compounds. The internal standards used for volatiles analyses are bromochloromethane, 1,4-difluorobenzene, chlorobenzene-d_5, and tetrahydrofuran-d_8. Concentrations of the labeled compounds and pollutants without labeled analogs are computed relative to the nearest eluting internal standard, as shown in Tables 3 and 4.

10.4.2.1 Response factors-Calibration requires the determination of response factors (RF) which are defined by the following equation:

$$RF = \frac{(A_s \times C_{is})}{(A_{is} \times C_s)}$$

Where:

A_s = *The EICP area at the characteristic m/z for the compound in the daily standard*

A_{is} = *The EICP area at the characteristic m/z for the internal standard*

C_{is} = *The concentration (µg/L) of the internal standard*

C_s = *The concentration of the pollutant in the daily standard*

10.4.2.2 The RF is determined at 10, 20, 50, 100, and 200 µg/L for the pollutants (optionally at 5 times or more these concentrations for highly water-soluble pollutants; see Section 7.8), in a way analogous to that for calibration by isotope dilution (Section 10.4.1). To produce a calibration curve, A_s*C_{is}/A_{is} is plotted against concentration (C_s) for each compound.

10.4.2.3 Linearity-If the relative standard deviation of the RFs for any compound is constant (less than 35%) over the five-point calibration range, an averaged RF may be used for that compound; otherwise, the complete calibration curve for that compound shall be used over the five-point range.

10.4.3 Combined calibration-By adding the isotopically labeled compounds and internal standards (Section 7.7) to the aqueous calibration standards (Section 7.8.1), a single set of analyses can be used to produce calibration curves for the isotope-dilution and internal-standard methods. These curves are verified each shift (Section 15.5) by analyzing the aqueous performance standard (Section 7.8.2). Recalibration is required only if calibration and ongoing performance (Section 15.5) criteria cannot be met.

11.0 Purge, Trap, and GC/MS Analysis

Samples containing less than 1% solids are analyzed directly as aqueous samples (Section 11.4). Samples containing 1% solids or greater are analyzed as solid samples utilizing one of two methods, depending on the levels of pollutants in the sample. Samples containing 1% solids or greater and low to moderate levels of pollutants are analyzed by purging a known weight of sample added to 5 mL of reagent water (Section 11.5). Samples containing 1% solids or greater and high levels of pollutants are extracted with methanol, and an aliquot of the methanol extract is added to reagent water and purged (Section 11.6).

11.1 Determination of percent solids.

11.1.1 Weigh 5 to 10 g of sample into a tared beaker.

11.1.2 Dry overnight (12 hours minimum) at 110°C (±5°C), and cool in a desiccator.

11.1.3 Determine percent solids as follows:

$$\%\ solids = \frac{weight\ of\ sample\ dry}{weight\ of\ sample\ wet} \times 100$$

11.2 Remove standards and samples from cold storage and bring to 20-25°C.

11.3 Adjust the purge gas flow rate to 40 mL/min (±4 mL/min).

11.4 Samples containing less than 1% solids.

11.4.1 Mix the sample by shaking vigorously. Remove the plunger from a 5-mL syringe and attach a closed syringe valve. Open the sample bottle and carefully pour the sample into the syringe barrel until it overflows. Replace the plunger and compress the sample. Open the syringe valve and vent any residual air while adjusting the sample volume to 5±0.1 mL. Because this process of taking an aliquot destroys the validity of the sample for future analysis, fill a second syringe at this time to protect against possible loss of data.

11.4.2 Add an appropriate amount of the labeled compound spiking solution (Section 7.7.1) through the valve bore, then close the valve.

11.4.3 Attach the syringe valve assembly to the syringe valve on the purging device. Open both syringe valves and inject the sample into the purging chamber. Purge the sample per Section 11.7.

11.5 Samples containing 1% solids or greater and low to moderate levels of pollutants.

11.5.1 Mix the sample thoroughly using a clean spatula and remove rocks, twigs, sticks, and other foreign matter.

11.5.2 Weigh 5±1 g of sample into a purging vessel (Figure 2). Record the weight to three significant figures.

11.5.3 Add 5±0.1 mL of reagent water to the vessel.

11.5.4 Using a metal spatula, break up any lumps of sample to disperse the sample in the water.

11.5.5 Add an appropriate amount of the labeled compound spiking solution (Section 7.7.1) to the sample in the purge vessel. Place a cap on the purging vessel and shake vigorously to further disperse the sample. Attach the purge vessel to the purging device, and purge the sample per Section 11.7.

11.6 Samples containing 1% solids or greater and high levels of pollutants, or samples requiring dilution by a factor of more than 100 (see Section 16).

11.6.1 Mix the sample thoroughly using a clean spatula and remove rocks, sticks, twigs, and other foreign matter.

11.6.2 Weigh 5±1 g of sample into a calibrated 15- to 25-mL centrifuge tube. Record the weight of the sample to three significant figures.

11.6.3 Add 10 mL of methanol to the centrifuge tube. Cap the tube and shake it vigorously for 15 to 20 seconds to disperse the sample in the methanol. Allow the sample to settle in the tube. If necessary, centrifuge the sample to settle suspended particles.

11.6.4 Remove approximately 0.1% of the volume of the supernatant methanol using a 15- to 25-µL syringe. This volume will be in the range of 10-15 µL.

11.6.5 Add this volume of the methanol extract to 5 mL reagent water in a 5-mL syringe, and analyze per Section 10.4.1.

11.6.6 For further dilutions, dilute 1 mL of the supernatant methanol (Section 10.6.4) to 10 mL, 100 mL, 1000 mL, etc., in reagent water. Remove a volume of this methanol extract/reagent water mixture equivalent to the volume in Section 10.6.4, add it to 5 mL reagent water in a 5-mL syringe, and analyze per Section 11.4.

11.7 Purge the sample for 11±0.1 minute at 45±2°C.

11.8 After the 11-minute purge time, attach the trap to the chromatograph and set the purge-and-trap apparatus to the desorb mode (Figure 5). Desorb the trapped compounds into the GC column by heating the trap to 170-180°C while backflushing with carrier gas at 20-60 mL/min for 4 minutes. Start MS data acquisition upon start of the desorb cycle, and start the GC column temperature program 3 minutes later. Section 6.3.3.1 provides the recommended operating conditions for the gas chromatograph. Table 3 provides the retention times and minimum levels that can be achieved under these conditions. An example of the separations achieved by the column listed is shown in Figure 8. Other columns may be used provided the requirements in Section 9 are met.

11.9 After desorbing the sample for 4 minutes, recondition the trap by purging with purge gas while maintaining the trap temperature at 170-180°C. After approximately 7 minutes, turn off the trap heater and stop the gas flow through the trap. When cool, the trap is ready for the next sample.

11.10 While analysis of the desorbed compounds proceeds, remove and clean the purge device. Rinse with tap water, clean with detergent and water, rinse with tap and distilled water, and dry for a minimum of 1 hour in an oven at a temperature greater than 150°C.

12.0 Direct Aqueous Injection and GC/MS Analysis

Samples containing less than 1% solids are analyzed directly as aqueous samples (Section 12.3). Samples containing 1% solids or greater are analyzed after equilibration with reagent water containing labeled PMI analytes and internal standards (Section 12.4).

12.1 Determine percent solids as in Section 11.1.

12.2 Remove standards and samples from cold storage and bring to 20-25 °C.

12.3 Samples containing less than 1% solids.

12.3.1 Allow solids to settle and remove 5 mL of sample.

12.3.2 Add an appropriate amount of the labeled compound spiking solution (Section 7.7.2).

12.3.3 Inject 1 mL or more directly into the GC injection port. The temperature of the injection block should be great enough to immediately vaporize the entire sample. An example of the separations achieved by the column listed is shown in Figure 9.

12.4 Samples containing 1% solids or greater.

12.4.1 Mix the sample thoroughly using a clean spatula and remove rocks, twigs, sticks and other foreign matter.

12.4.2 Add 5±1 g of sample to a 10-mL centrifuge tube. Using a clean metal spatula, break up any lumps of sample. Record the sample weight to three significant figures.

12.4.3 Add an appropriate amount of the labeled compound spiking solution (Section 7.7.2) to the sample in the centrifuge tube.

12.4.4 Add a measured quantity, Y, (to the nearest 0.1 mL) of reagent water to the tube so as to minimize headspace.

12.4.5 Place a cap on the centrifuge tube leaving little or no headspace. Place the tube in the sonicator for a minimum of 5 minutes, turning occasionally. For most samples this should be sufficient time to distribute labeled and native analytes between the solid and aqueous phases and to establish equilibrium. Some sample matrices may require more sonication.

12.4.6 On completion of sonication, centrifuge the sample and inject 1µL or more of supernate directly into the GC injection port. The temperature of the injection block should be great enough to immediately vaporize the entire sample.

12.5 Liquid samples containing high solids concentrations, such as sludges or mud, may be weighed into a 10-mL centrifuge tube, have labeled compound spiking solution (Section 7.7.2) added, and be sonicated as in Section 12.4.5. Centrifugation and injection are to be performed as in Section 12.4.6.

13.0 Qualitative Determination

Identification is accomplished by comparison of data from analysis of a sample or blank with data stored in the mass-spectral libraries. For compounds for which the relative retention times and mass spectra are known, identification is confirmed per Sections 13.1 and 13.2.

13.1 A labeled compound or pollutant having no labeled analog (Tables 1 and 2).

13.1.1 The signals for all characteristic m/z's stored in the spectral library (Section 10.1.1) shall be present and shall maximize within the same two consecutive scans.

13.1.2 Either (1) the background corrected EICP areas or (2) the corrected relative intensities of the mass-spectral peaks at the GC peak maximum shall agree within a factor of 2 (0.5-2 times) for all m/z's stored in the library.

13.1.3 The relative retention time (RRT) shall be within ±10% of the RRT in the system performance standard (Section 15.1)

13.2 Pollutants having a labeled analog (Tables 1 and 2).

13.2.1 The signals for all characteristic m/z's stored in the spectral library (Section 10.1.1) shall be present and shall maximize within the same two consecutive scans.

13.2.2 Either (1) the background corrected EICP areas or (2) the corrected relative intensities of the mass-spectral peaks at the GC peak maximum shall agree within a factor of 2 for all m/z's stored in the spectral library.

13.2.3 The RRT for the pollutant relative to its labeled analog shall be within -2% to +1% of the RRT in the system performance standard (Section 15.1).

13.3 The m/z's present in the sample mass spectrum that are not present in the reference mass spectrum shall be accounted for by contaminant or background ions. If the sample mass spectrum is contaminated, or if identification is ambiguous, an experienced spectrometrist (Section 1.4) is to determine the presence or absence of the compound.

14.0 Quantitative Determination

14.1 Isotope dilution-Because the pollutant and its labeled analog exhibit the same effects upon purging and desorption, or equilibration combined with gas chromatography, correction for recovery of the pollutant can be made by adding a known amount of a labeled compound to every sample prior to purging or equilibration. Relative response (RR) values for sample mixtures are used in conjunction with the calibration curves described in Section 10.4.1 to determine concentrations directly, so long as labeled compound spiking levels are constant. For the o-xylene example given in Figure 7 (Section 10.4.1.3), RR would be equal to 1.174. For this RR value, the o-xylene calibration curve given in Figure 6 indicates a concentration of 31.8 µg/L.

14.2 Internal standard-For the compounds for which the system was calibrated (Table 1 and Table 2) according to Section 10.4.2, use the response factor determined during the calibration to calculate the concentration from the equation below, where the terms are as defined in Section 10.4.2.1.

$$Concentration = \frac{(A_s \times C_{is})}{(A_{is} \times RF)}$$

14.3 Samples containing >1% solids—The concentration of the pollutant in the solid phase of the sample is computed using the concentration of the pollutant detected in the aqueous solution, as follows:

14.3.1 Samples containing low to moderate levels of pollutants (Section 11.5)

$$Concentration\ in\ solid\ (\mu g/kg) = \frac{Y\ (L) \times aqueous\ conc\ (\mu g/L)}{sample\ weight\ (kg) \times percent\ solids\ (g) \times DF}$$

where:

"percent solids" is from Section 11.1.3 or Section 12.1
Y = volume of water in liters (L) from Section 12.4.4
DF = dilution factor (as a decimal number), where necessary

14.3.2 Methanol extracts (Section 11.6)

$$Concentration\ in\ solid\ (\mu g/kg) = \frac{Y\ (L) \times F_m \times aqueous\ conc\ (\mu g/L)}{sample\ weight\ (kg) \times percent\ solids\ (g) \times DF}$$

where:

Y = volume of methanol in liters (L) from Section 11.6.3
F_m is the fraction of supernatant removed from the centrifuge tube (e.g., 0.001, Section 11.6.4), and the other terms are as defined in Section 14.3.1

14.3.3 Where the aqueous concentration is in mg/L, the result will be in mg/kg.

14.4 Sample dilution-If the EICP area at the quantitation m/z exceeds the calibration range of the system, the sample is diluted by successive factors of 10 until the area is within the calibration range. If dilution of high-solids samples by greater than a factor of 100 is required for purge-and-trap analysis, then extract the sample with methanol, as described in Section 11.6.

14.5 Dilution of samples containing high concentrations of compounds not in Table 1 or Table 2-When any peak in the mass spectrum is saturated, dilute the sample per Section 14.4.

14.6 Report results for all pollutants and labeled compounds found in all standards, blanks, and samples to three significant figures. For samples containing less than 1% solids, the units are micrograms or milligrams per liter (µg/L or mg/L); and for undiluted samples containing 1% solids or greater, units are micrograms or milligrams per kilogram (µg/kg or mg/kg).

14.6.1 Results for samples that have been diluted are reported at the least dilute level at which the area at the quantitation m/z is within the calibration range (Section 14.4), or at which no m/z in the spectrum is saturated (Section 14.5). For compounds having a labeled analog, results are reported at the least dilute level at which the area at the quantitation m/z is within the calibration range (Section 14.4) and the labeled compound recovery is within the normal range for the method (Section 16.2).

15.0 System Performance

15.1 At the beginning of each 12-hour shift during which analyses are performed, system calibration and performance shall be verified for the pollutants and labeled compounds (Table 1 or Table 2). For these tests, analysis of the aqueous performance standard (Section 7.8.2) shall be used to verify all performance criteria. Adjustment and/or recalibration (per Section 10) shall be performed until all performance criteria are met. Only after all performance criteria are met may blanks and samples be analyzed.

15.2 BFB spectrum validity-The criteria in Table 5 shall be met.

15.3 Retention times.

15.3.1 Purge-and-trap analysis-The absolute retention times of the internal standards shall fall within ±30 seconds of the following-bromochloromethane, 954 seconds; 1,4-difluorobenzene, 1052 seconds; chlorobenzene-d_5, 1359 seconds. The relative retention times of all pollutants and labeled compounds shall fall within 5% of the value given in Table 3.

15.3.2 Direct aqueous injection analysis-The absolute retention time of tetrahydrofuran-d_8 shall be 263±30 seconds. The relative retention times of all pollutants and labeled compounds shall fall within 10% of the value given in Table 4.

15.4 GC resolution-The valley height between o-xylene and o-xylene-d_{10} (at m/z 106 and 116 plotted on the same graph) shall be less than 10% of the taller of the two peaks.

15.5 Calibration verification and ongoing precision and accuracy-Compute the concentration of each pollutant (Table 1 or Table 2) by isotope dilution (Section 10.4.1) for those compounds that have labeled analogs. Compute the concentration of each pollutant that has no labeled analog by the internal standard method (Section 10.4.2). Compute the concentrations of the labeled compounds by the internal standard method. These concentrations are computed based on the calibration data determined in Section 10.

15.5.1 For each pollutant and labeled compound, compare the concentration with the corresponding limit for ongoing accuracy in Table 6. If all compounds meet the acceptance criteria, system performance is acceptable and analysis of blanks and samples may continue. If any individual value falls outside the range given, system performance is unacceptable for that compound.

Note: *The large number of compounds in Table 6 present a substantial probability that one or more will fail the acceptance criteria when all compounds are analyzed. To determine if the analytical system is out of control, or if the failure may be attributed to probability, proceed as follows.*

15.5.1.1 Analyze a second aliquot of the aqueous performance standard (Section 7.8.2).

15.5.1.2 Compute the concentration for only those compounds that failed the first test (Section 15.5.1). If these compounds now pass, system performance is acceptable for all compounds, and analyses of blanks and samples may proceed. If, however, any of the compounds fail again, the measurement system is not performing properly for these compounds. In this event, locate and correct the problem or recalibrate the system (Section 10), and repeat the entire test (Section 15.1) for all compounds.

15.5.2 It is suggested but not required that results that pass the specification in Section 15.5.1.2 be added to initial (Section 9.2) and previous ongoing data, that QC charts be updated to form a graphic representation of laboratory performance (Figure 8), and that a statement of accuracy be developed for each pollutant and labeled compound by calculating the average percent recovery (R) and the standard deviation of percent recovery (sr). Express the accuracy as a recovery interval from R - 2sr to R + 2sr. For example, if R = 95% and sr = 5%, the accuracy is 85-105%.

16.0 Analysis of Complex Samples

16.1 Some samples may contain high levels (>1000 µg/kg) of the compounds of interest and of interfering compounds. Some samples will foam excessively when purged. Others will overload the trap or the GC column.

16.2 When the recovery of any labeled compound is outside the range given in Table 6, dilute samples by a factor of 10 with reagent water and analyze this diluted sample. If the recovery remains outside of the range for this diluted sample, the aqueous performance standard shall be analyzed (Section 15.1) and calibration verified (Section 15.5). If the recovery for the labeled compound in the aqueous performance standard is outside the range given in Table 6, the analytical system is out of control. In this case, the instrument shall be repaired, the performance specifications in Section 15 shall be met, and the analysis of the undiluted sample shall be repeated. If the recovery for the aqueous performance standard is within the range given in Table 6, then the method does not apply to the sample being analyzed, and the result may not be reported for regulatory compliance purposes.

16.3 When a high level of the pollutant is present, reverse-search computer programs may misinterpret the spectrum of chromatographically unresolved pollutant and labeled compound pairs with overlapping spectra. Examine each chromatogram for peaks greater than the height of the internal standard peaks. These peaks can obscure the compounds of interest.

17.0 Method Performance

17.1 This method was developed and validated in a single laboratory.

17.2 Chromatograms of the aqueous performance standards (Sections 7.8.2 and 15.1) are shown in Figures 8 and 9.

18.0 Pollution Prevention

18.1 Pollution prevention encompasses any technique that reduces or eliminates the quantity or toxicity of waste at the point of generation. Many opportunities for pollution prevention exist in laboratory operation. EPA has established a preferred hierarchy of environmental management techniques that places pollution prevention as the management option of first choice. Whenever feasible, laboratory personnel should use pollution prevention techniques to address their waste generation. When wastes cannot be reduced feasibly at the source, the Agency recommends recycling as the next best option. The acids used in this Method should be reused as practicable by purifying by electrochemical techniques. The only other chemicals used in this Method are the neat materials used in preparing standards. These standards are used in extremely small amounts and pose little threat to the environment when managed properly. Standards should be prepared in volumes consistent with laboratory use to minimize the disposal of excess volumes of expired standards.

18.2 For information about pollution prevention that may be applied to laboratories and research institutions, consult *Less is Better: Laboratory Chemical Management for Waste Reduction*, available from the American Chemical Society's Department of Governmental Relations and Science Policy, 1155 16th Street NW, Washington DC 20036, 202/872–4477.

19.0 Waste Management

19.1 It is the laboratory's responsibility to comply with all Federal, State, and local regulations governing waste management, particularly the hazardous waste identification rules and land-disposal restrictions. In addition it is the laboratory's responsibility to protect air, water, and land resources by minimizing and controlling all releases from fume hoods and bench operations. Also, compliance is required with any sewage discharge permits and regulations.

19.2 Samples containing acids at a pH of less than 2 are hazardous and must be neutralized before being poured down a drain or must be handled as hazardous waste.

19.3 For further information on waste management, consult *The Waste Management Manual for Laboratory Personnel* and *Less is Better: Laboratory Chemical Management for Waste Reduction*, both available from the American Chemical Society's Department of Government Relations and Science Policy, 1155 16th Street NW, Washington, DC 20036.

20.0 References

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21.0 Tables

Table 1. Volatile PMI Analytes Amenable to Purge and Trap and Determined by GC/MS Using Isotope Dilution and Internal Standard Techniques

	Pollutant		Labeled Compound		
PMI Analyte	CASRN[1]	EPA-EGD	Analog	CASRN[1]	EPA-EGD
n-Amyl acetate	628-63-7	977			
n-Amyl alcohol	71-41-0	978			
n-Butyl acetate	123-86-4	979			
n-Butyl alcohol	71-36-3	1036			
Tert-butyl alcohol	75-65-0	1343	d_{10}	53001-22-2	1243
Cyclohexane	110-82-7	1333	d_{12}	1735-17-7	1233
Ethyl acetate	141-78-6	1736	^{13}C	84508-45-2	1636
Furfural[2]	98-01-1	981			
n-Heptane	142-82-5	1334	d_{16}	33838-52-7	1234
n-Hexane	110-54-3	1335	d_{14}	21666-38-6	1235
Isobutyraldehyde[2]	78-84-2	982			
Isopropanol	67-63-0	1044			
Isopropyl acetate	108-21-4	983			
Isopropylether	108-20-3	960			
Methyl formate	107-31-3	991			
Methylisobutyl ketone	108-10-1	1341			
N-pentane[3]	109-66-0	984			
Tetrahydrofuran	109-99-9	1345	d_8	1693-74-9	1245
Trichlorofluoromethane	75-69-4	552			
m+p-Xylene	136777-61-2	1332	d_{10}	41051-88-1	1232
o-Xylene	95-47-6	1331	d_{10}	56004-61-6	1231

[1] Chemical Abstracts Service Registry Number.
[2] These aldehydes may also be analyzed by Method 1667.
[3] n-Pentane is not explicitly a PMI analyte. However, the sum of the concentrations of n-pentane, n-hexane, and n-heptane are to be used to estimate the concentration of petroleum naphtha in PMI wastewaters.

Table 2. Volatile PMI Analytes Determined by Direct Aqueous Injection GCMS Using Isotope Dilution and Internal Standard Techniques

	Pollutant		Labeled Compound		
PMI Analyte	CASRN[1]	EPA-EGD	Analog	CASRN[1]	EPA-EGD
Acetonitrile	75-05-8	972	d_3	2206-26-0	1272
Diethylamine	109-89-7	986			
Dimethylamine	124-40-3	987			
Dimethyl sulfoxide	67-68-5	1037	d_6	2206-27-1	1237
Ethanol	64-17-5	1734	d_6	1516-08-1	1634
Ethylene glycol	107-21-1	1038			
Formamide	75-12-7	988			
Methanol	67-56-1	1735	d_3	1849-29-2	1635
Methylamine	74-89-5	989			
Methyl Cellosolve®	109-86-4	1040			
n-Propanol	71-23-8	755	1-d_1	not avail.	1255
Triethylamine	121-44-8	990			

[1] Chemical Abstracts Service Registry Number.

Table 3. Gas Chromatographic Retention Times and Minimum Levels for Volatile PMI Analytes Determined by Purge and Trap GC/MS

EGD		Retention Time			ML[2]
No.[1]	PMI Analyte	Mean (sec)	EGD	Relative	(µg/L)
991	Methyl formate	526	181	0.551	100
552	Trichlorofluoromethane	613	181	0.642	10
984	n-Pentane	622	181	0.652	10
1344	Isopropanol	687	181	0.720	200
1243	Tert-butyl alcohol-d_{10}	730	181	0.765	
1343	Tert-butyl alcohol	741	1243	1.016	100
1235	n-Hexane-d_{14}	820	181	0.860	
982	Isobutyraldehyde	823	181	0.863	10
1335	n-Hexane	839	1235	1.023	10
960	Isopropylether	865	181	0.907	5
1636	Ethyl acetate-^{13}C	925	181	0.970	
1736	Ethyl acetate	925	1636	1.000	10
181	Bromochloromethane(I.S.)	954	181	1.000	
1245	Tetrahydrofuran-d_8	956	181	1.002	
1345	Tetrahydrofuran	964	181	1.012	20
1233	Cyclohexane-d_{12}	981	181	1.028	
1333	Cyclohexane	996	1233	1.015	5
1234	n-Heptane-d_{16}	1013	985	0.963	
1336	n-Butanol	1015	985	0.964	500
1334	n-Heptane	1033	1234	1.020	10
985	1,4-Difluorobenzene(I.S.)	1052	985	1.000	
983	Isopropyl acetate	1128	985	1.072	10
1341	Methylisobutyl ketone	1157	985	1.100	10
978	n-Amyl alcohol	1202	985	1.143	500
979	n-Butyl acetate	1268	207	0.933	5
981	Furfural	1354	207	0.996	500
207	Chlorobenzene-d_5 (I.S.)	1359	207	1.000	
1232	p-Xylene-d_{10}	1368	207	1.007	
1332	m,p-Xylene	1379	1232	1.008	10
1231	o-Xylene-d_{10}	1413	207	1.040	
977	n-Amyl acetate	1417	207	1.043	5
1331	o-Xylene	1424	1231	1.008	5

[1] Three digit EGD numbers beginning with 0, 1, 5, or 9 indicate a pollutant quantified by the internal standard method; EGD numbers beginning with 2 or 6 indicated a labeled compound quantified by the internal standard method; EGD numbers beginning with 3 or 7 indicate a pollutant quantified by isotope dilution. The initial "1" in four digit EGD numbers is to be ignored in applying these rules.

[2] This is a minimum level at which the entire analytical system shall give recognizable mass spectra (background corrected) and acceptable calibration points, taking into account method-specific sample and injection volumes. The concentration in the aqueous or solid phase is determined using the equations in Section 14.

Table 4. Gas Chromatographic Retention Times and Minimum Levels for Volatile PMI Analytes by Direct Aqueous Injection GC/MS

EGD No.[1]	PMI Analyte	Retention Time			ML[2] (mg/L)
		Mean (sec)	EGD Ref	Relative	
989	Methylamine	81	1245	0.308	200
1635	Methyl alcohol-d_3	85	1245	0.323	
1735	Methyl alcohol	85.5	1635	1.006	50
987	Diethylamine	93	1245	0.354	200
1634	Ethyl alcohol-d_5	103	1245	0.394	
1734	Ethyl alcohol	104	1634	1.010	20
1272	Acetonitrile-d_3	119	1245	0.452	
972	Acetonitrile	121	1272	1.017	5
1255	n-Propanol-1-d_1	170	1245	0.464	
755	n-Propanol	170.5	1255	1.003	20
986	Diethylamine	188	1245	0.717	200
1245	Tetrahydrofuran-d_8 (I.S.)	263	1245	1.000	
1040	Methyl Cellosolve® (2-Methoxyethanol)	290	1245	1.103	50
990	Triethylamine	372	1245	1.414	200
1038	Ethylene glycol	398	1245	1.513	200
988	Formamide	400	1245	1.521	1000
1237	Dimethyl sulfoxide-d_6	639	1245	2.431	
1037	Dimethyl sulfoxide	643	1237	1.006	100

[1] Three digit EGD numbers beginning with 0, 1, 5, or 9 indicate a pollutant quantified by the internal standard method; EGD numbers beginning with 2 or 6 indicated a labeled compound quantified by the internal standard method; EGD numbers beginning with 3 or 7 indicate a pollutant quantified by isotope dilution. The initial "1" in four digit EGD numbers is to be ignored in applying these rules.

[2] This is a minimum level at which the entire analytical system shall give recognizable mass spectra (background corrected) and acceptable calibration points, taking into account method-specific sample and injection volumes. The concentration in the aqueous or solid phase is determined using the equations in Section 14.

Table 5. BFB Mass-Intensity Specifications

m/z	Intensity Required
50	15-40% of m/z 95
75	30-60% of m/z 95
95	base peak, 100%
96	5-9% of m/z 95
173	less than 2% of m/z 174
174	greater than 50% of m/z 95
175	5-9% of m/z 174
176	95-101% of m/z 174
177	5-9% of m/z 176

Table 6. Quality Control Acceptance Criteria for PMI Analytes

EGD No.	PMI Analyte	Spike Level	Acceptance Criteria for Performance Tests (% of Spike Level)			
			Labeled and Native PMI Analyte Initial Precision and Recovery		Labeled PMI Analyte Recovery (P)	Labeled and Native PMI Analyte On-going Recovery (R)
			s	X		
972	Acetonitrile	50 mg/L	20	70-130	70-130	70-130
977	Amyl acetate	10 µg/L	20	70-130		70-130
978	Amyl alcohol	200 µg/L	75	16-166		10-172
979	n-Butyl acetate	10 µg/L	20	70-130		70-130
1036	n-Butyl alcohol	200 µg/L	108	d-190		d-199
1343	tert-Butyl alcohol	50 µg/L	121	d-202		d-212
1333	Cyclohexane	10 µg/L	26	70-134	8-156	70-136
986	Diethylamine	250 mg/L	31	70-132		68-134
987	Diethylamine	250 mg/L	38	61-136		58-139
1037	Dimethyl sulfoxide	250 mg/L	20	70-130	59-122	70-130
1734	Ethanol	50 mg/L	15	66-130	70-130	65-130
1736	Ethyl acetate	10 µg/L	48	60-157	58-159	57-160
1038	Ethylene glycol	250 mg/L	195	d-310		d-326
988	Formamide	500 mg/L	113	60-286		51-296
981	Furfural	100 µg/L	186	d-282		d-297
1334	n-Heptane	10 µg/L	37	70-161	14-128	70-164
1335	n-Hexane	10 µg/L	34	70-154	5-157	70-157
982	Isobutyraldehyde	10 µg/L	54	67-176		63-180
1044	Isopropanol	100 µg/L	284	d-418		d-441

983	Isopropyl acetate	10 µg/L	32	70-147		70-150
960	Isopropyl ether	10 µg/L	21	70-127		70-129
1735	Methanol	50 mg/L	26	57-109	70-130	55-111
989	Methylamine	250 mg/L	36	61-133		59-136
1040	Methyl cello solve	250 mg/L	20	70-130		70-130
991	Methyl formate	50 µg/L	73	20-165		14-171
1341	Methylisobutyl ketone	10 µg/L	42	70-162		70-165
984	n-Pentane	10 µg/L	52	51-155		47-159
755	n-Propanol	50 mg/L	25	42-130	54-149	40-130
975	Tetrahydrofuran	10 µg/L	89	35-214	42-178	28-221
552	Trichlorofluoromethane	20 µg/L	20	70-130		70-130
990	Triethylamine	250 mg/L	31	70-133		69-135
1332	m,p-Xylene	20 µg/L	20	70-130	70-130	70-130
1331	o-Xylene	10 µg/L	20	70-130	70-130	70-130

Table 7. Characteristic m/z's for Volatile PMI Analytes

PMI Analyte	Spike Level (µg/L)	Spike Level (mg/L)	Labeled Analog	Primary m/z (Native/Labeled)	Reference Compound
Acetonitrile		50	d_3	41/44	1272
n-Amyl acetate	10			43	207
n-Amyl alcohol	100			70	985
n-Butyl acetate	10			43	207
n-Butyl alcohol	200			56	985
Tert-butyl alcohol	50		d_{10}	59/66	1234
Cyclohexane	10		d_{12}	56/96	1233
Diethylamine		250		58	1245
Diethylamine		250		44	1245
Dimethyl sulfoxide		250	d_6	47/50	1237
Ethanol		50	d_5	31/33	1634
Ethyl acetate	10		^{13}C	43/44	1636
Ethylene glycol		250		31	1245
Formamide		500		45	1245
Furfural	100			96	207
n-Heptane	10		d_{16}	71/82	1234
n-Hexane	10		d_{14}	57/66	1235
Isobutyraldehyde	10			72	181
Isopropanol	100			45	181
Isopropyl acetate	10			43	985
Isopropyl ether	10			45	181
Methanol		50	d_3	31/33	1635
Methylamine		250		30	1245
Methyl Cellosolve® (2-Methoxyethanol)		250		45	1245

Methyl formate	50			60	181
Methylisobutyl ketone	10			43	
n-Pentane	10			43	181
n-Propanol		50	1-d_1	31/32	1255
Tetrahydrofuran	10		d_8	72/80	1245
Trichlorofluoromethane	20			101	181
Triethylamine		250		86	1245
m,p-Xylene	20		d_{10}	106/116	1232
o-Xylene	10		d_{10}	106/16	1231

Table 8. Maximum Recoveries for PMI Analytes by Purge-and-Trap GC/MS

PMI Analyte	Maximum Recovery (%)
n-Amyl acetate	130
n-Amyl alcohol	300
n-Butyl acetate	130
n-Butyl alcohol	440
tert-Butyl alcohol	130
Cyclohexane	130
Ethyl acetate	130
Furfural	170
n-Heptane	140
n-Hexane	140
Isobutyraldehyde	150
Isopropanol	250
Isopropyl acetate	130
Isopropyl ether	130
Methyl formate	130
Methylisobutyl ketone	130
n-Pentane	130
Tetrahydrofuran	150
Trichlorofluoromethane	130
m,p-Xylene	130
o-Xylene	130

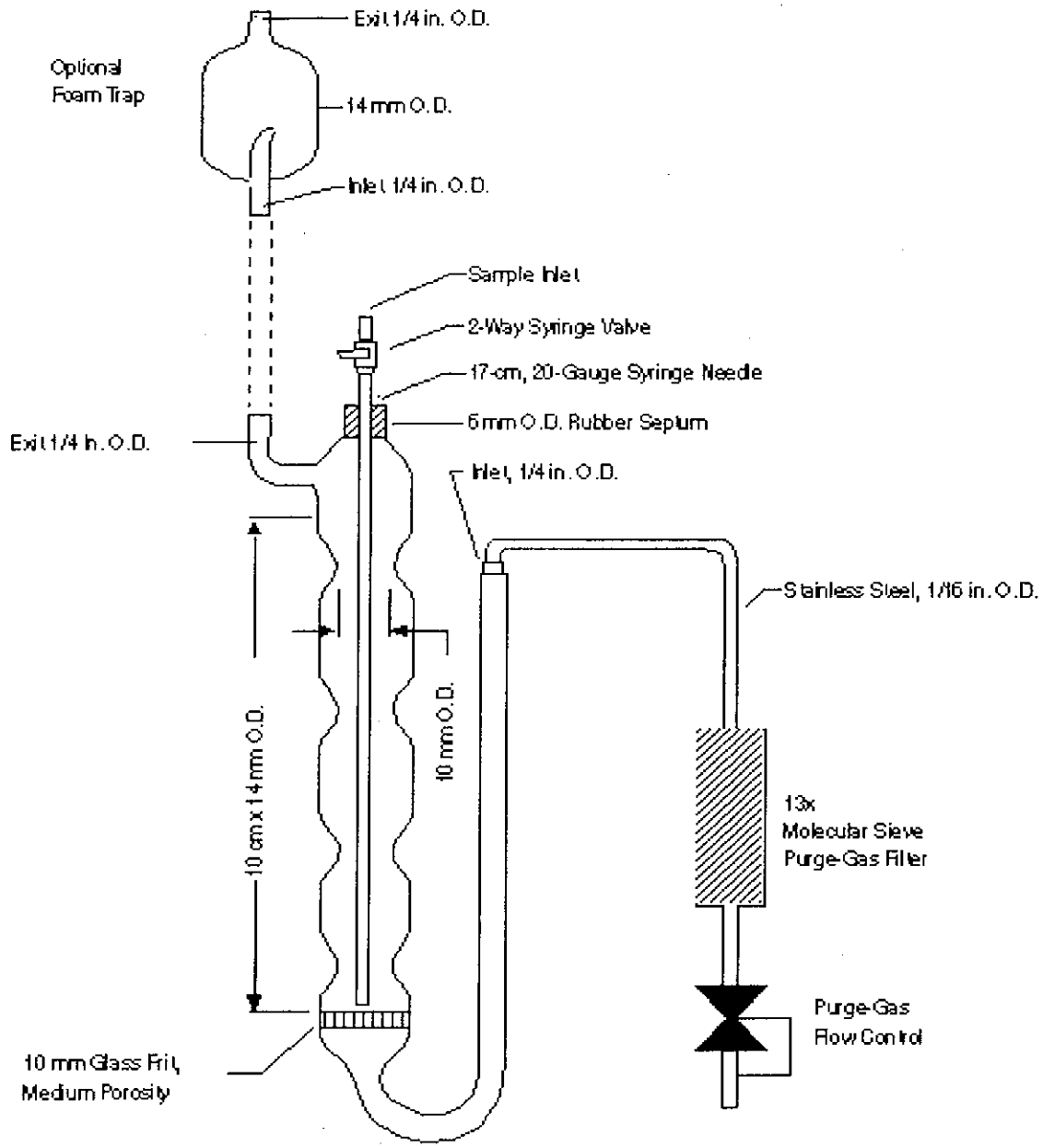


Figure 1. Purging Device for Waters

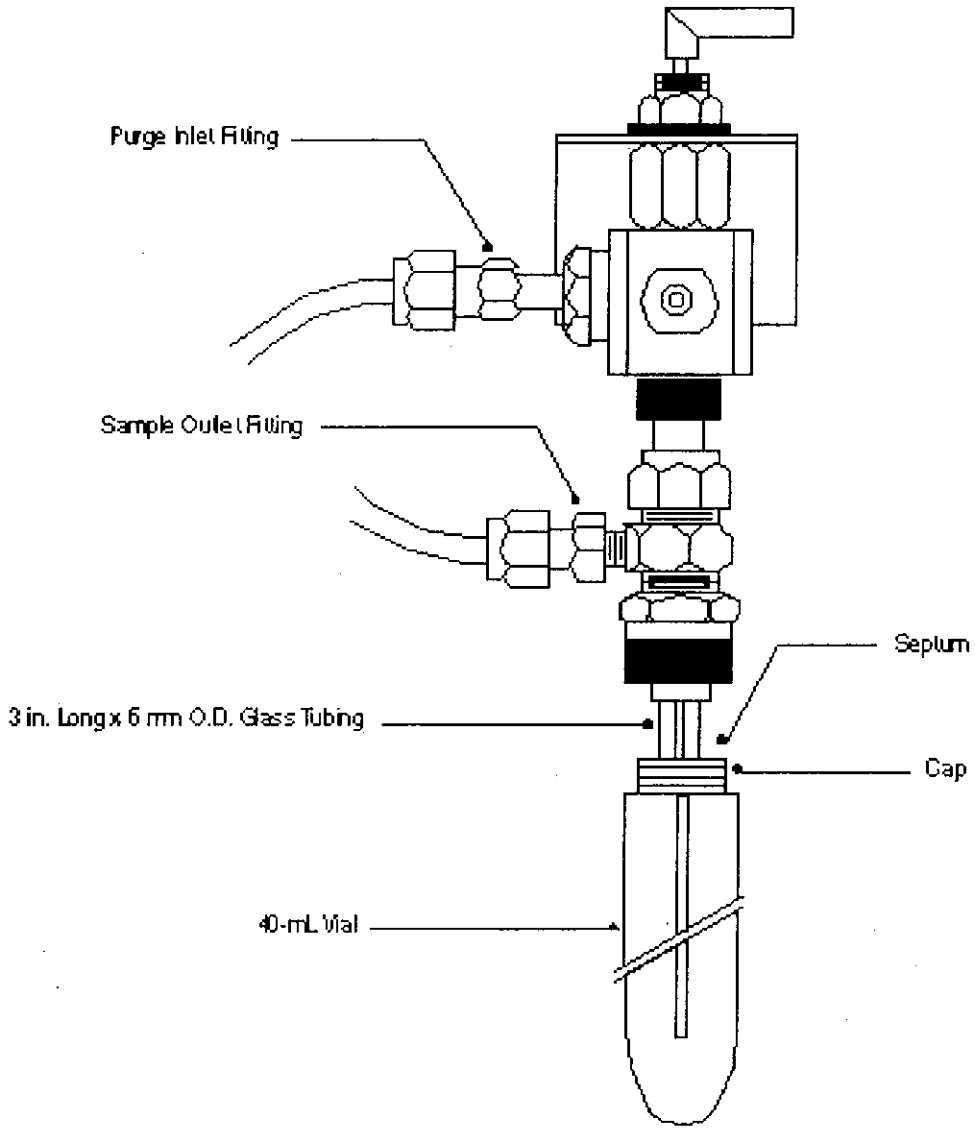


Figure 2. Purging Device for Soils or Waters

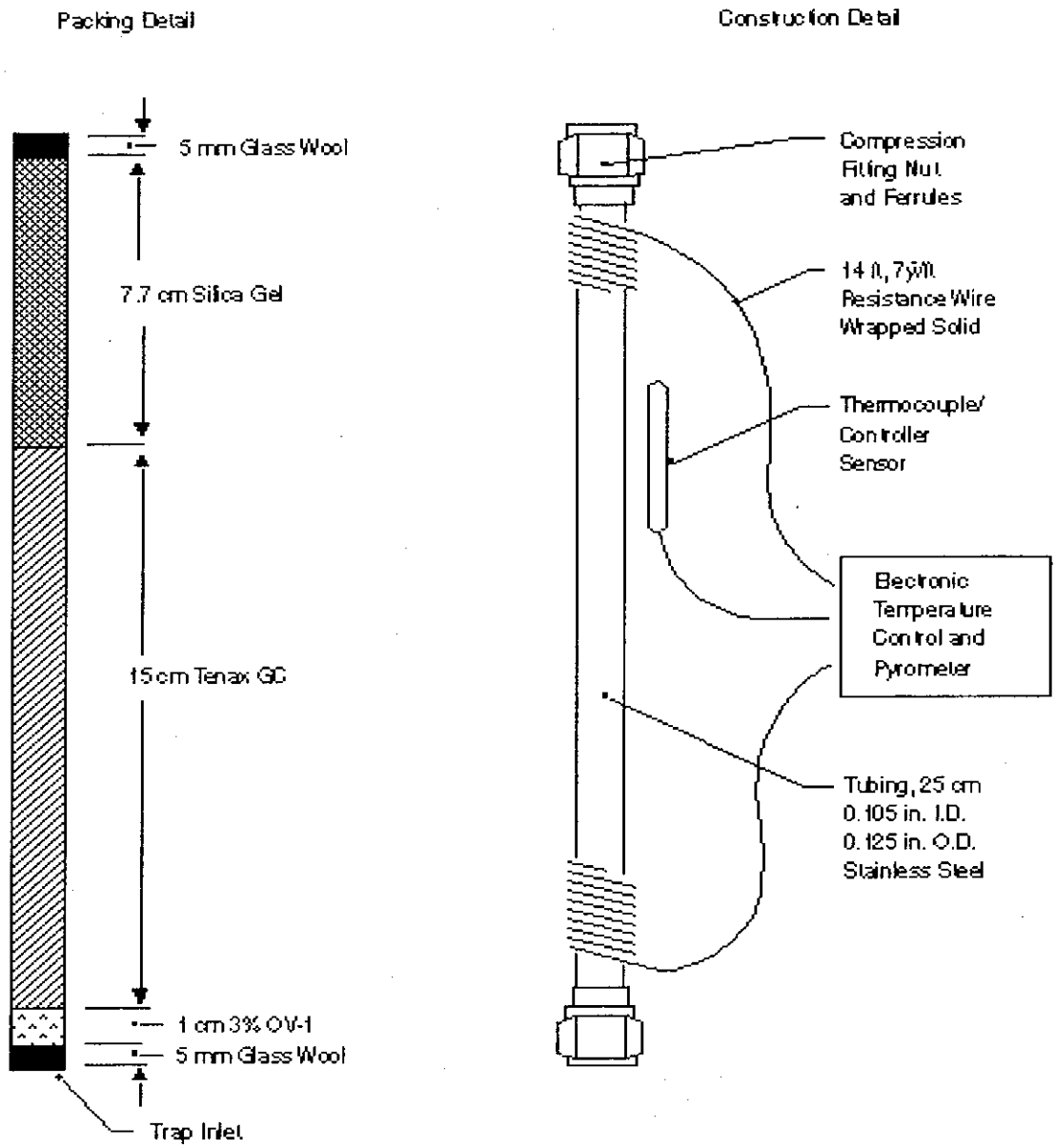


Figure 3. Trap Construction and Packings

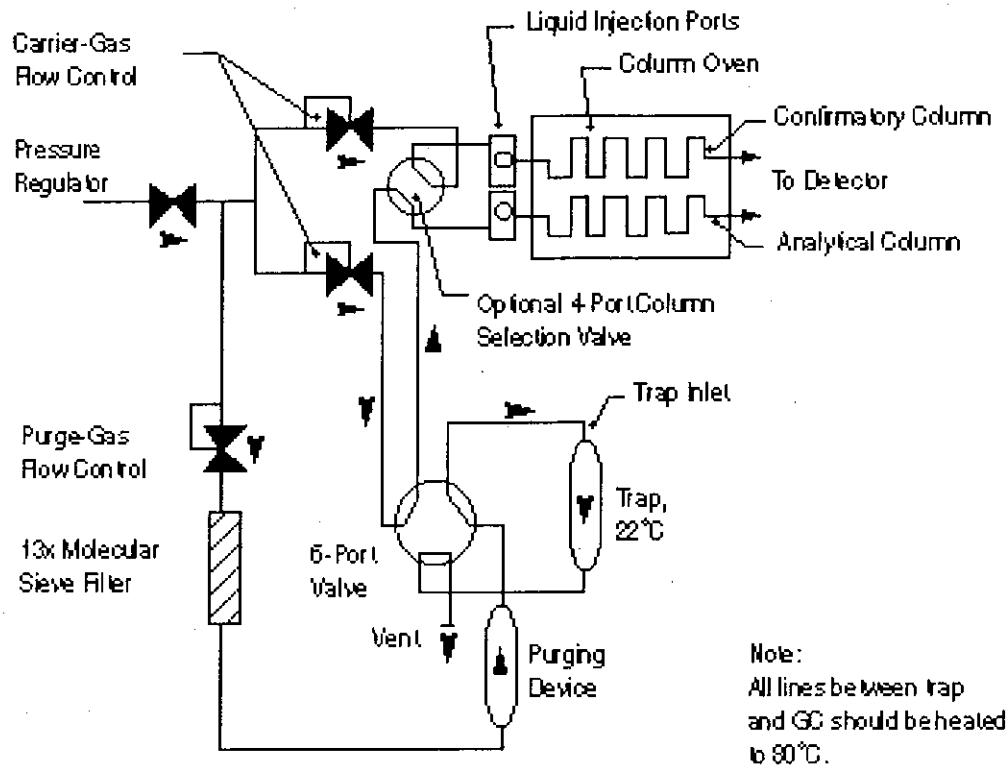


Figure 4. Schematic of Purge-and-Trap Device—Purge Mode

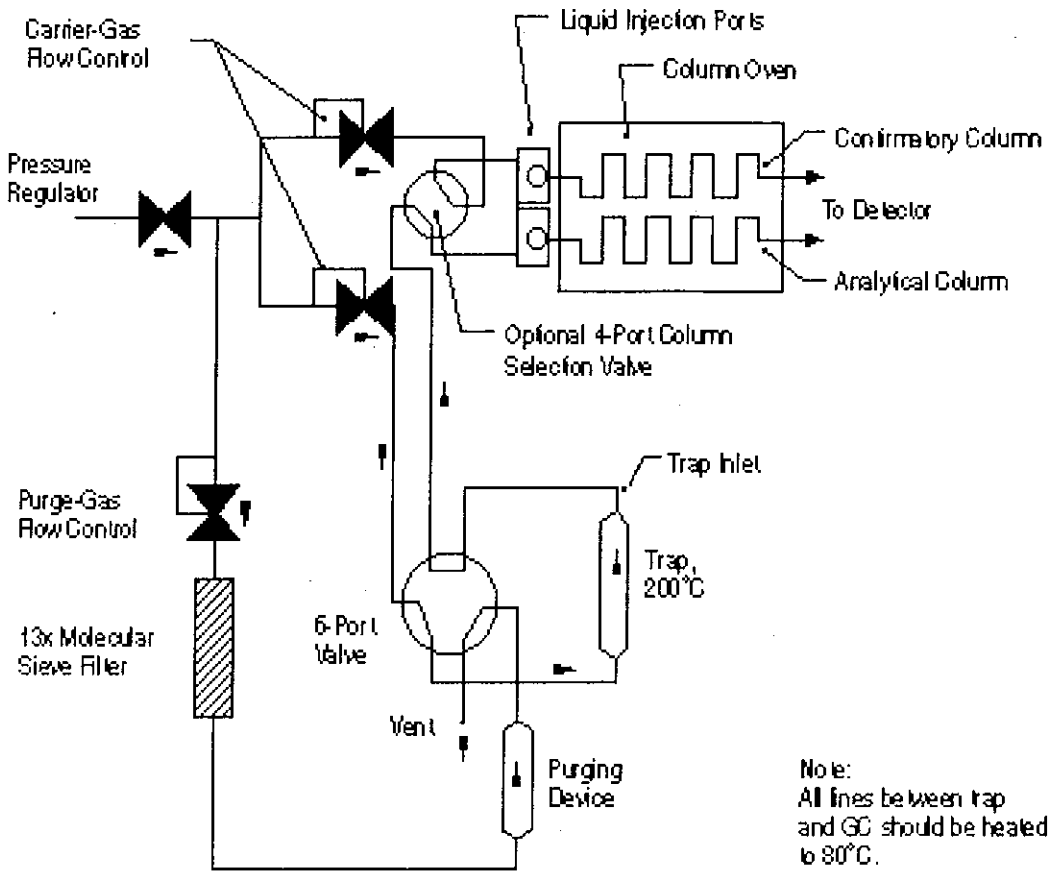
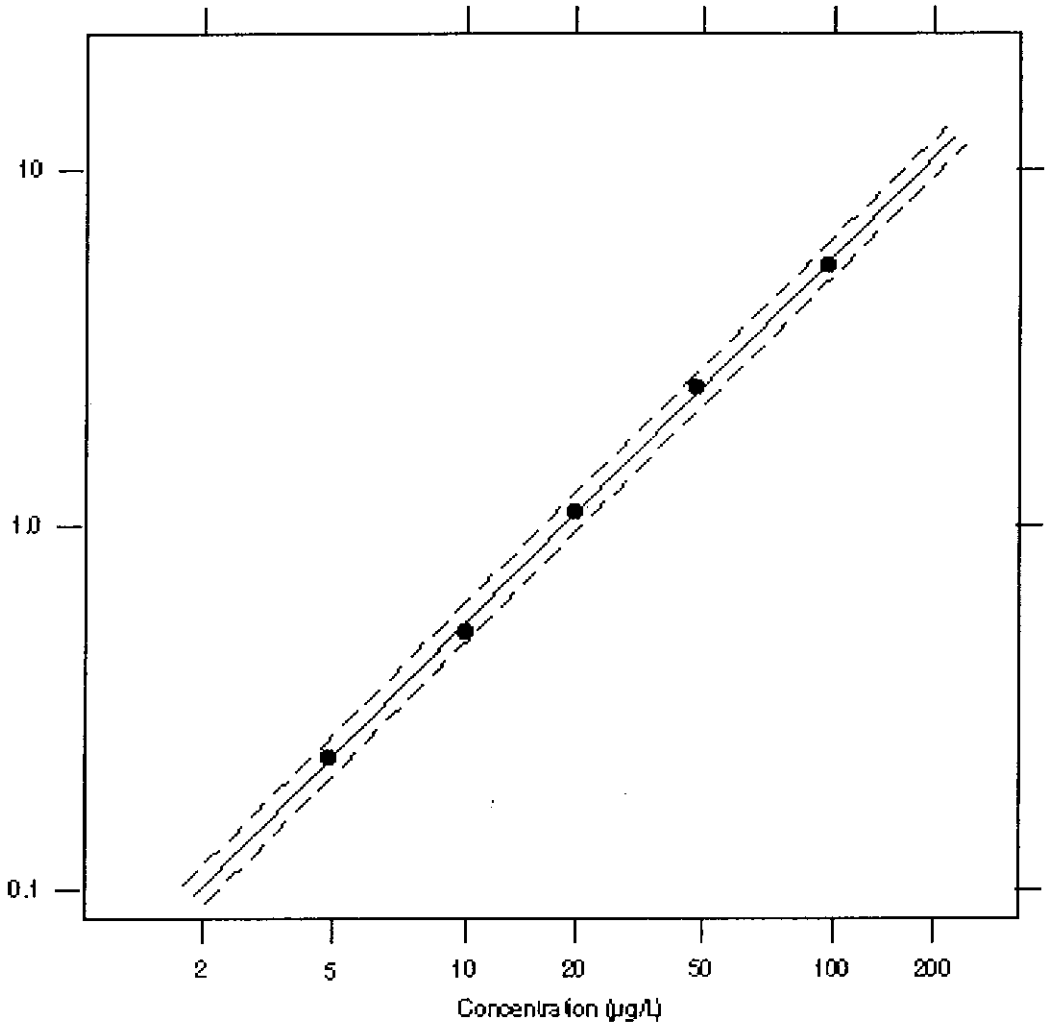


Figure 5. Schematic of Purge-and-Trap Device—Desorb Mode



The Dotted Lines Enclose a ±10% Error Window.

Figure 6. Relative Response Calibration Curve for o-Xylene

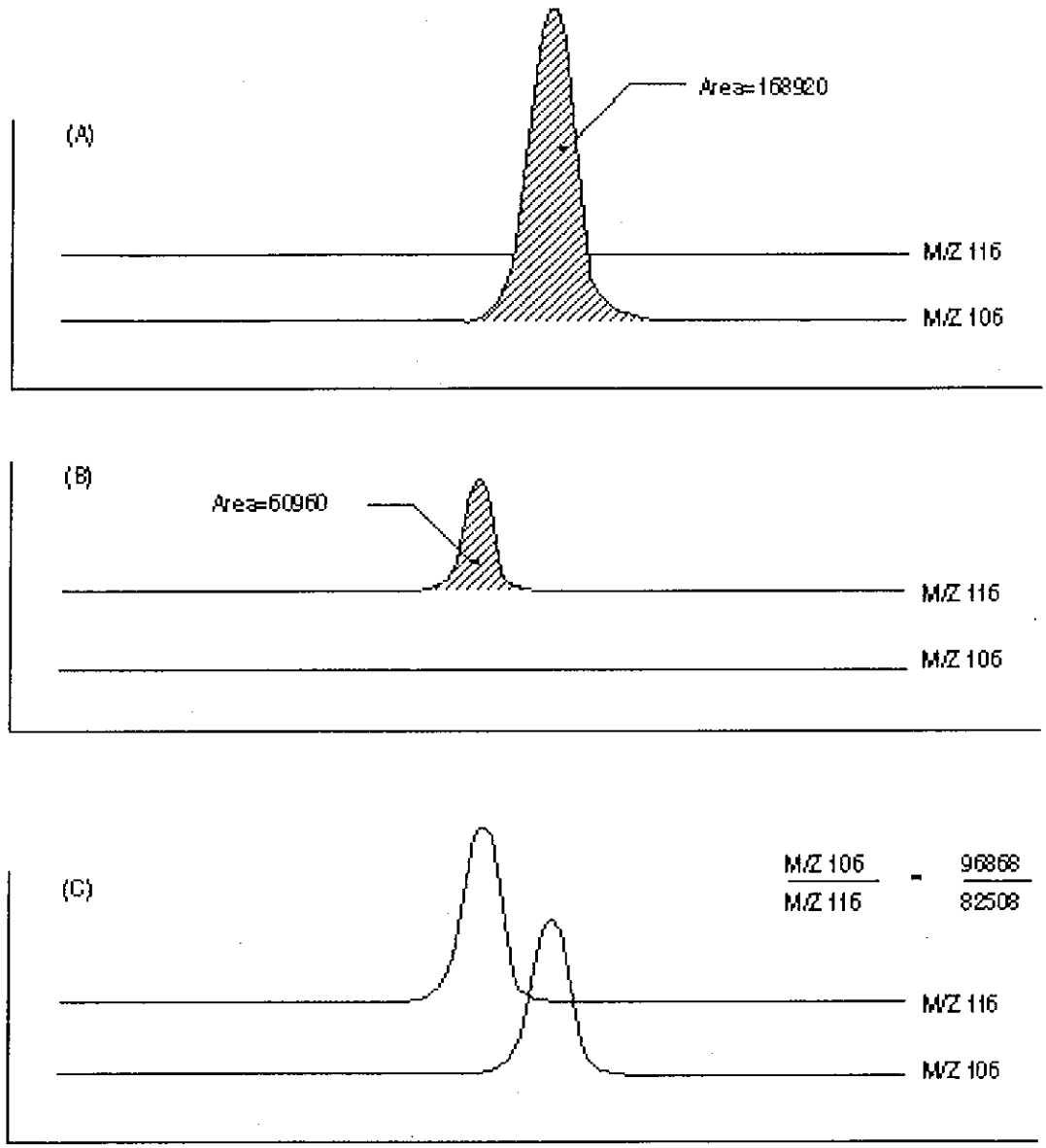


Figure 7. Extracted Ion Current Profiles for (A) o-Xylene, (B) o-Xylene-d_{10} and (C) a Mixture of o-Xylene and o-Xylene-d_{10}

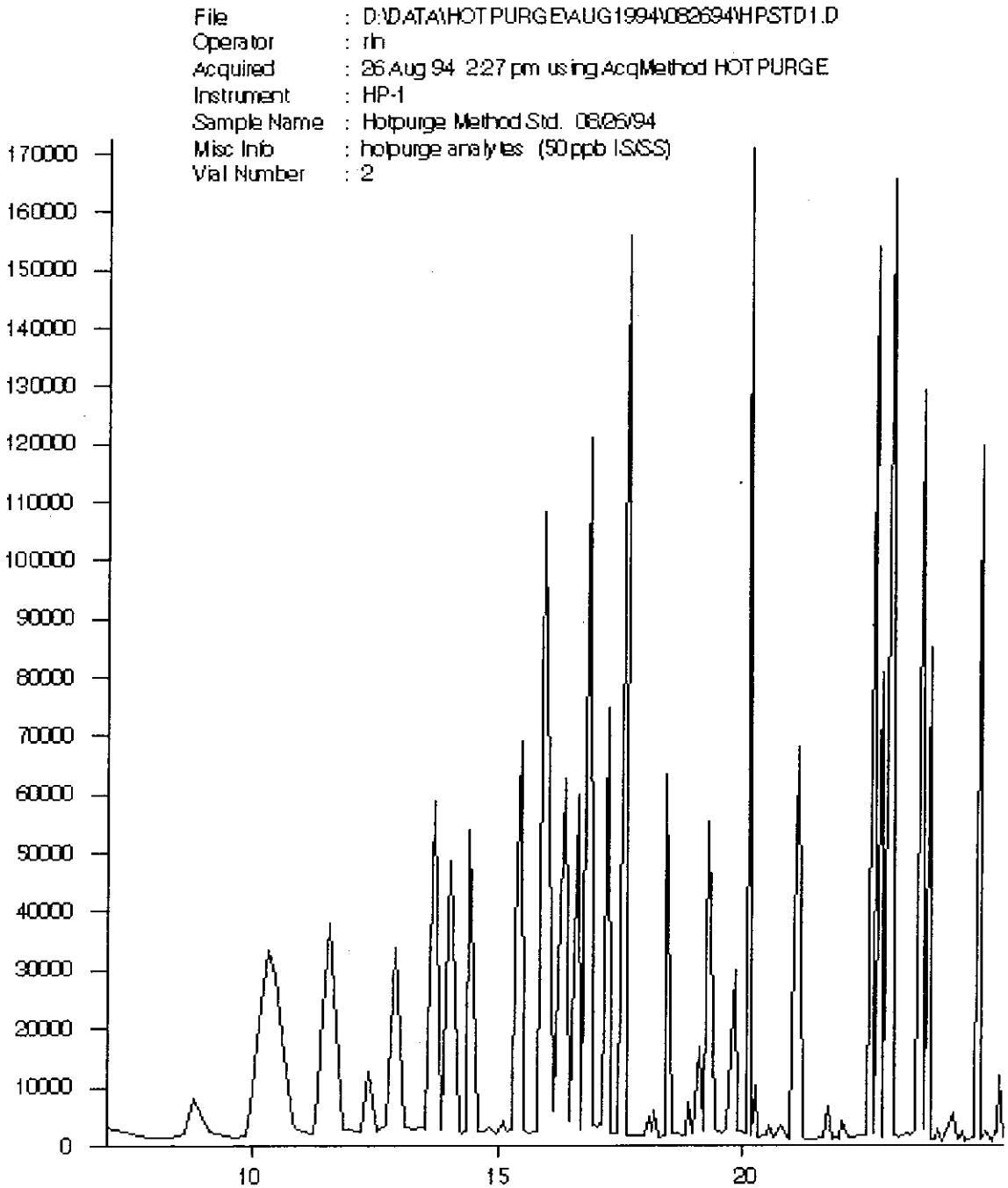


Figure 8. Chromatogram of Aqueous Performance Standard of Analytes from Table 1

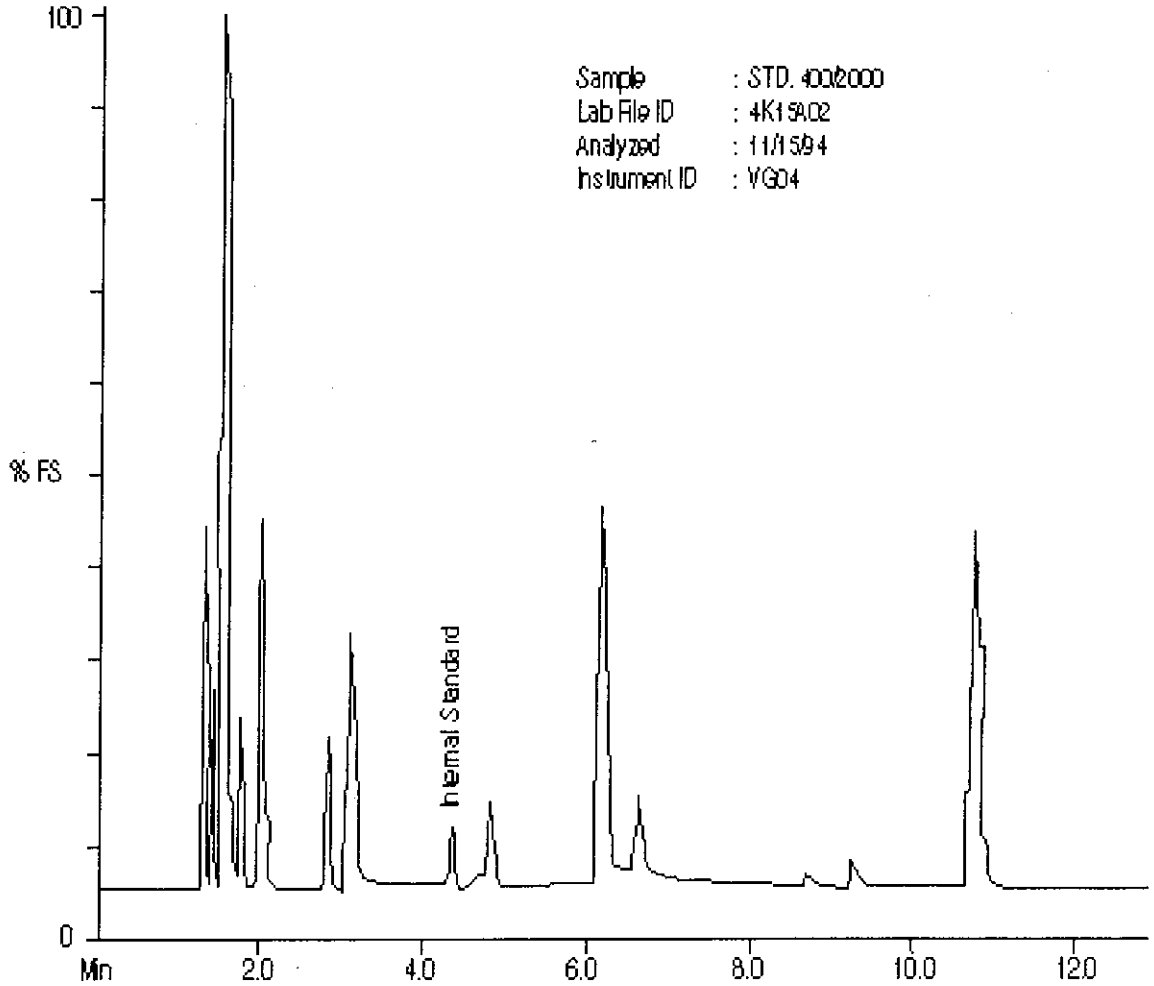


Figure 9. Chromatogram of Aqueous Performance Standard of Analytes from Table 2

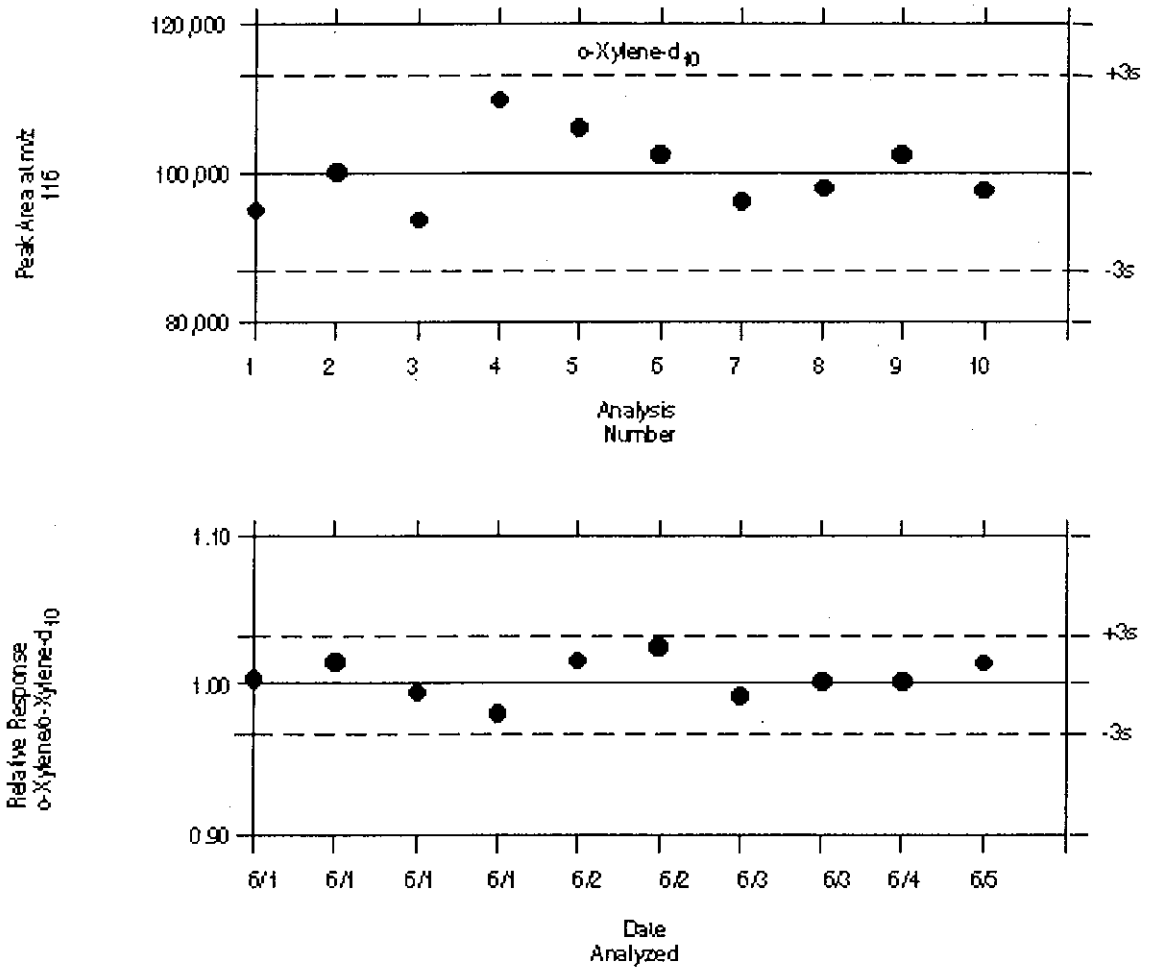


Figure 10. Quality Control Charts Showing Area (top graph) and Relative Response of o-Xylene to o-Xylene-d_{10} (lower graph) Plotted as Function of Time or Analysis Number

Method 1667

Formaldehyde, Isobutyraldehyde, and Furfural by Derivatization Followed by High Performance Liquid Chromatography

Revision A, July 1998

Method 1667, Revision A

Formaldehyde, Isobutyraldehyde, and Furfural by Derivatization Followed by High Performance Liquid Chromatography

1.0 Scope and Application

1.1 This method is for surveying and monitoring under the Clean Water Act. It is used to determine certain organic pollutants specific to the pharmaceutical manufacturing industry (PMI) that can be derivatized and analyzed by high-performance liquid chromatography (HPLC).

1.2 The chemical compounds listed in Table 1 may be determined in waters, soils, and municipal sludges by this method.

1.3 The detection limits of the method are usually dependent on the level of interferences rather than instrumental limitations. The limits in Table 2 are the minimum levels that can be reliably quantified by this method with no interferences present.

Furfural (2-furaldehyde) forms two relatively stable geometric isomers upon derivatization with 2,4-dinitrophenylhydrazine (DNPH). The first isomer (probably anti-) elutes after the formaldehyde derivative and before the isobutyraldehyde derivative. The second isomer (probably syn-) elutes after the isobutyraldehyde derivative. Experience with this system has shown that the best quantitative results (lowest detection limits) are obtained using the area from the first eluted peak rather than that from the second peak or the sum of the two areas. This method is for use only by analysts experienced with HPLC or under the close supervision of such qualified persons.

1.4 This method is performance-based. The analyst is permitted to modify the method to overcome interferences or to lower the cost of measurements, provided that all performance criteria in this method are met. The requirements for establishing method equivalency are given in Section 9.1.2.

2.0 Summary of the Method

2.1 For solid wastes or for aqueous wastes containing significant amounts of solid material, the aqueous phase, if any, is separated from the solid phase and stored for later analysis. If necessary, the particle size of the solids in the waste is reduced. The solid phase is extracted with an amount of extraction fluid equal to 20 times the weight of the solid phase. The extraction fluid employed is a function of the alkalinity of the solid phase of the waste. Following extraction, the aqueous extract is separated from the solid phase by filtration employing 0.6 to 0.9-µm glass-fiber filter.

2.2 If compatible (i.e., multiple phases will not form on combination), the initial aqueous phase of the waste is added to the aqueous extract, and these liquids are analyzed together. If incompatible, the liquids are analyzed separately and the results are mathematically combined to yield a volume-weighted average concentration.

2.3 A measured volume of aqueous sample or an appropriate amount of solids leachate is buffered to pH=5 and derivatized with 2,4-dinitrophenylhydrazine (DNPH), using either the solid-sorbent or

methylene chloride derivatization/extraction option. If the solid-sorbent option is used, the derivative is extracted using solid-sorbent cartridges, followed by elution with ethanol. If the methylene chloride option is used, the derivative is extracted with methylene chloride. The methylene chloride extracts are concentrated using the Kuderna-Danish (K-D) procedure and solvent exchanged into methanol prior to HPLC analysis. Liquid chromatographic conditions are described that permit the separation and measurement of formaldehyde, isobutyraldehyde, and furfural derivatives in the extract by absorbance detection at 365 nm.

2.4 The quality of the analysis is assured through reproducible calibration and testing of the derivatization/extraction procedure and the HPLC system.

3.0 Definitions

There are no specific definitions unique to this method.

4.0 Interferences

4.1 Method interferences may be caused by contaminants in solvents, reagents, glassware, and other sample processing hardware that lead to discrete artifacts and/or elevated baselines in chromatograms. All of these materials must be routinely demonstrated to be free from interferences under the conditions of the analysis by analyzing laboratory reagent blanks as described in Section 9.3.

4.1.1 Glassware must be scrupulously cleaned. Clean all glassware as soon as possible after use by rinsing with the last solvent used. This should be followed by detergent washing with hot water, and rinses with tap water and reagent water. It should then be drained, dried, and heated in a laboratory oven at 130°C for several hours before use. Solvent rinses with methanol may be substituted for the oven heating. After drying and cooling, glassware should be stored in a clean environment to prevent any accumulation of dust or other contaminants.

4.1.2 The use of high-purity reagents and solvents helps to minimize interference problems. Purification of solvents by distillation in all-glass systems may be required.

4.2 Analysis of formaldehyde is complicated by its ubiquitous occurrence in the environment. Acetic acid, even high-purity acetic acid, is often contaminated with formaldehyde. For this reason, a phthalate buffer is used in this method instead of an acetate buffer. Wherever acetic acid is used, it must be demonstrated to be formaldehyde free.

4.3 Matrix interferences may be caused by contaminants that are coextracted from the sample. The extent of matrix interferences will vary considerably from source to source, depending upon the nature and diversity of the matrix being sampled. If matrix interferences occur, some additional cleanup may be necessary.

4.4 The extent of interferences that may be encountered using liquid chromatographic techniques has not been fully assessed. Although the HPLC conditions described allow for resolution of the specific compounds covered by this method, other matrix components may interfere.

5.0 Safety

5.1 The toxicity or carcinogenicity of each compound or reagent used in this method has not been precisely determined; however, each chemical compound should be treated as a potential health hazard. Exposure to these compounds should be reduced to the lowest possible level. The laboratory is responsible for maintaining a current awareness file of OSHA regulations regarding the safe handling of the chemicals specified in this method. A reference file of material safety data sheets should also be made available to all personnel involved in these analyses. Additional information on laboratory safety can be found in References 1 through 3.

5.2 Formaldehyde has been classified as a potential carcinogen. Primary standards of formaldehyde should be prepared in a hood, and a NIOSH/MESA approved toxic gas respirator should be worn when high concentrations are handled.

6.0 Apparatus and Materials

Disclaimer: The mention of trade names or commercial products in this Method is for illustrative purposes only and does not constitute endorsement or recommendation for use by the Environmental Protection Agency. Equivalent performance may be achievable using apparatus, materials, or cleaning procedures other than those suggested here. The laboratory is responsible for demonstrating equivalent performance.

6.1 Reaction vessel—250-mL Florence flask.

6.2 Separatory funnel—250-mL, with polytetrafluoroethylene (PTFE) stopcock.

6.3 Kuderna-Danish (K-D) apparatus.

6.3.1 Concentrator tube—10-mL, graduated (Kontes K-570050 or equivalent). A ground-glass stopper is used to prevent evaporation of extracts.

6.3.2 Evaporation flask—500-mL (Kontes K-570001-500 or equivalent). Attach to concentrator tube with springs, clamps, or equivalent.

6.3.3 Snyder column—Three-ball macro (Kontes K-503000-0121 or equivalent).

6.3.4 Snyder column—Two-ball micro (Kontes K569001-0219 or equivalent).

6.3.5 Springs—½", (Kontes K-662750 or equivalent).

6.4 Vials—10- and 25-mL glass, with PTFE-lined screw-caps or crimp-tops.

6.5 Boiling chips—Solvent-extracted with methylene chloride, approximately 10/40 mesh (silicon carbide or equivalent).

6.6 Balance—Analytical, capable of accurately weighing to the nearest 0.0001 g.

6.7 pH meter—Capable of measuring to the nearest 0.01.

6.8 High-performance liquid chromatograph (modular).

6.8.1 Pumping system—Isocratic, with constant flow control capable of 1.00 mL/min.

6.8.2 High-pressure injection valve with 20-µL loop.

6.8.3 Column—250 mm long × 4.6 mm inside diameter (i.d.), 5-µm particle size, C_{18} (or equivalent).

6.8.4 Absorbance detector—365 nm.

6.8.5 Strip-chart recorder compatible with the detector. Use of a data system is recommended.

6.9 Glass-fiber filter paper, 0.6 to 0.9-µm.

6.10 Solid-sorbent cartridges—Packed with 500 mg C_{18} (Baker or equivalent).

6.11 Vacuum manifold—Capable of simultaneous extraction of up to 12 samples (Supelco or equivalent).

6.12 Sample reservoirs—50-mL capacity (Supelco or equivalent).

6.13 Pipet—Capable of accurately delivering 0.10 mL of solution (Pipetman or equivalent).

6.14 Water bath—Heated, with concentric ring cover, capable of temperature control of ± 2 °C at 80-90 °C. The bath should be used in a hood.

7.0 Reagents and Standards

7.1 Reagent grade chemicals shall be used in all tests. Unless otherwise indicated, it is intended that all reagents shall conform to the specifications of the Committee on Analytical Reagents of the American Chemical Society, where such specifications are available. Other grades may be used, provided it is first ascertained that the reagent is of sufficiently high purity to permit its use without lessening the accuracy of the determinations.

7.2 Reagent water—Water in which the compounds of interest and interfering compounds are not detected by this method. It may be generated by any of the methods in this subsection.

7.2.1 Activated carbon—Pass tap water through a carbon bed (Calgon Filtrasorb-300, or equivalent).

7.2.2 Water purifier—Pass tap water through a purifier (Millipore Super Q, or equivalent).

7.2.3 Boil and purge—Heat tap water to 90-100°C and bubble contaminant-free inert gas through it for approximately 1 hour. While still hot, transfer the water to screw-cap bottles and seal with a PTFE-lined cap.

7.3 Methylene chloride—HPLC grade or equivalent.

7.4 Methanol—HPLC grade or equivalent.

7.5 Ethanol (absolute)—HPLC grade or equivalent.

7.6 2,4-Dinitrophenylhydrazine (DNPH, 70% w/w) in reagent water.

7.7 Formalin (37.6% w/w) in reagent water.

7.8 Acetic acid (glacial), demonstrated to be formaldehyde-free.

7.9 Potassium acid phthalate.

7.10 Sodium hydroxide solutions, 1 N, and 5 N.

7.11 Sodium chloride.

7.12 Sodium sulfate solution, 0.1 M.

7.13 Hydrochloric acid, 0.1 N.

7.14 Extraction fluid—Dilute 64.3 mL of 1.0 N sodium hydroxide and 5.7 mL of glacial acetic acid to 900 mL with reagent water. Further dilute to 1 L with reagent water. The pH should be 4.93 ± 0.02. If not, adjust with acid or base.

7.15 Stock standard solutions.

7.15.1 Stock formaldehyde (approximately 1.00 mg/mL)—Prepare by diluting 265 µL formalin to 100 mL with reagent water.

Standardization of formaldehyde stock solution—Transfer a 25-mL aliquot of a 0.1 M sodium sulfite solution to a beaker and record the pH. Add a 25-mL aliquot of the formaldehyde stock solution (Section 7.15.1) and record the pH. Titrate this mixture back to the original pH using 0.1 N hydrochloric acid. The formaldehyde concentration is calculated using the following equation:

$$Concentration\ (mg/mL) = 30.03 \times (N\ HCl) \times (mL\ HCl) \times 25$$

where:

N HCl = Normality of the HCl solution

mL HCl = mL of standardized HCl solution; and

30.03 = *Molecular weight of formaldehyde.*

7.15.2 Stock formaldehyde, isobutyraldehyde, and furfural—Prepare by adding 265 µL of formalin, 0.100 g of isobutyraldehyde, and 0.100 g of furfural to 90 mL of reagent water and dilute to 100 mL. The concentrations of isobutyraldehyde and furfural in this solution are 1.00 mg/mL. Calculate the concentration of formaldehyde in this solution using the results of the assay performed in Section 7.15.1.

7.15.3 Stock standard solutions must be replaced after six months, or sooner if comparison with check standards indicates a problem.

7.15.4 Aqueous performance standard—An aqueous performance standard containing formaldehyde (nominally 100 µg/L), isobutyraldehyde at 100 µg/L, and furfural at 100 µg/L shall be prepared daily and analyzed each shift to demonstrate performance (Section 9).

7.15.5 Preparation of calibration standards.

7.15.5.1 Prepare calibration standard solutions of formaldehyde, isobutyraldehyde, and furfural in reagent water from stock standard solution (Section 7.15.2). Prepare these solutions at the following concentrations (in µg/mL) by serial dilution of the stock standard solution: 50, 20, 10. Prepare additional calibration standard solutions at the following concentrations, by dilution of the appropriate 50, 20, or 10 µg/mL standard: 5, 0.5, 2, 0.2, 1, 0.1. Make further dilutions if appropriate.

7.16 Reaction solutions.

7.16.1 DNPH (1.00 mg/mL)—Dissolve 142.9 mg 70% (w/w) reagent in 100 mL of absolute ethanol. Slight heating or sonication may be necessary to effect dissolution.

7.16.2 Phthalate buffer (0.1 N)—Prepare by dissolving 20.42 g of potassium acid phthalate in 1 L of reagent water. Adjust pH to 5 by addition of sodium hydroxide or hydrochloric acid, as necessary.

7.16.3 Sodium chloride solution (saturated)—Prepare by mixing an excess of the reagent-grade solid with reagent water.

8.0 Sample Collection, Preservation, and Storage

8.1 Grab samples are collected in glass containers having a total volume greater than 20 mL. For aqueous samples that pour freely, fill sample bottles so that no air bubbles pass through the sample as the bottle is filled and seal each bottle so that no air bubbles are entrapped. Maintain the hermetic seal on the sample bottle until time of analysis.

8.2 Samples are maintained at 0-4°C from the time of collection until analysis. Samples must be derivatized within five days of collection and analyzed within three days of derivatization.

9.0 Quality Control

9.1 Each laboratory that uses this method is required to operate a formal quality assurance program (Reference 4). The minimum requirements of this program consist of an initial demonstration of laboratory capability and analysis of standards and blanks as tests of continued performance. Laboratory performance is compared to established performance criteria to determine if the results of analyses meet the performance characteristics of the method.

9.1.1 The analyst shall make an initial demonstration of the ability to generate acceptable accuracy and precision with this method. This ability is established as described in Section 9.2.

9.1.2 In recognition of advances that are occurring in analytical technology, and to allow the analyst to overcome sample matrix interferences, the analyst is permitted certain options to improve separations or lower the costs of measurements. These options include alternative extraction, concentration, cleanup procedures, and changes in columns and detectors. Alternative techniques, such as substitution of immunoassay, and changes that degrade method performance are not allowed. If an analytical technique other than the techniques specified in this method is used, that technique must have a specificity equal to or better than the specificity of the techniques in this method for the analytes of interest.

9.1.2.1 Each time a modification is made to this method, the analyst is required to repeat the procedure in Section 9.2. If the detection limit of the method will be affected by the change, the laboratory is required to demonstrate that the method detection limit (MDL; 40 CFR Part 136, Appendix B) is lower than one-third the regulatory compliance level. If calibration will be affected by the change, the analyst must recalibrate the instrument per Section 10.

9.1.2.2 The laboratory is required to maintain records of modifications made to this method. These records include the information below, at a minimum.

9.1.2.2.1 The names, titles, addresses, and telephone numbers of the analyst(s) who performed the analyses and modification, and of the quality control officer who witnessed and will verify the analyses and modification.

9.1.2.2.2 A list of pollutant(s) measured, including name and CAS Registry Number.

9.1.2.2.3 A narrative stating the reason(s) for the modification.

9.1.2.2.4 Results from all quality control (QC) tests comparing the modified method to this method, including:

(a) Calibration (Section 10.1.2)

(b) Calibration verification (Section 10.1.2.2)

(c) Initial precision and accuracy (Section 9.2)

(d) Analysis of blanks (Section 9.3)

(e) Accuracy assessment (Section 9.5)

9.1.2.2.5 Data that will allow an independent reviewer to validate each determination by tracing the instrument output (peak height, area, or other signal) to the final result. These data are to include:

(a) Sample numbers and other identifiers

(b) Extraction dates

(c) Analysis dates and times

(d) Analysis sequence/run chronology

(e) Sample weight or volume (Section 11)

(f) Extract volume prior to each cleaning step (Section 11.1.2)

(g) Final extract volume prior to injection (Section 11.3.4.5 or Section 11.3.5.5)

(h) Injection volume (Section 12)

(I) Dilution data, differentiating between dilution of a sample or an extract

(j) Instrument and operating conditions

(k) Column and operating conditions (nature of column, dimensions, flow rates, solvents, etc.)

(l) Detector operating conditions (wavelength, etc.)

(m) Chromatograms, printer tapes, and other recording of raw data

(n) Quantitation reports, data system outputs, and other data necessary to link raw data to the results reported

9.1.3 Analyses of blanks are required to demonstrate freedom from contamination and that the compounds of interest and interfering compounds have not been carried over from a previous analysis (Section 4). The procedures and criteria for analysis of a blank are described in Section 9.3.

9.1.4 The laboratory shall, on an ongoing basis, demonstrate through the analysis of the aqueous performance standard (Section 7.15.4) that the analysis system is in control. This procedure is described in Section 10.

9.1.5 The laboratory shall maintain records to define the quality of data that is generated.

9.2 Initial precision and accuracy—To establish the ability to generate acceptable precision and accuracy, the analyst shall perform the following operations for compounds to be calibrated.

9.2.1 Analyze four aliquots of the aqueous performance standard (Section 7.15.4) according to the method beginning in Section 11. Use the solid-sorbent option or the methylene chloride option, whichever will be used routinely.

9.2.2 Using results from Section 9.2.1, compute the average percent recovery (X) and the standard deviation of the recovery (s) for each compound.

9.2.3 For each compound, compare s and X with the corresponding limits for initial precision and recovery found in Table 3. If s and X for all compounds meet the acceptance criteria, system performance is acceptable and analysis of blanks and samples may begin. If, however, any individual s exceeds the precision limit or any individual X falls outside the range for accuracy, system performance is unacceptable for that compound. This is an indication that the analytical system is not performing properly for the compound(s) in question. In this event, correct the problem and repeat the entire test (Section 9.2.1).

9.3 Blanks—Reagent water blanks are analyzed to demonstrate freedom from contamination.

With each sample lot (samples analyzed on the same 12-hour shift), a blank shall be analyzed immediately after analysis of the aqueous performance standard (Section 9.1.4) to demonstrate freedom from contamination. If any of the compounds of interest or any potentially interfering

compound is found in a blank at greater than 10 µg/L, analysis of samples is halted until the source of contamination is eliminated and a blank shows no evidence of contamination at this level.

9.4 The specifications contained in this method can be met if the apparatus used is calibrated properly, then maintained in a calibrated state. The standards used for calibration (Section 7.15.5), calibration verification (Section 10.1.2.2) and for initial (Section 9.2) and ongoing (Section 9.1.4) precision and accuracy should be identical, so that the most precise results will be obtained.

9.5 Depending on specific program requirements, field replicates may be collected to determine the precision of the sampling technique, and spiked samples may be required to determine the accuracy of the analysis.

10.0 Calibration

10.1 Establish liquid chromatographic operating parameters to produce a retention time equivalent to that indicated in Table 2 for formaldehyde derivative. Suggested chromatographic conditions are provided in Section 12.1. Prepare derivatized calibration standards according to the procedure in Section 10.1.1. Calibrate the chromatographic system using the external standard technique (Section 10.1.2).

10.1.1 Process each calibration standard solution through the derivatization option used for sample processing (Section 11.3.4 or 11.3.5).

10.1.2 External standard calibration procedure.

10.1.2.1 Analyze each derivatized calibration standard using the chromatographic conditions specified in Section 12.1, and tabulate peak area against concentration injected. The results may be used to prepare calibration curves for formaldehyde, isobutyraldehyde, and furfural.

10.1.2.2 The working calibration curve must be verified at the beginning of each 12-hour shift or every 20 samples, whichever is more frequent, by the measurement of one or more calibration standards. If the response for any analyte varies from the previously established responses by more than 10%, the test must be repeated using a fresh calibration standard after it is verified that the analytical system is in control. Alternatively, a new calibration curve may be prepared for that compound. If an autosampler is available, it is convenient to prepare a calibration curve daily by analyzing standards along with test samples.

11.0 Sample Extraction, Cleanup, and Derivatization

11.1 Extraction of solid samples.

11.1.1 All solids must be homogeneous. When the sample is not dry, determine the dry weight of the sample using a representative aliquot.

11.1.1.1 Determination of dry weight—In certain cases, sample results are desired based on a dry weight basis. When such data is desired, a portion of the sample is weighed out at the same time as the portion used for the analytical determination.

Warning: *The drying oven should be contained in a hood or vented. Significant laboratory contamination may result from drying a heavily contaminated hazardous waste sample.*

11.1.1.2 Immediately after weighing the sample for extraction, weigh 5-10 g of the sample into a tared crucible. Determine the percent dry weight of the sample by drying overnight at 105°C. Allow to cool in a desiccator before weighing.

$$\%\ dry\ weight = \frac{g\ of\ dry\ sample}{g\ of\ sample} \times 100$$

11.1.2 Measure 25 g of solid into a 500-mL bottle with a PTFE-lined screw-cap or crimp-top, and add 500 mL of extraction fluid (Section 6.13). Extract the solid by rotating the bottle at approximately 30 rpm for 18 hours. Filter the extract through glass-fiber filter paper and store in a sealed bottle at 4°C. Each mL of extract represents 0.050 g of solid.

11.2 Cleanup and separation.

11.2.1 Cleanup procedures may not be necessary for a relatively clean sample matrix. The cleanup procedures recommended in this method have been used for the analysis of various sample types. If particular circumstances demand the use of an alternative cleanup procedure, the analyst must meet the specifications in Section 9.1.2.

11.2.2 If the sample is not clean, or the complexity is unknown, the entire sample should be centrifuged at 2500 rpm for 10 minutes. Decant the supernatant liquid from the centrifuge bottle and filter through glass-fiber filter paper into a container that can be tightly sealed.

11.3 Derivatization.

11.3.1 For aqueous samples, measure a 50- to 100-mL aliquot of sample. Quantitatively transfer the sample aliquot to the reaction vessel (Section 6.1).

11.3.2 For solid samples, 1-10 mL of leachate (Section 11.1.2 or Section 11.2.2) will usually be required. The amount used for a particular sample must be determined through preliminary experiments.

11.3.3 Derivatization and extraction of the derivative can be accomplished using the solid-sorbent (Section 11.3.4) or methylene chloride option (Section 11.3.5).

11.3.4 Solid Sorbent Option

11.3.4.1 Add 4 mL of phthalate buffer (Section 7.16.2) and adjust the pH to 5.0±0.1 with sodium hydroxide or hydrochloric acid. Add 10 mL of DNPH reagent, adjust the total volume to approximately 100 mL with reagent water, seal the container and place on a wrist-action shaker at room temperature for 1 hour. Samples or standards containing high analyte concentrations may require more DNPH reagent for complete reaction.

11.3.4.2 Assemble the vacuum manifold and connect to a water aspirator or vacuum pump. Assemble solid sorbent cartridges containing a minimum of 1.5 g of C_{18} sorbent, using connectors supplied by the manufacturer, and attach the sorbent train to the vacuum manifold. Condition each cartridge by passing 10 mL dilute phthalate buffer (10 mL 5 N phthalate buffer dissolved in 250 mL of reagent water) through the sorbent cartridge train.

11.3.4.3 Remove the reaction vessel from the shaker and add 10 mL of saturated sodium chloride solution to the vessel.

11.3.4.4 Add the reaction solution to the sorbent train and apply a vacuum so that the solution is drawn through the cartridges at a rate of 3 to 5 mL/min. After the solution has eluted, allow air to be drawn through the cartridge for approximately 2 minutes to remove all traces of solution, then release the vacuum.

11.3.4.5 Elute each cartridge train with approximately 9 mL of absolute ethanol, directly into a 10-mL volumetric flask. Dilute the solution to volume with absolute ethanol, mix thoroughly, and place in a tightly sealed vial until analyzed.

11.3.5 Methylene chloride option.

11.3.5.1 Add 5 mL of phthalate buffer (Section 7.16.2) and adjust the pH to 5.0±0.1 with sodium hydroxide or hydrochloric acid. Add 10 mL of DNPH reagent, adjust the volume to approximately 100 mL with reagent water, seal the container, and place on a wrist-action shaker at room temperature for 1 hour. Samples or standards with high analyte concentrations may require more DNPH reagent for complete reaction.

11.3.5.2 Extract the solution with three 20-mL portions of methylene chloride, using a 250-mL separatory funnel, and combine the methylene chloride layers. If an emulsion forms upon extraction, remove the entire emulsion and centrifuge at 2000 rpm for 10 minutes. Separate the layers and proceed with the next extraction.

11.3.5.3 Assemble a K-D concentrator by attaching a 10-mL concentrator tube to a 500-mL evaporator flask. Wash the K-D apparatus with 25 mL of extraction solvent to complete the quantitative transfer.

11.3.5.4 Add one or two clean boiling chips to the evaporation flask and attach a three-ball Snyder column. Prewet the Snyder column by adding about 1 mL of methylene chloride to the top. Place the K-D apparatus on a hot water bath (80-90 °C) so that the concentrator tube is partially immersed in the hot water and the entire lower rounded surface of the flask is bathed with hot vapor. Adjust the vertical position of the apparatus and the water temperature, as required, to complete the concentration in 10-15 minutes. At the proper rate of distillation, the balls of the column will actively chatter, but the chambers will not flood with condensed solvent. When the apparent volume of the liquid reaches 10 mL, remove the K-D apparatus and allow it to drain and cool for at least 10 minutes.

11.3.5.5 Prior to liquid chromatographic analysis, the solvent must be exchanged to methanol. The analyst must ensure quantitative transfer of the extract concentrate. The exchange is performed as described below.

11.4 After cooling and draining as described in Section 11.3.5.4, momentarily remove the Snyder column and add 5 mL of methanol and a new boiling chip. Attach the micro Snyder column. Concentrate the extract using 1 mL of methanol to prewet the Snyder column. Place the K-D apparatus on the water bath so that the concentrator tube is partially immersed in the hot water. Adjust the vertical position of the apparatus and the water temperature, as required, to complete the concentration. When the apparent volume of the liquid reaches less than 5 mL, remove the K-D apparatus and allow it to drain and cool for at least 10 minutes.

Remove the Snyder column and rinse the flask and its lower joint with 1-2 mL of methanol and add to the concentrator tube. A 5-mL syringe is recommended for this operation. Adjust the extract volume to 10-mL with methanol. Stopper the concentrator tube and store refrigerated at 4 °C if further processing will not be performed immediately. If the extract will be stored longer than two days, it should be transferred to a vial with a PTFE-lined screw-cap or crimp-top. Proceed with the liquid chromatographic analysis if further cleanup is not required.

12.0 High-Performance Liquid Chromatography

12.1 Chromatographic conditions.

Column: C_{18}, 250 mm long × 4.6 mm i.d., 5-µm particle size (or equivalent).

Mobile Phase: Methanol/water, 75:25 (v/v), isocratic at 30°C.

Flow Rate: 1.0 mL/min.

UV Detector: 365 nm.

Injection Vol.: 20 µL.

12.2 Analysis.

12.2.1 Analyze samples by HPLC using conditions described in Section 12.1. Table 2 lists the retention times and MLs that were obtained under these conditions. Other HPLC columns, chromatographic conditions, or detectors may be used if the requirements of Section 9 are met.

12.2.2 The width of the retention-time window used to make identifications should be based upon measurements of actual retention-time variations of standards over the course of a day. Three times the standard deviation of the retention time for a compound can be used to calculate a suggested window size; however, the experience of the analyst should weigh heavily in the interpretation of chromatograms.

12.2.3 If the peak area exceeds the linear range of the calibration curve, a smaller sample volume should be used. Alternatively, the final solution may be diluted with ethanol or methanol, as appropriate, and reanalyzed.

12.2.4 If the peak area measurement is prevented by the presence of observed interferences, further cleanup may be required.

12.3 Calculations.

12.3.1 Calculate the calibration factor (CF) at each concentration and the mean calibration factor (CF_m) as follows (mean value based on 5 points):

$$CF = \frac{area\ response\ (A_s)}{concentration\ (C_s)}$$

$$mean\ CF = CF_m = \frac{\sum_{i=1}^{5} CF}{5}$$

12.3.2 Aqueous samples—Calculate the concentration of each analyte as follows:

$$\mu g/L = \frac{A_s * V_e * DF}{CF_m * V_s}$$

where:

RF_m is the mean response factor
A_s is the area signal from the analyte
V_e is the extract volume
DF is the dilution factor; e.g. 10, if the sample is diluted by a factor of 10
V_s is the sample volume

12.3.3 Solid samples—Calculate the concentration of each analyte using the equation below. A factor must be included in the equation to account for the weight of the sample used and, if desired, to correct for dry weight.

$$mg/kg = \frac{A_s * V_e * DF}{CF_m \times W_s * (1 - \frac{\%m}{100})}$$

where:

W_s is the sample weight
%m is the percent moisture of the sample
the other symbols are the same as in Section 12.3.2

13.0 Method Performance

13.1 The MDLs listed in Table 2 were obtained using reagent water and methylene chloride extraction. Similar results can be obtained using the solid-sorbent method.

13.2 This method has been tested for linearity of recovery from spiked reagent water and has been demonstrated to be applicable over the range from the ML to 50 times the ML.

13.3 A representative chromatogram is presented as Figure 1.

14.0 Pollution Prevention

14.1 Pollution prevention encompasses any technique that reduces or eliminates the quantity or toxicity of waste at the point of generation. Many opportunities for pollution prevention exist in laboratory operation. EPA has established a preferred hierarchy of environmental management techniques that places pollution prevention as the management option of first choice. Whenever feasible, laboratory personnel should use pollution prevention techniques to address their waste generation. When wastes cannot be reduced feasibly at the source, the Agency recommends recycling as the next best option. The acids used in this Method should be reused as practicable by purifying by electrochemical techniques. The only other chemicals used in this Method are the neat materials used in preparing

standards. These standards are used in extremely small amounts and pose little threat to the environment when managed properly. Standards should be prepared in volumes consistent with laboratory use to minimize the disposal of excess volumes of expired standards.

14.2 For information about pollution prevention that may be applied to laboratories and research institutions, consult *Less is Better: Laboratory Chemical Management for Waste Reduction*, available from the American Chemical Society's Department of Governmental Relations and Science Policy, 1155 16th Street NW, Washington DC 20036, 202/872–4477.

15.0 Waste Management

15.1 It is the laboratory's responsibility to comply with all Federal, State, and local regulations governing waste management, particularly the hazardous waste identification rules and land-disposal restrictions. In addition it is the laboratory's responsibility to protect air, water, and land resources by minimizing and controlling all releases from fume hoods and bench operations. Also, compliance is required with any sewage discharge permits and regulations.

15.2 Samples containing acids at a pH of less than 2 are hazardous and must be neutralized before being poured down a drain or must be handled as hazardous waste.

15.3 For further information on waste management, consult *The Waste Management Manual for Laboratory Personnel* and *Less is Better: Laboratory Chemical Management for Waste Reduction*, both available from the American Chemical Society's Department of Government Relations and Science Policy, 1155 16th Street NW, Washington, DC 20036.

16.0 References

1. "Working with Carcinogens," DHEW, PHS, NIOSH, Publication 77-206 (1977).

2. "OSHA Safety and Health Standards, General Industry," 29 CFR 1910, OSHA 2206, (1976).

3. "Safety in Academic Chemistry Laboratories," American Chemical Society Publication, Committee on Chemical Safety (1979).

4. "Handbook of Analytical Quality Control in Water and Wastewater Laboratories," U.S. EPA, EMSL Cincinnati, OH 45268, EPA-600/4-79-019 (March 1979).

17.0 Tables

Table 1. PMI Analytes to Which This Method Applies

PMI Analyte	CASRN[1]
Formaldehyde	50-00-0
Furfural	98-01-1
Isobutyraldehyde	78-84-2

[1] Chemical Abstracts Service Registry Number.

Table 2. Retention Times and Minimum Levels (MLs) for PMI Analytes

PMI Analyte	Retention Time[1] (seconds)	ML[2] (µg/L)
Formaldehyde	326	50
Furfural	495	50
Isobutyraldehyde	714	50

[1] Retention times are for the DNPH derivative.

[2] This is the minimum level at which the entire analytical system shall give a recognizable signal and an acceptable calibration point, taking into account method-specific sample and injection volumes.

Table 3. Quality Control Acceptance Criteria for Initial Precision and Recovery

PMI Analyte	Spike Level (µg/L)	Average Percent Recovery (X)	Standard Deviation (s)
Formaldehyde	50	25-187	81
Furfural	100	70-102	16

Isobutyraldehyde	50	45-121	38

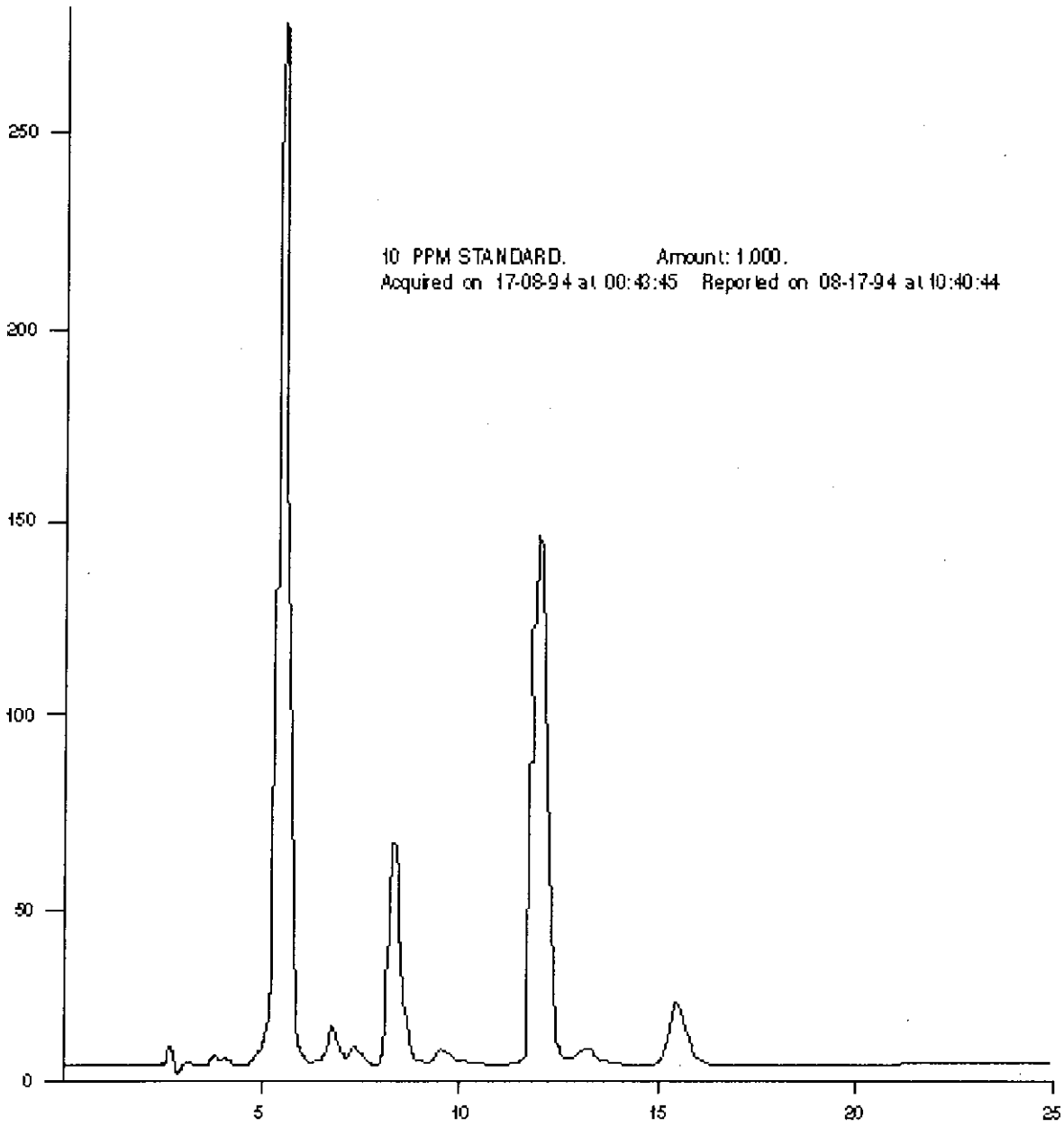


Figure 1. Chromatogram of the 2,4-DNPH Derivative of Formaldehyde, Furfural, and Isobutyraldehyde

Method 1671

Volatile Organic Compounds Specific to the Pharmaceutical Manufacturing Industry by GC/FID

Revision A, July 1998

Method 1671, Revision A

Volatile Organic Compounds Specific to the Pharmaceutical Manufacturing Industry by GC/FID

1.0 Scope and Application

1.1 This method is for surveying and monitoring under the Clean Water Act. The method is used to determine certain non-purgeable volatile organic pollutants specific to the pharmaceutical manufacturing industry (PMI) that are amenable to direct aqueous injection gas chromatography (GC) and detection by a flame ionization detector (FID).

1.2 The PMI analytes listed in Table 1 may be determined in waters, soils, and municipal sludges by this method.

1.3 The detection limits of Method 1671 are usually dependent on the level of interferences rather than instrumental limitations. The minimum levels (MLs) in Table 2 are the level that can be attained with no interferences present.

1.4 This method is recommended for use by, or under the supervision of, analysts experienced in the operation of gas chromatographs and in the interpretation of chromatograms.

1.5 This method is performance-based. The analyst is permitted to modify the method to overcome interferences or to lower the cost of measurements, provided that all performance criteria in this method are met. The requirements for establishing method equivalency are given in Section 9.2.

2.0 Summary of the Method

2.1 The percent solids content of the sample is determined. If the solids content is less than 1%, an internal standard(s) is added to a 5-mL sample. If the solids content of the sample is greater than 1%, 5 mL of reagent water and an internal standard(s) is added to a 5-g aliquot of sample.

The mixture is sonicated in a centrifuge tube with little or no headspace for 5 minutes. During this period the analytes and the internal standard will equilibrate between the solid and aqueous phases. In some cases, additional sonication will be necessary to establish equilibrium. The resulting suspension is centrifuged and the supernatant liquid analyzed.

2.2 An appropriate amount of the aqueous solution (or supernate) is injected into the GC. The compounds are separated by the GC and detected by the FID.

3.0 Definitions

There are no definitions specific to this method.

4.0 Interferences

4.1 Impurities in the carrier gas, organic compounds outgassing from the GC plumbing, and solvent vapors in the laboratory account for the majority of contamination problems encountered with this method. The analytical system is demonstrated to be free from interferences under conditions of the analysis by analyzing reagent water blanks initially and with each sample batch (samples analyzed on the same 12-hour shift), as described in Section 9.4.

4.2 Samples can be contaminated by diffusion of volatile organic compounds through the bottle seal during shipment and storage. A field blank prepared from reagent water and carried through the sampling and handling protocol may serve as a check on such contamination.

4.3 Contamination by carryover can occur when high-level and low-level samples are analyzed sequentially. To reduce carryover, the syringe is cleaned or replaced with a new syringe after each sample is analyzed. When an unusually concentrated sample is encountered, it is followed by analysis of a reagent water blank to check for carryover. Syringes are cleaned by washing with soap solution, rinsing with tap and distilled water, and drying in an oven at 100-125 °C. Other parts of the system are also subject to contamination; therefore, frequent bakeout and purging of the entire system may be required.

4.4 Interferences resulting from samples will vary considerably from source to source, depending on the diversity of the site being sampled.

5.0 Safety

The toxicity or carcinogenicity of each analyte, compound, or reagent used in this method has not been precisely determined; however, each chemical compound should be treated as a potential health hazard. Exposure to these compounds should be reduced to the lowest possible level. The laboratory is responsible for maintaining a current awareness file of OSHA regulations regarding the safe handling of the chemicals specified in this method. A reference file of material safety data sheets should also be made available to all personnel involved in these analyses. Additional information on laboratory safety can be found in References 2-4.

6.0 Equipment and Supplies

6.1 Sample bottles and septa

6.1.1 Bottles**S**25- to 40-mL with polytetrafluoroethylene (PTFE)-lined screw-cap (Pierce 13075, or equivalent). Detergent wash, rinse with tap and distilled water, and dry at >105 °C for a minimum of 1 hour before use.

6.1.2 Septa**S**PTFE-faced silicone (Pierce 12722, or equivalent), cleaned as above and baked at 100-200 °C for a minimum of 1 hour.

6.2 Gas chromatographSShall be linearly temperature programmable with initial and final holds, and shall produce results which meet the calibration (Section 10), quality assurance (Section 9), and performance tests (Section 13) of this method.

6.2.1 ColumnS30 m long × 0.32 mm i.d. fused-silica microbore column coated with 4-µm of bonded poly(dimethylpolysiloxane) (Supelco SPB-1 Sulfur, or equivalent).

6.2.2 GC operating conditions.

Temperatures:

ColumnS2 minutes at 40°C, 10°C per minute to 180°C.

Injection portS200°C

FIDS300°C

Carrier gasSHydrogen at a head pressure of 10 psig.

An injector split may be used in order to optimize peak shape and repeatability.

6.3 SyringesS5-mL, gas-tight glass hypodermic, with Luer-lok tips.

6.4 Micro syringesS10-, 25-, and 100-µL.

6.5 Syringe valvesS2-way with Luer ends, PTFE.

6.6 BottlesS15-mL, screw-cap with PTFE liner.

6.7 Balances.

6.7.1 Analytical, capable of weighing 0.1 mg.

6.7.2 Top-loading, capable of weighing 10 mg.

6.8 Equipment for determining percent moisture.

6.8.1 Oven, capable of being temperature-controlled at 110°C (±5°C).

6.8.2 Desiccator.

6.8.3 BeakersS50-, 100-mL.

6.9 Centrifuge apparatus.

6.9.1 Centrifuge capable of rotating 10-mL centrifuge tubes at 5000 rpm.

6.9.2 Centrifuge tubes, 10-mL, with screw-caps (PTFE-lined) to fit centrifuge.

6.10 Sonication apparatus capable of sonicating 10-mL centrifuge tubes and thoroughly agitating contents.

7.0 Reagents and Standards

7.1 Reagent water: Water in which the compounds of interest and interfering compounds are not detected by this method. It may be generated by any of the following methods:

7.1.1 Activated carbon**S**pass tap water through a carbon bed (Calgon Filtrasorb-300, or equivalent).

7.1.2 Water purifier**S**Pass tap water through a purifier (Millipore Super Q, or equivalent).

7.1.3 Boil and purge**S**Heat tap water to between 90 and 100°C and bubble contaminant-free inert gas through it for approximately 1 hour. While still hot, transfer the water to screw-cap bottles and seal with a PTFE-lined cap.

7.2 Sodium thiosulfate**S**ACS granular.

7.3 Standard solutions**S**Purchased as solutions or mixtures with certification to their purity, concentration, and authenticity, or prepared from materials of known purity and composition. If compound purity is 96% or greater, the weight may be used without correction to calculate the concentration of the standard.

7.3.1 Place approximately 8 mL of reagent water in a 10-mL ground-glass-stoppered volumetric flask. Allow the flask to stand unstoppered for approximately 10 minutes or until all wetted surfaces have dried. For each analyte, weigh the stoppered flask, add the compound, restopper, then immediately reweigh to prevent evaporation losses from affecting the measurement.

7.3.2 Liquids**S**Using a microsyringe, add sufficient liquid (about 100 mg) so that the final solution will have a concentration of about 10 mg/mL.

7.3.3 Gases**S**Fill a valved 5-mL gas-tight syringe with the compound. Lower the needle to approximately 5 mm above the meniscus. Slowly introduce the compound above the surface of the meniscus. The gas will dissolve in the solvent. Repeat if necessary to reach desired concentration.

7.3.4 Fill the flask to volume, stopper, then mix by inverting several times. Calculate the concentration in milligrams per milliliter (mg/mL, equivalent to micrograms per microliter [µg/µL]) from the weight gain.

7.3.5 Transfer the stock solution to a PTFE-sealed screw-cap bottle. Store, with minimal headspace, in the dark at approximately 4 °C. Do not freeze.

7.3.6 Replace standards after one month, or sooner if comparison with check standards indicate a change in concentration. Quality control check standards that can be used to determine the accuracy of calibration standards may be available from the National Institute of Standards and Technology, Gaithersburg, MD.

7.4 Secondary standardsSUsing standard solutions (Section 7.3), prepare a secondary standard to contain each pollutant at a concentration of 100 mg/L or 500 mg/L for compounds with higher MLs. Where necessary, a concentration of 1000 mg/L may be used.

7.4.1 Aqueous calibration standardsSUsing a syringe or a microsyringe, add sufficient secondary standard (Section 7.4) to five reagent water aliquots to produce concentrations in the range of interest.

7.4.2 Aqueous performance standardSAn aqueous standard containing all pollutants and internal standard(s) is prepared daily, and analyzed each shift to demonstrate performance (Section 13). This standard shall contain concentrations of pollutants and internal standard(s), as appropriate, within a factor of 1 to 5 times the MLs of the pollutants listed in Table 1. It may be one of the aqueous calibration standards described in Section 7.4.1.

8.0 Sample Collection, Preservation, and Handling

8.1 Grab samples are collected in glass containers having a total volume greater than 20 mL. For aqueous samples that pour freely, fill sample bottles so that no air bubbles pass through the sample as the bottle is filled and seal each bottle so that no air bubbles are entrapped. Maintain the hermetic seal on the sample bottle until time of analysis.

8.2 Maintain samples at 4 °C from the time of collection until analysis. Do not freeze. If an aqueous sample contains residual chlorine, add sodium thiosulfate preservative (10 mg/40 mL) to the empty sample bottles just prior to shipment to the sample site. EPA Methods 330.4 and 330.5 may be used for measurement of residual chlorine (Reference 5). If preservative has been added, shake the bottle vigorously for 1 minute immediately after filling.

8.3 For aqueous samples, experimental evidence indicates that some PMI analytes are susceptible to rapid biological degradation under certain environmental conditions. Refrigeration alone may not be adequate to preserve these compounds in wastewaters for more than seven days. For this reason, a separate sample should be collected, acidified, and analyzed when compounds susceptible to rapid biological degradation are to be determined. Collect about 500 mL of sample in a clean container. Adjust the pH of the sample to about 2 by adding hydrochloric acid (1:1) while stirring. Check pH with narrow range (1.4 to 2.8) pH paper. Fill a sample bottle as described in Section 8.1. If residual chlorine is present, add sodium thiosulfate to a separate sample bottle and fill as in Section 8.1.

8.4 All samples shall be analyzed within 14 days of collection.

9.0 Quality Assurance/Quality Control

9.1 Each laboratory that uses this method is required to operate a formal quality assurance program (Reference 6). The minimum requirements of this program consist of an initial demonstration of laboratory capability (Section 9.5) and analysis of standards (Sections 9.6 and 13) and blanks (Section 9.4) as tests of continued performance. Each time a batch of samples is analyzed or there is a change in reagents or procedures, a method blank must be analyzed as a safeguard against contamination.

9.2 In recognition of advances that are occurring in analytical technology, and to allow the analyst to overcome sample matrix interferences, the analyst is permitted certain options to improve separations or lower the costs of measurements. These options include alternative concentration and cleanup procedures, and changes in columns and detectors. Alternative techniques, such as the substitution of spectroscopy or immunoassay, and changes that degrade method performance are not allowed. If an analytical technique other than the techniques specified in this method is used, that technique must have a specificity equal to or better than the specificity of the techniques in this method for the analytes of interest.

9.2.1 If the detection limit of the method will be affected by the change, the laboratory is required to demonstrate that the method detection limit (MDL; 40 CFR 136, Appendix B) is lower than one-third the regulatory compliance level. If calibration will be affected by the change, the analyst must recalibrate the instrument per Section 10.

9.2.2 The laboratory is required to maintain records of modifications made to this method. These records include the information in this subsection, at a minimum.

9.2.2.1 The names, titles, addresses, and telephone numbers of the analyst(s) who performed the analyses and modification, and of the quality control officer who witnessed and will verify the analyses and modification.

9.2.2.2 A listing of pollutant(s) measured, by name and CAS Registry Number.

9.2.2.3 A narrative stating the reason(s) for the modification.

9.2.2.4 Results from all quality control (QC) tests comparing the modified method to this method including:

(a) calibration (Section 10);
(b) calibration verification (Section 13);
(c) initial precision and accuracy (Section 9.5);
(d) analysis of blanks (Section 9.4); and
(e) accuracy assessment (Section 9.6 and 13).

9.2.2.5 Data that will allow an independent reviewer to validate each determination by tracing the instrument output (peak height, area, or other signal) to the final result. These data are to include:

(a) sample numbers and other identifiers;
(b) analysis dates and times;
(c) injection logs;
(d) analysis sequence/run chronology;
(e) sample weight or volume;
(f) sample volume prior to each cleanup step, if applicable;
(g) sample volume after each cleanup step, if applicable;
(h) final sample volume prior to injection;
(I) injection volume;
(j) dilution data, differentiating between dilution of a sample or an extract;
(k) instrument and operating conditions;
(l) column (dimensions, liquid phase, solid support, film thickness, etc.);
(m) operating conditions (temperature, temperature program, flow rates, etc.);
(n) detector (type, operating condition, etc.);
(o) chromatograms, printer tapes, and other recording of raw data; and
(p) quantitation reports, data system outputs, and other data necessary to link raw data to the results reported.

9.3 With each sample batch, a matrix spike (MS) and matrix spike duplicate (MSD) are analyzed to assess precision and accuracy of the analysis. The relative percent difference (RPD) between the MS and MSD shall be less than 30% and compound recoveries shall fall within the limits specified in Table 3. If the recovery of any compound falls outside its warning limit, method performance is unacceptable for that compound in that sample and the results may not be reported for regulatory compliance purposes.

9.4 Analyses of blanks are required to demonstrate freedom from contamination and that the compounds of interest and interfering compounds have not been carried over from a previous analysis (Section 4.3).

9.4.1 With each sample batch (samples analyzed on the same 12-hour shift), a blank shall be analyzed immediately after analysis of the aqueous performance standard (Sections 9.6 and 13) to demonstrate freedom from contamination. If any of the compounds of interest or any potentially interfering compound is found in a blank at greater than the ML (assuming a response factor of 1 relative to the nearest-eluted internal standard for compounds not listed in Table 1), analysis of samples is halted until the source of contamination is eliminated and a blank shows no evidence of contamination at this level.

9.5 Initial precision and recovery—To establish the ability to generate acceptable precision and accuracy, the analyst shall perform the following operations for compounds to be calibrated.

9.5.1 Analyze two sets of four 5-mL aliquots (eight aliquots total) of the aqueous performance standard (Section 7.4.2) containing the PMI analytes listed in Table 1.

9.5.2 Using the first set of four analyses, compute the average recovery (X) in percent of spike level and standard deviation of the recovery (s) in percent of spike level, for each compound.

9.5.3 For each compound, compare s and X with the corresponding limits for initial precision and accuracy found in Table 3. If s and X for all compounds meet the acceptance criteria, system performance is acceptable and analysis of blanks and samples may begin. If, however, any individual s exceeds the precision limit or any individual X falls outside the range for accuracy, system performance is unacceptable for that compound.

9.5.4 Using the results of the second set of analyses, compute s and X for only those compounds that failed the test of the first set of four analyses (Section 9.5.3). If these compounds now pass, the system performance is acceptable for all compounds, and analysis of blanks and samples may begin. If, however, any of the same compounds fail again, the analysis system is not performing properly for the compound(s) in question. In this event, correct the problem and repeat the entire test (Section 9.5).

9.6 The laboratory shall, on an ongoing basis, demonstrate through the analysis of the aqueous performance standard (Section 7.4.2) that the analysis system is in control. This procedure is described in Section 13.

9.7 Where available, field replicates may be used to validate the precision of the sampling technique.

9.8 The laboratory shall maintain records to define the quality of data that is generated.

10.0 Calibration

10.1 Inject standards into the GC and adjust the sensitivity to detect an amount of each compound less than or equal to one-third of the ML listed in Table 2 for the analyte.

10.2 Internal standard calibration procedure. The analyst must select one or more internal standards that are similar in analytical behavior to the compounds of interest. The analyst must further demonstrate that the measurement of the internal standard(s) is not affected by method or matrix interferences. Because of these limitations, no internal standard that would be applicable to all samples can be required in the method. The method was developed using tetrahydrofuran (THF) as an internal standard. Where THF is not present in the sample matrix and no interference precludes its use, THF is to be used as an internal standard for application of this method. If interferences preclude use of THF and other internal standards, external standard calibration may be used.

10.2.1 Prepare aqueous calibration standards at a minimum of five concentration levels for each analyte by carefully adding an appropriate amount of secondary standard to reagent water or to the matrix under study. One of the concentrations should be at or below the ML. The concentration range should bracket the concentrations expected in the samples and should not exceed the dynamic range of the GC/FID instrument. These aqueous standards must be prepared daily.

10.2.2 Prepare a spiking solution containing the internal standard(s) using the procedures described in Sections 7.3 and 7.4 and add an appropriate amount of internal standard to each aqueous calibration standard.

10.2.3 Using injections appropriate to optimize system sensitivity and separation of the analytes, analyze each calibration standard and tabulate peak height or area responses against concentration for each compound and internal standard. Calculate response factors (RF) for each compound as follows:

$$RF = \frac{A_s \times C_{is}}{A_{is} \times C_s}$$

where:
A_s = *Response for the analyte to be measured*
A_{is} = *Response for the nearest eluting internal standard*
C_{is} = *Concentration of the nearest eluting internal standard*
C_s = *Concentration of the analyte to be measured*

If the RF value over the working range is a constant (less than 10% relative standard deviation), the RF can be assumed to be invariant and the average RF can be used for calculations. Alternatively, the results can be used to plot a calibration curve of relative response, A_s*C_{is}/A_{is}, against analyte concentration (C_s).

11.0 Sample Preparation

Samples containing less than 1% solids are analyzed directly as aqueous samples. Samples containing 1% solids or greater are analyzed after equilibration with reagent water containing internal standard(s).

11.1 Determination of percent solids.

11.1.1 Weigh 5-10 g of sample into a tared beaker.

11.1.2 Dry overnight (12 hours minimum) at 110±5°C, and cool in a desiccator.

11.1.3 Determine the percent solids as follows:

$$\% \text{ solids} = \frac{\text{weight of sample dry}}{\text{weight of sample wet}} \times 100$$

11.2 Remove standards and samples from cold storage and bring to 20-25 °C.

11.3 Samples containing less than 1% solids.

11.3.1 Allow solids to settle and remove 5 mL of sample.

11.3.2 Add an appropriate amount of internal standard spiking solution.

11.3.3 Inject a sample directly into the GC. The temperature of the injection block should be great enough to immediately vaporize the entire sample. An example of the separations achieved by the column listed is shown in Figure 1.

Note: Use of a 0.2-µL injection has been found to improve method sensitivity over a larger injection combined with a split sample. Where possible, splitless injection should be used. All requirements of this Method must be met regardless of type of injection used.

11.4 Samples containing 1% solids or greater.

11.4.1 Mix the sample thoroughly using a clean spatula and remove rocks, twigs, sticks, and other foreign matter.

11.4.2 Add 5±1 g of sample to a tared 10-mL centrifuge tube. Using a clean metal spatula, break up any lumps of sample. Record the sample weight to three significant figures.

11.4.3 Add an appropriate amount of internal standard spiking solution to the sample in the centrifuge tube.

11.4.4 Add a measured quantity (Y ± 0.1 mL) of reagent water to the tube so as to minimize head space.

11.4.5 Place a cap on the centrifuge tube leaving little or no headspace. Place the tube in the sonicator for a minimum of 5 minutes, turning occasionally. For most samples this should be sufficient time to distribute the analytes and standard(s) between the solid and aqueous phases and to establish equilibrium. Some sample matrices may require more sonication.

11.4.6 On completion of sonication, centrifuge the sample and inject the same amount of supernate into the GC that was injected for the calibration standards.

11.5 For liquid samples containing high-solids concentrations, such as sludges or muds, weigh approximately 5 g (to three significant figures) into a 10-mL centrifuge tube, add an appropriate amount of internal standard solution, sonicate, centrifuge, and inject as in Section 11.4.6.

12.0 Quantitative Determination

12.1 The calibration curve or averaged response factor determined during calibration is used to calculate the concentration. For calculation using the averaged RF, the equation below is used, and the terms are as defined in Section 10.2.3.

$$Concentration = \frac{A_s \times C_{is}}{A_{is} \times RF}$$

12.2 The concentration of the pollutant in the solid phase of the sample is computed using the concentration of the pollutant detected in the aqueous solution, as follows:

$$\text{Concentration in solid (mg/kg)} = \frac{\text{YL x aqueous conc (mg/L)}}{\text{sample wt (kg)}} \text{ x percent solids x DF}$$

where:
percent solids is from Section 11.1
Y = Volume of water in liters (L) from 11.4.4
DF = Dilution factor (as a decimal number), if necessary

12.3 Sample dilution—If the calibration range of the system is exceeded, the sample is diluted by successive factors of 10 until the sample concentration is within the calibration range.

12.4 Report results for all pollutants found in standards, blanks, and samples to three significant figures. For samples containing less than 1% solids, the units are milligrams per liter (mg/L); and for samples containing 1% solids or greater, units are milligrams per kilogram (mg/kg).

13.0 System Performance

13.1 At the beginning of each 12-hour shift during which analyses are performed, system calibration and performance shall be verified. Acceptance criteria for each compound (R) are found in Table 3. Adjustment and/or recalibration shall be performed until all performance criteria are met. Only after all performance criteria are met may blanks and samples be analyzed.

13.2 Where THF is used as the internal standard, the absolute retention time of THF shall be 416 seconds (± 30 seconds). The relative retention times of all pollutants shall fall within 10% of the value given in Table 2.

14.0 Method Performance

14.1 This method was developed and validated in a single laboratory.

14.2 A chromatogram of the aqueous performance standard is shown in Figure 1.

15.0 Pollution Prevention

15.1 Pollution prevention encompasses any technique that reduces or eliminates the quantity or toxicity of waste at the point of generation. Many opportunities for pollution prevention exist in laboratory operation. EPA has established a preferred hierarchy of environmental management techniques that places pollution prevention as the management option of first choice. Whenever feasible, laboratory personnel should use pollution prevention techniques to address their waste generation. When wastes cannot be reduced feasibly at the source, the Agency recommends recycling as the next best option.

The acids used in this Method should be reused as practicable by purifying by electrochemical techniques. The only other chemicals used in this Method are the neat materials used in preparing standards. These standards are used in extremely small amounts and pose little threat to the environment when managed properly. Standards should be prepared in volumes consistent with laboratory use to minimize the disposal of excess volumes of expired standards.

15.2 For information about pollution prevention that may be applied to laboratories and research institutions, consult *Less is Better: Laboratory Chemical Management for Waste Reduction*, available from the American Chemical Society's Department of Governmental Relations and Science Policy, 1155 16th Street NW, Washington DC 20036, 202/872–4477.

16.0 Waste Management

16.1 It is the laboratory's responsibility to comply with all Federal, State, and local regulations governing waste management, particularly the hazardous waste identification rules and land-disposal restrictions. In addition, it is the laboratory's responsibility to protect air, water, and land resources by minimizing and controlling all releases from fume hoods and bench operations. Also, compliance is required with any sewage discharge permits and regulations.

16.2 Samples containing acids at a pH of less than 2 are hazardous and must be neutralized before being poured down a drain or must be handled as hazardous waste.

16.3 For further information on waste management, consult *The Waste Management Manual for Laboratory Personnel* and *Less is Better: Laboratory Chemical Management for Waste Reduction*, both available from the American Chemical Society's Department of Government Relations and Science Policy, 1155 16th Street NW, Washington, DC 20036.

17.0 References

1. "Standard Test Method for Volatile Alcohols in Water by Direct Aqueous-Injection Gas Chromatography." 1994 Annual Book of ASTM Standards, Volume 11.02 (Water (II)). ASTM, 1916 Race Street, Philadelphia, PA 19103-1187.

2. "Working with Carcinogens," DHEW, PHS, NIOSH, Publication 77-206 (1977).

3. "OSHA Safety and Health Standards, General Industry," 29 CFR 1910, OSHA 2206 (1976).

4. "Safety in Academic Chemistry Laboratories," American Chemical Society Publication, Committee on Chemical Safety (1979).

5. "Methods 330.4 and 330.5 for Total Residual Chlorine," USEPA, EMSL Cincinnati, OH 45268.

6. "Method of Analytical Quality Control in Water and Wastewater Laboratories," USEPA, EMSL Cincinnati, OH 45268, EPA-4-79-019 (March, 1979).

7. Technical Report to PhRMA from Tichler & Kocurek by Malcolm Pirnie Laboratory, EPA Water Docket for Pharmaceutical Manufacturing Industry rule proposed May 2, 1995 (60 FR 21592), Document Control Number 8166 at Record Section 13.2.4. (February 13, 1997).

18.0 Tables

Table 1. Non-purgeable Water Soluble PMI Analytes to be Analyzed by Direct Aqueous Injection GC/FID and Internal Standard Techniques

PMI Analyte	CASRN[1]	EPA-EGD
Acetonitrile	75-05-8	972
Diethylamine	109-89-7	986
Dimethylamine	124-40-3	987
Dimethyl sulfoxide	67-68-5	1037
Ethanol	64-17-5	134
Ethylene glycol	107-21-1	1038
Formamide	75-12-7	988
Methanol	67-56-1	135
Methylamine	74-89-5	989
Methyl Cellosolve® (2-methoxyethanol)	109-86-4	1040
n-Propanol	71-23-8	955
Triethylamine	121-44-8	990

[1] Chemical Abstracts Service Registry Number

Table 2. Gas Chromatographic Retention Times and Minimum Levels for Non-purgeable Water Soluble PMI Analytes by Direct Aqueous Injection GC/FID

EGD No.	PMI Analyte	Retention Time			ML[1]
		Mean (sec)	EGD Ref	Relative	(mg/L)
989	Methylamine	128	975	0.307	50
135	Methanol	139	975	0.334	2[(2)]
987	Dimethylamine	165	975	0.396	50
134	Ethanol	188	975	0.452	2[(2)]
972	Acetonitrile	203	975	0.488	50
955	n-Propanol	307	975	0.737	50
986	Diethylamine	341	975	0.819	50
975	Tetrahydrofuran (int std)	416	975	1.000	
1040	Methyl Cellosolve®	429	975	1.030	20
988	Formamide	473	975	1.136	100
1038	Ethylene glycol	495	975	1.189	100
990	Triethylamine	518	975	1.244	50
1037	Dimethyl sulfoxide	676	975	1.624	20

[1] This is a minimum level at which the entire analytical system shall give an acceptable calibration point, taking into account method-specific sample and injection volumes. The concentration in the aqueous or solid phase is determined using the equations in Section 12.

[2] The minimum level for this analyte was developed from data provided in Reference 7.

Table 3. Acceptance Criteria for Performance Tests

EGD No.	PMI Analyte	Spike Level	Acceptance Criteria (% of Spike Level)		
			Initial Precision and Accuracy		On-going Accuracy
			s	X	R
972	Acetonitrile	50	30	70 - 146	70 - 148
986	Diethylamine	50	20	65 - 130	70 - 130
987	Dimethylamine	50	27	70 - 153	70 - 155
1037	Dimethyl sulfoxide	50	20	31 - 130	30 - 130
134	Ethanol	50	20	70 - 131	70 - 132
1038	Ethylene glycol	100	22	70 - 149	70 - 150
988	Formamide	200	20	70 - 130	70 - 130
135	Methanol	50	21	70 - 130	70 - 130
989	Methylamine	50	20	70 - 130	70 - 130
1040	Methyl Cellosolve®	50	20	64 - 130	64 - 130
955	n-Propanol	50	25	70 - 137	70 - 139
990	Triethylamine	50	47	70 - 165	68 - 168

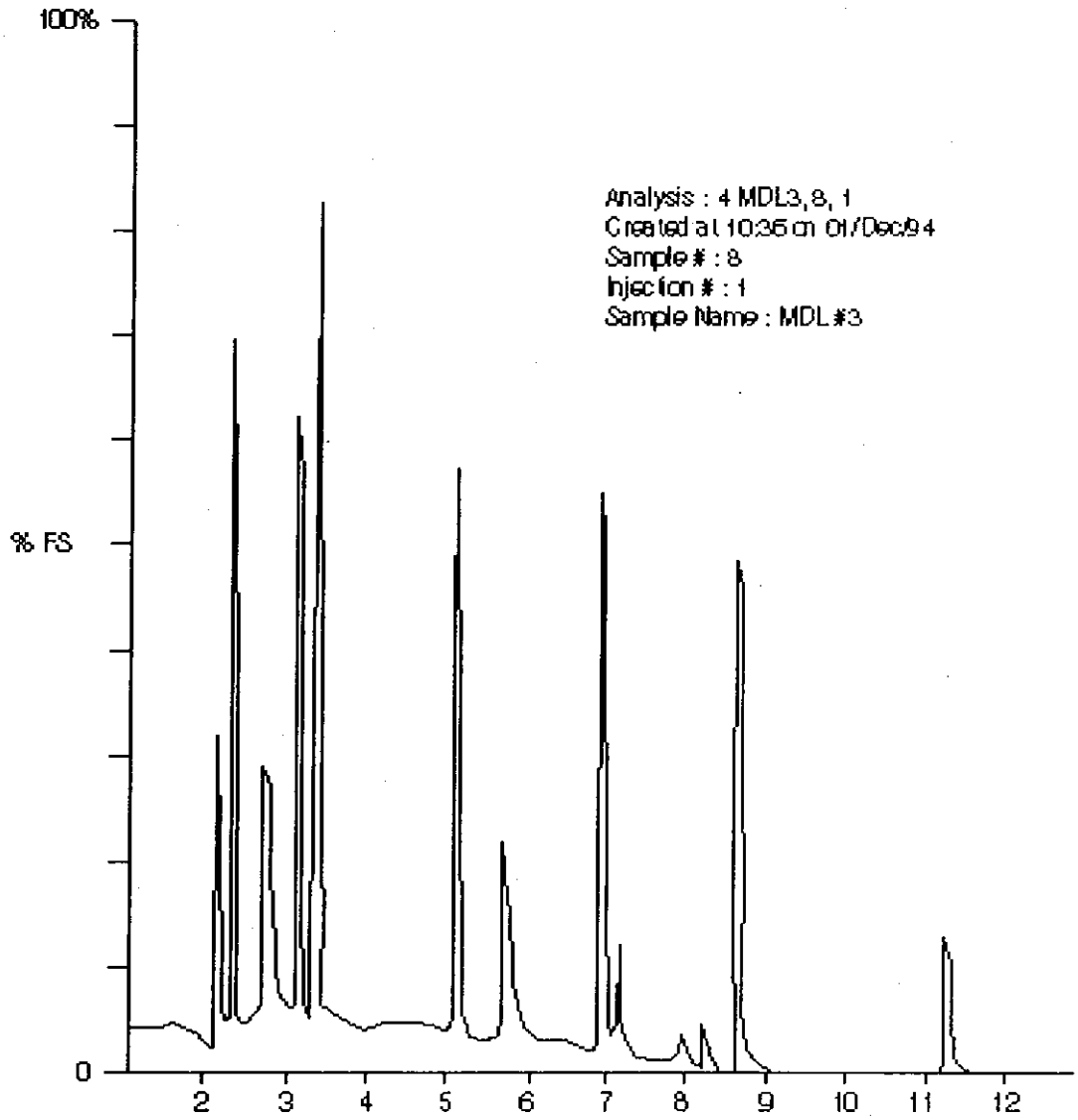


Figure 1. Chromatogram of Aqueous Performance Standard of Analytes from Table 1