SAMPLING AND ANALYTICAL METHODS

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OSHA Method Guideline 1, Sampling and Analytical Methods

Content

Introduction

This guideline provides a uniform and practical means for validating sampling and analytical methods for workplace exposure monitoring of hazardous chemicals by the Occupational Safety and Health Administration (OSHA). The overall goal is to provide OSHA with usable sampling and analytical methods that produce reliable results. It defines required laboratory tests and statistical calculations with acceptance criteria for determining sampling and analytical parameters. This guideline replaces previous method validation guidelines used by OSHA[1,2,3] and harmonizes validation tests, statistical calculations, terms, and definitions. This guideline also explains how OSHA will evaluate sources of both sampling and analytical uncertainty and report a combined uncertainty value for sampling and analysis using the approach outlined in the International Organization for Standardization (ISO) standard ISO 20581:2016.[4] Unique methods and procedures that do not fit within the framework of this guideline may also be developed to fulfill the needs of the agency using other appropriate tests and procedures.

Before approval and use, all validated methods will be reviewed by technically competent individuals, and found to demonstrate that a method is clearly written using standardized language, that terms and numerical data are correctly used and presented, that consideration for inclusion of method target analytes in a group that may use the same sampling media and conditions for simultaneous analysis has been made, and that the validation requirements of this guideline have been met. All traceability documentation and data associated with a method must be stored in a standardized format and made accessible during the process of development and review, and for future reference.

1 Preliminary Considerations

Review the literature, regulatory standards, and other appropriate sources of information to determine how and where the chemical substance to be sampled and analyzed is used in workplaces and how it is or may be regulated. Review existing or related sampling and analytical methods to identify the potential to add the chemical substance to an existing or prospective sampling group. Identify other common chemicals present in those workplaces that could cause sampling and analytical interferences.

Consider the relevant chemical and physical properties in determining appropriate sampling, sample preparation, and analytical techniques. If possible, incorporate sampling and analysis into a current OSHA sampling group method so that common samplers, reagents, and instrumentation can be used, or consider creation of a new sampling group as appropriate. For example, a non-polar analyte that can be collected on coconut shell charcoal for desorption with carbon disulfide, and that may be analyzed by gas chromatography with flame-ionization detection should be evaluated for inclusion into OSHA Method 5000.[5] For stand-alone methods, explore ways to use common instrumentation configurations aligned with other methods, and/or eliminate preparation steps as well as hazardous waste generation when this is compatible with acceptable quality and usefulness for enforcement sampling.

1.1 Target Concentration Selection

Determine the concentration of the chemical substance at which the validation will be performed. This value, referred to as the target concentration (T_C), may be an OSHA Permissible Exposure Limit (PEL), an American Conference of Governmental Industrial Hygienists (ACGIH)Threshold Limit Value (TLV), or some other occupational exposure limit (OEL). The method can be validated at more than one concentration if

the chemical substance has multiple exposure limits; for example, an 8-hour time weighted average (TWA), and one or more of the following: a ceiling, peak, short-term exposure limit (STEL), or action level. The equivalent analyte mass collected on a sampler at T_C with the proposed sampling volume (dependent on the sampling time and rate) is referred to as the target mass (T_M).

1.2 Sampling

1.2.1 Active Sampling

Active sampling methods determine the concentration of an airborne chemical substance by actively pumping air presumed to contain the substance into a vessel, or through a sampling medium, followed by prescribed quantitative analytical procedures.

Use an appropriately designed sampling medium, such as a sorbent tube with separate front and back sections, or a cassette with adequate support for a filter, to allow the production of results with required quality and certainty. Consider how the analyte will interact with the sampling medium and any components such as sorbent separators, supports, and cassette walls. For aerosol sampling, select a sampler that will collect the appropriate size fraction (e.g., respirable) when this is required.

If possible, use a 4-hour sampling time for substances with an 8-hour TWA exposure limit. Select a flow rate that will provide sufficient time for the analyte to collect, react, or adsorb to the sampling medium. Flow rates between 50-200 mL/min for sorbent tubes, and 1-2 L/min for filters and OSHA Versatile Samplers (OVS), are recommended. Optimal sampling time and rate will depend on the lowest mass per sample reportable, defined as the limit of quantitation (LOQ) in Section 2.1, and the sampler capacity defined in Section 2.7. If the LOQ for a prepared sample would be ≥ one-tenth the T_M value, evaluate the use of a higher flow rate or longer sampling time. If sampler capacity is exceeded evaluate the use of a lower flow rate or shorter sampling time.

For substances that have a peak, ceiling, or other short-term exposure limit, optimize the sampling rate to collect sufficient analyte mass so that the LOQ is ≤ one-half the corresponding T_M value for the specific exposure limit when sampling for a period relevant to the short-term exposure limit.

At each proposed sampling rate, measure the pressure drop across the sampler and confirm a commercial sampling pump is available that can maintain a constant flow at the measured pressure drop with adequate flow rate precision and accuracy.

1.2.2 Surface Sampling

Surface sampling is used to determine possible exposure to hazards that may be absorbed through the skin or be ingested. A potentially contaminated surface is wiped with an appropriate sampling medium to collect a target analyte.

Assure the wipe medium is large enough to have the capacity to handle the required analyte mass expected within the area sampled, yet small enough to be practical for preparation in the laboratory. The sampling medium should allow sampling of a 10×10 cm area, and be durable enough to withstand the wiping procedure without tearing. Determine if the medium will need a wetting agent or if it can be used dry. If a wetting agent is used, verify it will not interfere with detection of the target analyte.

1.2.3 Bulk Sampling

Bulk sampling is not specifically addressed in this guideline. However, bulk sampling should be addressed when necessary, for example, if required by an expanded standard, or if needed as an appropriate reference material for performing supporting tests and analyses needed to correctly analyze samples collected in the field. When specifying special requirements related to shipment of a bulk material, assure the recommended shipping vessel is compatible chemically and physically, and is gas tight if the sampled material is expected to contain volatile components.

1.3 Sampler Testing Techniques

1.3.1 Test Atmosphere

The use of a dynamically generated controlled test atmosphere is preferred for evaluating sampling approaches when air contaminants are encountered in the gas phase. When safety concerns or other problems prevent the use of a dynamic test atmosphere generation system, consider the use of a static test atmosphere (e.g., target analyte injected into a gas-sampling bag). All test atmospheres generated must be non-condensing. Generate test atmospheres using either dry or humid air as specified in Section 2, Validation Tests. Generate humid test atmospheres with an absolute humidity of 15.7 ± 3.0 milligrams of water per liter of air, and dry test atmospheres with an absolute humidity of 3.92 ± 1.6 milligrams of water per liter of air. These water concentration values represent 80% and 20% relative humidity respectively at 22.2 °C. Perform sampling for testing using the proposed sampling time and sampling rate.

1.3.2 Direct Spiking

Use vapor spiking to test air samplers for air contaminants expected to be encountered in the vapor phase when test atmosphere generation is not possible. This involves injecting the analyte, or the analyte dissolved in a non-interfering solvent, directly onto a glass wool plug immediately upstream of a sampler. Air is then drawn through the plug and sampler using the proposed sampling time and rate to move analyte into the sampler. As a general rule, no more than 20 µL of solution should be used when vapor spiking.

pike analyte onto media when vapor spiking is not possible. This involves spiking onto the first media section intended to capture analyte that airflow encounters in an air sampler (e.g., the front section of a sorbent tube). When using this technique ensure the analyte is loaded only onto the front section of a sampler that contains more than one section. For samplers that contain a filter supported by a backup pad, or a filter placed in front of a sorbent bed, be sure to spike in such a way that the analyte is not immediately transferred to the support pad or sorbent bed. This can be done by removing a filter and placing it on a suitable support, such as the rim of a small beaker so that only the outside edge of the filter touches the support. Then carefully deliver liquid to about 5-10 small spots across the face of the filter. Once the delivery solvent has evaporated, the filter can be placed back into its sampler and have air drawn through it for testing where this is required.

Also use direct spiking to test wipe sample media that have been prepared using a proposed sampling technique (e.g., when media is to be moistened before use). Spike the analyte directly onto the wipe medium to test recovery, or onto a non-porous smooth surface such as a glass plate to test sampling efficiency and recovery, as specified in Section 2. The testing surface should be the same dimensions as the sampling area recommended in the method.

1.4 Internal Standard Selection

Where an internal standard may be used in an analytical process, identify an internal standard that can be used to correct for sample introduction, matrix interferences, instrument drift, and variable signal noise. Assure internal standards are compatible with the sampling medium, analytical technique, instrumentation, and are not typically found in the workplace.

1.5 Interference

The effect of water vapor on sampling and analysis must always be considered. Water vapor effects have been known to include altered sampler capacity, analytical recovery, and sampler storage stability. OSHA's experience is that water will usually have a detrimental effect on sampling and analysis, thus air sampler testing is mostly done using humid air; however, testing is also done using dry air as in some cases this has also been shown to be detrimental.

Besides the effect of water, test other potential sampling and analytical interferences as needed. Interferences can result in reduced sampler capacity, may react with an analyte or a derivatizing agent, or negatively impact instrument performance.

2 Validation Testing

Validation tests are presented in logical order; however, the order in which tests are completed is not important. All reference and calibration materials should be accredited to ISO 17034:2016[6] and traceable to National Institute of Standards and Technology (NIST) or equivalent national or international standards, where possible. Use reagents of acceptable purity (e.g., reagent grade or better). Ensure that supplier information (including lot numbers) for reagents, standards, and sampling media, and expiration dates are captured in the traceability system used to document method development activities. Evaluate and respect expiration dates for standards, reagents, and sampling media. Validation testing instrumentation must be properly maintained and must be verified to be performing properly. Optimize analytical parameters so that analyses may be completed at all required validation levels. Record all needed details regarding instrument performance and maintenance status, traceability, and testing details to allow evaluation and re-creation of all tests completed. Ensure that all relevant testing is documented, whether successful or not, to leave a data trail that may be important for future method development work. Compliance with these traceability and documentation requirements will result in a digitized data packet for validation work. Complete all final validation tests of record using the sampling and analytical conditions described in the final method.

2.1 Limits of Detection and Quantitation

Determine the limit of detection (LOD) and limit of quantitation (LOQ) for each sample collection medium using the following procedure:

1. Estimate the background response from analysis of a sample medium blank.

2. Directly spike three separate samples at each of five evenly spaced levels, for a total of fifteen spiked media samples, with the highest spiking level producing an instrument response about ten times the background response of the media blank, and the lowest spiking level producing a response about two times the background response.

3. Prepare the fifteen spiked samples for analysis, along with three media blanks, and analyze in a random order.

4. Plot instrument response versus calculated mass per sample and determine the slope (m) from an ordinary least-squares (OLS) linear regression line equation.

5. Calculate the standard error of estimate for the OLS line equation using Equation 1:

$$S_{y/x} = \sqrt{\frac{\sum(y_i - \hat{y})^2}{n - k}} \quad (1)$$

where $S_{y/x}$ is the standard error of estimate; y_i is the observed instrument response; $\hat{y}$ is the calculated response from the line equation; n is the number of samples and blanks (eighteen); and k is 2 for linear regression.

6. Calculate the LOD using Equation 2:

$$\text{LOD} = \frac{3.3 \times S_{y/x}}{m} \quad (2)$$

where LOD is the limit of detection in terms of mass per sample; $S_{y/x}$ is the standard error of estimate; and m is the slope of the OLS line. Equation 2 assumes that the probability of a false positive and of a false negative detection occurrence are both 5%, each sample will be analyzed once, and results are not blank corrected.[7-11]

7. Calculate the LOQ using Equation 3:

$$\text{LOQ} = \frac{10 \times S_{y/x}}{m} \quad (3)$$

where LOQ is the limit of quantitation in terms of mass per sample and is set to approximately 3 times the LOD; $S_{y/x}$ is the standard error of estimate; and m is the slope of the OLS line.

2.2 Analytical Calibration

Determine the analytical calibration procedure using the following procedure:

1. Establish a reporting limit (RL) value by selecting a mass that is ≥ LOQ and ≤ 0.1× the T_M value. If the LOQ is greater than one-tenth the T_M value, select the LOQ as the RL value.

2. Prepare three separate analytical standards at ten evenly spaced levels, for a total of thirty standards, covering the RL to at least 2.2× the T_M value.

3. Analyze each of the thirty standards in a random order.

4. Plot instrument response versus mass per sample as an OLS regression. Then, calculate the residuals and plot residuals versus mass per sample. Visually examine both the OLS regression and residual plots to assess the quality of the regression model and fit. [12,13,14]

5. Perform a Shapiro–Wilk test, at the 95% confidence level, to assess normality of the residuals.[15] If the test leads to rejection of the null hypothesis that residuals are normally distributed (i.e., *p*-value < 0.05), examine the use of a weighted least-squares (WLS) fitting technique[16] (e.g., x^{-1} weighting factor), or transform[17] the data and return to Step 4.

6. Perform a Levene test, using means at the 95% confidence level, to assess the equality of variances of the residuals.[18] If the test leads to rejection of the null hypothesis that variances are equal (i.e., *p*-value < 0.05), examine the use of a WLS fitting technique or transform the data and return to Step 4.

7. Perform a lack-of-fit test, at the 95% confidence level, to assess the appropriateness of the model and fit (e.g., WLS linear regression using a weighting factor of x^{-1}).[12,19] If the test leads to rejection of the null hypothesis that the data fit the model (i.e., *p*-value < 0.05), examine the use of a polynomial model (e.g., quadratic, cubic) and return to Step 4.

8. After determining the regression model and fitting technique, establish the analytical calibration procedure to be used in the method validation test and presented in the method. For example, "analytical calibration will be performed with five equally spaced standards, over the range of the RL to 2.2× the T_M value using WLS linear regression with a weighting factor of x^{-1}."

9. Prepare six spiked media samples at the RL and analyze using the proposed analytical calibration procedure. Calculate percent recovery for each sample, correcting for the analytical recovery value determined in Section 2.3, and the mean recovery. If the mean recovery of the spiked samples is not within ±25% of the calculated value, adjust the regression model, fitting technique, or RL of the proposed analytical calibration procedure and complete this test again.

2.3 Analytical Recovery

Determine analytical recovery for each type of sample collection medium/analyte tested using the following procedure:

1. Directly spike six samples at each of five mass loading levels (i.e., 0.1, 0.5, 1.0, 1.5, and 2.0× the T_M value) for a total of thirty spiked media samples. The 0.1× T_M value is not needed for peak, ceiling, or other short-term exposure limits. For an OEL that may include multiple compounds, such as for lead, perform analytical recovery tests using a reasonable subset of the possible compound types (e.g., one soluble and two or three insoluble compounds that may be reasonably expected to be found in the workplace).

2. Set the spiked samples aside for one hour to assure complete analyte sorption.

3. Prepare four control standard replicates, without media, corresponding to each equivalent concentration that would be obtained from processing samples with no preparation loss at the same levels as in paragraph 1, for a total of twenty standards if five mass loading values are used. Use the same equipment (e.g., syringe), technique, reagents, working standards, and spiking volumes to prepare the control standards as used to prepare the directly spiked samples.

4. Prepare the spiked samples for analysis. Analyze control standards and samples at each level, grouping each level together and evenly spacing the samples between the corresponding control standards.

5. Calculate percent recovery for each sample using Equation 4:

$$R_i = \frac{I_s}{\bar{I}_{std}} \times 100 \quad (4)$$

where R_i is the recovery of an individual spiked sample, in percent; I_s is the instrument response for the spiked sample; and $\bar{I}_{std}$ is the mean response signal of the four control standards at the equivalent level.

6. Calculate the mean recovery and variance for each of the five levels tested.

7. Apply a Dixon *Q* test for possible mean recovery outlier values, and a Cochran *C* test for within-level variance outlier values across the five levels tested (both at the 95% confidence level).[20] A mean recovery outlier, or a difference in variance between levels, is usually an indicator of a poor analytical practice, such as using a 50-µL syringe to spike 1.00 µL of analyte.

8. Calculate the analytical recovery (R_A) as the mean of the 30 individual sample recoveries. The R_A must be within 75 to 125%; however, a value between 95% and 105% is preferred, and the mean recovery of each level should be within ±5% of the R_A value.

9. Apply a two-tailed Student's *t*-test at the 95% confidence level to determine if the bias of the analytical recovery is significant compared to the reference value of 100%. If bias is significant, sample results should be corrected, or include the bias as an uncertainty component of analytical recovery.

2.4 Stability of Prepared Samples

Determine the stability of prepared samples for each type of sample collection media tested using the following procedure:

1. Directly spike six samples at the T_M value. Set the resulting spiked media samples aside for one hour to assure complete analyte sorption. (Note: The 1.0× T_M value samples prepared for Section 2.3, can be used for this stability determination.)

2. Prepare four control standards, without media, corresponding to the equivalent concentration that would be obtained from processing samples loaded at the T_M value with no preparation loss. Use

the same equipment (e.g., syringe), technique, reagents, working standards, and spiking volumes to prepare the control standards as used to prepare the spiked samples.

3. Prepare the spiked samples for analysis and immediately analyze. Analyze control standards and samples, evenly spacing the samples between the corresponding control standards.

4. Reanalyze the same prepared samples again approximately one, two, and three days after the initial analysis using four freshly prepared control standards for each analysis.

5. Calculate the recovery of each spiked sample using Equation 4. Plot percent recovery versus days of storage and obtain an OLS linear regression line equation. Stability of prepared samples (Δ_{ps}) is calculated as the absolute difference between the final and initial test day recoveries calculated using the line equation. If recovery changes by more than 5%, provide appropriate directions for timely analysis in the method (e.g., could include requirements to perform analysis within 24 hours, change storage conditions, or recap).

2.5 Post Sampling Storage

Determine the post sampling storage limitations for each type of sample collection medium/analyte combination tested using the following procedure:

1. Collect eighteen air samples at the T_C from a humid test atmosphere at the recommended sampling time and with the recommended sampling rate, or for analytes where test atmosphere generation is not possible, spike samples at the T_M value followed by drawing humid air through the samplers for the recommended sampling time at the recommended sampling rate. For wipe samples, prepare eighteen samples by spiking the analyte onto the sampling medium as it is to be used in the field (e.g., moistened).

2. Prepare and analyze three samples on the day of preparation (Day 0) using the analytical calibration procedure determined in paragraph 8 of Section 2.2.

3. Store the remaining fifteen samples on a bench-top at room temperature.

4. Prepare and analyze three samples every third or fourth day, using freshly prepared calibration standards, so that the duration of the entire storage test is about eighteen days.

5. Calculate the recovery for each sample, but do not correct sample results for analytical recovery using the mean recovery value determined in Section 2.3. Plot percent recovery versus days of storage and obtain an OLS linear regression line equation. Calculate the final and initial test day recoveries using the line equation, then calculate post sampling storage stability (Δ_{ss}) as the absolute difference between the final and initial test day recoveries using the OLS line equation to obtain these. Recovery after eighteen days must be ≥75% and Δ_{ss} must be ≤10%.

6. Perform a refrigerated post sampling storage stability test if recovery from room temperature storage is ≤75% or Δ_{ss} is >10%. Freezer storage can also be tested if necessary.

2.6 Method Precision and Bias

Determine method precision and bias for each type of sample collection medium tested using the following procedure:

1. Collect six air samples at each of five levels (i.e., 0.1, 0.5, 1.0, 1.5, and 2.0× the T_C) from a humid test atmosphere using the recommended sampling time and sampling rate, or for analytes where test atmosphere generation is not possible, spike six samples at each of five levels (i.e., 0.1, 0.5, 1.0, 1.5, and 2.0× the T_M value) followed by drawing humid air through the samplers for the recommended sampling time at the recommended sampling rate. The 0.1× T_M can be excluded for peak, ceiling, or other short-term exposure limits.

   For wipe samples, collect six samples at each of five levels (i.e., 0.1, 0.5, 1.0, 1.5, and 2.0× the T_M value) by spiking the analyte onto a surface, and then wiping the surface with the sampling medium using the proposed wiping technique. Use a surface that is extremely smooth and non-porous such as a glass plate. A suggested technique is to draw a 10 cm × 10 cm square with a marker on a glass plate and then spike the analyte on the reverse side. The analyte need not be uniformly distributed within the confines of the test area. If the analyte is delivered onto the surface in solution, allow any solvent used to evaporate before proceeding. If the analyte is volatile proceed as rapidly as possible.

2. Prepare and analyze samples at each level as an independent application of the proposed method, including use of new calibration standards prepared using the analytical calibration procedure determined in paragraph 8 of Section 2.2.

3. Calculate percent recovery for each sample, correcting for analytical recovery using the mean recovery value determined in Section 2.3.

4. Calculate the mean recovery and variance for each of the five levels tested.

5. Apply a Dixon *Q* test for possible mean recovery outlier values, and a Cochran *C* test for within-level variance outliers across the five levels tested (both at the 95% confidence level).[20] A statistical difference in variance between levels, or a mean recovery outlier, should be investigated to determine if the cause is due to the testing procedure or method performance.

2.7 Sampler Capacity

Determine sampler capacity for each type of air sample collection medium/analyte combination tested using the following procedure:

1. Assemble three test systems with each consisting of two samplers connected in series. If a sampler contains a back section, it should be removed from the first sampler.

2. Sample at the recommended sampling rate through each system in parallel from a humid test atmosphere containing the analyte at 2.0× the T_C for 1.2× the proposed sampling time. Beginning at 50 to 80% of the recommended sampling time replace the second sampler in each of the three

sample test systems at short time intervals. The time intervals will vary with the sampling medium, analyte, and sampling time; however, intervals of 15-30 minutes are preferred. Shorter intervals will lead to more samples requiring analysis and the potential for recovery of insufficient mass for analysis but will also provide more precise data on breakthrough time at the specified flow rate. These factors should be considered, and some experimentation may be needed to empirically determine an optimized approach for this.

3. Prepare and analyze the resulting samples using the analytical calibration procedure determined in paragraph 8 of Section 2.2.

4. If analyte is not detected on the back samplers after 1.2× the proposed sampling time, report "capacity is not exceeded." If analyte is detected on the back samplers, determine if the cumulative analyte mass found on the second samplers is ≥5% of the mass that corresponds to that calculated to have been present in the sampling volume. The 5% breakthrough volume can be determined by plotting percent breakthrough versus sampled air volume, fitting the data with a curve, and using regression to determine the volume corresponding to 5% breakthrough. The recommended sampling time for a given sampling rate should be 80% of the calculated 5% breakthrough time determined by the 5% breakthrough volume at a constant sampling rate.

5. Repeat this test by sampling dry air if the absence of water is expected to decrease sampler capacity.

Sampler capacity can also be determined by monitoring the downstream effluent of a sampler with an instrument, such as a total hydrocarbon analyzer or infrared spectroscopy instrument, after the response to the upstream concentration has been established.

When it is not possible to use a dynamically generated controlled test atmosphere, determine sampler capacity for each type of sample collection medium/analyte combination tested using the following procedure:

1. Assemble three sampler test systems with two samplers connected in series and no back section (if applicable) in the front sampler, as described above.

2. Spike each test system with 2.0× the T_M value and then draw humid air through each for 1.2× the proposed sampling time at the recommend sampling rate.

3. Prepare and analyze samples using the analytical calibration procedure determined in paragraph 8 of Section 2.2.

4. Breakthrough will be determined to have occurred if the average mass found on the three back samplers is ≥5% of the total mass spiked.

2.8 Effect of Humidity

Determine the effect of humidity for each type of sample collection medium/analyte combination tested using the following procedure:

1. Using dry air, prepare six samples at 2.0× the T_C in the same manner used to prepare the method precision samples in Section 2.6.

2. Prepare and analyze samples using the analytical calibration procedure determined in paragraph 8 of Section 2.2.

3. Calculate the percent recovery for each sample, correcting for analytical recovery using the mean recovery value determined in Section 2.3, and the mean recovery value obtained for these test samples.

4. Calculate the effect of humidity (Δ_h) as the absolute difference between the mean dry recovery and the mean humid recovery taken from the 2.0× T_C method precision test described in Section 2.6. If Δ_h is >10%, modify the sampling or analytical procedure if possible and repeat the test.

2.9 Cassette Wall Wiping Removal Efficiency

When a cassette is used in sampling, determine the efficiency of a proposed cassette interior wall wiping removal technique using the following procedure:

1. Spike the interior wall of six sampler cassettes at the T_M value. The analyte need not be uniformly distributed within the cassette. If the analyte is delivered onto the cassette wall in solution, allow any solvent used to evaporate before proceeding. Also, if a solvent is used ensure that it does not react with the cassette material.

2. Wipe the interior of each cassette separately with an individual medium to be tested.

3. Prepare four control standards corresponding to the equivalent concentration that would be obtained from processing samples loaded at the T_M value with no preparation loss. Use the same equipment (e.g., syringe), technique, reagents, working standards, and spiking volumes to prepare the analytical standards as used to spike the cassettes.

4. Prepare the media used to wipe the spiked surfaces for analysis. Analyze the control standards and samples at each level, grouping each level together and evenly spacing the wipe samples between the control standards. Calculate the recovery of each spiked sample using Equation 4 and the mean recovery. Do not correct for analytical recovery using the mean recovery value determined in Section 2.3.

5. Calculate the cassette wall wiping removal efficiency (Δ_{cw}) as the absolute difference between the mean recovery of the 1.0× test for analytical recovery, using the mean recovery value determined in Section 2.3, and the mean cassette wall wiping recovery. If Δ_{cw} is >10%, determine if removal efficiency can be increased with the use of a second wipe. The Δ_{cw} value must be ≤25%.

2.10 Sampling and Analytical Interferents

Sampling and analytical interferents selected for testing should be based, in part, on interferents possibly present in workplaces similar to those in which the method may be used. For testing, set the suspected interferent concentration at an appropriate level, such as its PEL, TLV, or level anticipated to be found in the workplace

2.10.1 Sampling Interferents

Determine the effect of a suspected sampling interferent by using the following procedure:

1. Prepare six samples at 1.0× the T_C in the same manner as used to prepare the method precision samples described in Section 2.6 but include the potential interferent. For example, if a test atmosphere is used in Section 2.6, generate a test atmosphere containing both the analyte and potential interferent.

2. Prepare and analyze samples using the analytical calibration procedure determined in paragraph 8 of Section 2.2.

3. Calculate the recovery of each sample, correcting for analytical recovery using the mean recovery value determined in Section 2.3, and the mean recovery value obtained from these test samples.

4. Calculate the effect of the sampling interferent (Δ_{si}) as the absolute difference between the mean corrected recovery value for the interferent samples and the mean recovery taken from the 1.0× the T_C method precision test in Section 2.6. If Δ_{si} is >10%, modify the sampling or analytical procedure if possible and repeat the test.

2.10.2 Analytical Interferents

Determine the effect of a suspected analytical interferent by using the following procedure:

1. Spike twelve samples at 1.0× the T_C, six with analyte only and the other six with both the analyte and potential interferent.

2. Prepare and analyze samples using the analytical calibration procedure determined in paragraph 8 of Section 2.2.

3. Calculate the recovery for each sample, correcting for analytical recovery using the mean recovery value determined in Section 2.3. Calculate the mean corrected recovery of the six samples with potential interferent and the six without.

4. Calculate the effect of the potential analytical interferent (Δ_{ai}) as the absolute difference between the mean corrected recovery values for the samples with and without interferent. If Δ_{ai} is >10%, modify the sampling or analytical procedure if possible and repeat the test.

2.11 Analytical Reproducibility

Determine if the analytical procedure is reproducible using the following procedure:

1. Prepare six samples at 1.0× the T_C for each sample collection medium/analyte combination in the same manner used to prepare the method precision samples described in Section 2.6.

2. Submit the samples to the SLTC Production Chemistry Team for analysis along with a complete draft copy of the proposed method. The analyst assigned these sample will prepare and analyze them relying solely on the draft method for guidance. If possible, the analyst should use different analytical equipment and ancillary support equipment to prepare and analyze the samples than were used to gather method validation data. All sample results must fall within the calculated expanded uncertainty bounds determined in Section 3.3. If the bounds are exceeded, steps must be taken to determine and eliminate the cause (e.g., lack of clarity in the method instructions provided in the draft copy), followed by a repeat of the test.

2.12 Confirmation Analysis

When a non-orthogonal analytical technique is used, determine alternate analytical conditions to aid in confirming the identity or purity of the analyte (or relevant derivative). Mass spectrometry can often provide conclusive identification when combined with another method such as gas chromatography and should be considered first when possible. Peak response ratios and analysis with alternate detectors may also provide confirmation.

3 Estimation of Method Uncertainty

For each sampler/analyte combination and target concentration (T_C), calculate the relevant sampling and analytical uncertainty components as described below in Sections 3.1 and 3.2, and then calculate the combined standard uncertainty and expanded uncertainty as described in Section 3.3. For an analyte sampled as both a vapor and particulate, where each phase is collected on a separate sampling medium (e.g., filter preceding a sorbent tube), calculate combined standard uncertainties for each medium and then calculate a combined standard uncertainty for the sampling procedure.[21]

3.1 Sampling and Storage Uncertainty

3.1.1 Air Volume Sampled

3.1.1.1 Flow Rate Measurement

Calculate the uncertainty associated with the flow rate measurement of the flow meter, using Equation 5:

$$u_{fr} = \frac{CV_{fr}}{\sqrt{n}} \tag{5}$$

where u_{fr} is the percent relative standard uncertainty of the flow rate measurement, and CV_{fr} is the flow rate coefficient of variation (expressed as percent), of n flow measurements. Determine CV_{fr} from

reproducibility measurements using the flow meter with a representative sampler inline at the recommended flow rate. Take at least three measurements (n = 3).

3.1.1.2 Flow Rate Calibration

Calculate the uncertainty associated with the calibration of the flow meter, assuming a rectangular probability distribution, using Equation 6:

$$u_{fc} = \frac{\Delta_{fc}}{\sqrt{3}} \tag{6}$$

where u_{fc} is the percent relative standard uncertainty of the flow meter calibration, and Δ_{fc} is the manufacturer's reported tolerance specification expressed as a percent value.

3.1.1.3 Pump Flow Stability

Calculate the uncertainty associated with the flow stability of the sampling pump, assuming a rectangular probability distribution, using Equation 7:

$$u_{fs} = \frac{\Delta_{fs}}{\sqrt{3}} \tag{7}$$

where u_{fs} is the percent relative standard uncertainty of the sampling pump flow stability, and Δ_{fs} is the flow stability of the sampling pump expressed as percent, assuming the flow rate does not change by more than ±5% or ±3 mL/min, whichever is greater, during the sampling period.

3.1.1.4 Sampling Time

Calculate the uncertainty associated with sampling time, assuming a triangular probability distribution, using Equation 8:

$$u_{st} = \frac{(B_{st} \times t_{st}^{-1})}{\sqrt{6}} \times 100 \tag{8}$$

where u_{st} is the percent relative standard uncertainty of the sampling time, t_{st} is the sampling time in min, and B_{st} is the sum of maximum bias at the beginning and end of the sampling period (e.g., when sampling to nearest minute B_{st} = 0.5 min + 0.5 min = 1 min).

3.1.2 Sampling Efficiency

3.1.2.1 Gas and Vapor Sampling

The relative standard uncertainty associated with gas and vapor sampling efficiency (u_{se}) is negligible when sampling volume is limited to ensure sampler capacity is not exceeded as determined in Section 2.7.

3.1.2.2 Aerosol Sampling

Components associated with the relative standard uncertainty of aerosol sampling efficiency depend on the type of sampler and can include the following:

- deviation from the sampling convention (e.g., inhalable, respirable);
- variability between samplers;
- sampler test system calibration;
- sampled concentration.

These uncertainty components are described in ISO 21832:2020 and estimate values are provided.[22] Calculate the relative standard uncertainty for the sampling efficiency (u_{se}) by propagation of errors using the appropriate uncertainty components.

3.1.2.3 Wipe Sampling

Calculate the uncertainty associated with wipe sampling efficiency, assuming a rectangular probability distribution, using Equation 9:

$$u_{se} = \frac{55\%}{\sqrt{3}} \tag{9}$$

where u_{se} is the percent relative standard uncertainty of the sampling efficiency, and 55% is the calculated difference between 100% and 45%.[a]

3.1.3 Post Sampling Storage

Calculate the uncertainty associated with post-sampling storage stability, assuming a rectangular probability distribution, using Equation 10:

$$u_{ss} = \frac{\Delta_{ss}}{\sqrt{3}} \tag{10}$$

where u_{ss} is the percent relative standard uncertainty of post sampling storage, and Δ_{ss} is the storage loss or gain calculated in Section 2.5.

3.1.4 Sampling Interferent

Calculate the uncertainty associated with a sampling interferent, assuming a rectangular probability distribution, using Equation 11:

[a] It has been demonstrated that across a range of surface types a repeat wipe of a surface, on average, will remove 55% of the contaminant concentration of the initial wipe.[23] Assuming the ratio of 0.55 remains constant for further repeat wipes, the average amount of contaminant removed from the surface by the initial wipe can be determined using the equation for an infinite geometric series: $S = a_1/(1-r)$. Setting S to 1 as the total amount of contaminant on the surface, r to 0.55 as the common ratio between repeatwipes, and solving for a_1 as the amount of contaminant removed by the initial wipe gives 0.45 (45%).

$$u_{si} = \frac{\Delta_{si}}{\sqrt{3}} \quad (11)$$

Where u_{si} is the percent relative standard uncertainty of the effect of a sampling interferent, and Δ_{si} is the effect of a sampling interferent (expressed as percent) calculated in Section 2.10.1.

3.2 Analytical Uncertainty

3.2.1 Calibration Standards

Determine the uncertainty components associated with the concentration of the calibration standards. These components depend on how the calibration standards are made and can include the following:

- purity of the starting material (e.g., purity >99.0%);
- uncertainty associated with measuring the starting material (e.g., weighing, pipetting);
- uncertainty associated with diluting;
- laboratory temperature.

Calculate the relative standard uncertainty for the calibration standards (u_{cs}) by propagation of errors using the appropriate uncertainty components. Examples of the calculation of u_{cs} can be found in the Eurachem guide *Quantifying Uncertainty in Analytical Measurement*.[24]

3.2.2 Analytical Recovery

Calculate the uncertainty associated with sample results corrected for analytical recovery using Equation 12:

$$u_{ar} = \sqrt{\left(\frac{CV_{R_A}}{\sqrt{n}}\right)^2} \quad (12)$$

where u_{ar} is the percent relative standard uncertainty of the analytical recovery, CV_{R_A} is the coefficient of variation of the thirty analytical recovery samples analyzed per Section 2.3 (expressed as a percent value), n is thirty.

Calculate the uncertainty associated with sample results not corrected for analytical recovery using Equation 13:

$$u_{ar} = \sqrt{\left(\frac{B_{R_A}}{\sqrt{3}}\right)^2 + \left(\frac{CV_{R_A}}{\sqrt{n}}\right)^2} \quad (13)$$

where $B_{R_A}$is the absolute difference between the mean percent recovery of the thirty analytical recovery samples analyzed per Section 2.6, and the calculated 100% recovery value. If multiple compounds were tested (e.g., one soluble and two insoluble) calculate u_{ar} for each compound and use the largest u_{ar} value to calculate the combined standard uncertainty in Section 3.3.

3.2.3 Stability of Prepared Samples

Calculate the uncertainty associated with the stability of prepared samples, assuming a rectangular probability distribution, using Equation 14:

$$u_{ps} = \frac{\Delta_{ps}}{\sqrt{3}} \tag{14}$$

where u_{ps} is the percent relative standard uncertainty of the stability of prepared samples processed and maintained as required by the method, and Δ_{ps} is the storage loss or gain calculated in Section 2.4.

3.2.4 Method Precision

Calculate the uncertainty associated with method precision as described in Section C.6.2 of ISO/DIS 22065:2018[25], using Equation 15:

$$u_{mp} = \sqrt{(CV_m)^2 + \left(1 - \frac{1}{n}\right)\left(CV_{pl}\right)^2} \tag{15}$$

where u_{mp} is the percent relative standard uncertainty of method precision, CV_m is the coefficient of variation for the means of the five levels tested in Section 2.6 (expressed as percent), n is the number of replicate samples tested per level (six); CV_{pl} is the pooled coefficient of variation of the five levels tested in Section 2.6 (expressed as percent), calculated using Equation 16:

$$CV_{pl} = \sqrt{\frac{(CV_1)^2 + (CV_2)^2 + \cdots + (CV_5)^2}{5}} \tag{16}$$

where CV_1 through CV_5 are the coefficients of variation of the five levels tested expressed as percent values.

3.2.5 Method Bias

Calculate the uncertainty associated with method bias using Equation 17:

$$u_{mb} = \sqrt{\left(\frac{B_{mb}}{\sqrt{3}}\right)^2 + \left(\frac{CV_{mb}}{\sqrt{n}}\right)^2 + (u_{rc})^2} \tag{17}$$

where u_{mb} is the percent relative standard uncertainty of the method bias, B_{mb} is the absolute difference between the mean percent recovery of the thirty method precision samples analyzed per Section 2.6, and the calculated 100% recovery value; CV_{mb} is the percent coefficient of variation of the recovery of the thirty samples analyzed per Section 2.6, n is thirty, and u_{rc} is the percent relative standard uncertainty of the reference concentration sampled or mass spiked. For gas and vapor dynamic test atmosphere generation use an estimated u_{rc} value of 3% as suggested in ISO/DIS 22065:2018.[25]

3.2.6 Effect of Humidity

Calculate the uncertainty associated with humidity effect, assuming a rectangular probability distribution, using Equation 18:

$$u_h = \frac{\Delta_h}{\sqrt{3}} \tag{18}$$

where u_h is the percent relative standard uncertainty of the effect of humidity, and Δ_h is the effect of humidity difference calculated in Section 2.8, expressed as a percent value.

3.2.7 Cassette Wall Removal Efficiency

When a cassette is used in sampling, calculate the uncertainty associated with cassette wall wiping removal efficiency, assuming a rectangular probability distribution, using Equation 19:

$$u_{cw} = \frac{\Delta_{cw}}{\sqrt{3}} \tag{19}$$

where u_{cw} is the percent relative standard uncertainty of analyte removal from cassette walls, and Δ_{cw} is the percent cassette wall wiping removal efficiency calculated in Section 2.9, expressed as a percent value.

3.2.8 Analytical Interferent

Calculate the uncertainty associated with an analytical interferent, assuming a rectangular probability distribution, using Equation 20:

$$u_{ai} = \frac{\Delta_{ai}}{\sqrt{3}} \tag{20}$$

where u_{ai} is the percent relative standard uncertainty of the effect of an analytical interferent, and Δ_{ai} is the of an analytical interferent calculated in Section 2.10.2, expressed as a percent value.

3.2.9 Instrument Response Drift

Calculate the uncertainty associated with instrument response drift, assuming a rectangular probability distribution, using Equation 21:

$$u_{dr} = \frac{d_{max}}{\sqrt{3}} \tag{21}$$

where u_{dr} is the percent relative standard uncertainty of the instrument response drift, and d_{max} is the percent maximum allowed instrument response drift of a continuing calibration standard.

3.3 Combined Standard Uncertainty and Expanded Uncertainty

Calculate the sampling and storage uncertainty using Equation 22:

$$u_s = \sqrt{\sum_{i=1}^{n_s} (u_{s_i})^2} \tag{22}$$

where u_s is the percent relative standard sampling and storage uncertainty, u_{s_i} is the ith sampling uncertainty component expressed as percent calculated in Section 3.1, and n_s is the total number of relevant sampling uncertainty components addressed in Section 3.1.

Calculate the analytical uncertainty using Equation 23:

$$u_a = \sqrt{\sum_{i=1}^{n_a} (u_{a_i})^2} \tag{23}$$

where u_a is the percent relative standard analytical uncertainty, u_{a_i} is the ith sampling uncertainty component expressed as percent, calculated in Section 3.2, and n_a is the total number of relevant analytical uncertainty components calculated in Section 3.2.

Calculate the combined uncertainty using Equation 24:

$$u = \sqrt{(u_s)^2 + (u_a)^2} \tag{24}$$

where u is the combined percent relative standard uncertainty for sampling and analysis, u_s is the percent relative standard sampling uncertainty, and u_a is the percent relative standard analytical uncertainty.

Calculate the expanded uncertainty using Equation 25:

$$U = k \times u \tag{25}$$

where U is the percent expanded uncertainty of the sampling and analysis procedure, u is the combined percent relative standard uncertainty for sampling and analysis; and k is the coverage factor. For a two-sided 95% confidence interval use a coverage factor of 2.

4 Preparation of Written Method

Include the following sections in OSHA sampling and analytical methods:

- Cover Page
- Introduction
- Sampling Procedure

- Analytical Procedure
- Method Validation and Estimation of Measurement Uncertainty
- References

The following information will be included in the header of every page: version number, state, date, method number, and title. The cover page will include, CAS No., OSHA PEL, type(s) of PEL (e.g., “general industry,” “construction,” and/or “shipyard” as applicable), other appropriate OEL values, a brief description of the sampling and analytical procedure, recommended sampling time and rate, LOQ, RL, uncertainty, any special requirements (e.g., cold shipping), and author. A version number beginning with 1 will be assigned to new methods and incremented by 1 for any change. When a method is updated and approved, the new approval date will be in the header of the document and a description of the changes will be included in the Introduction. All methods with a reported combined uncertainty will be considered validated.

In the Introduction section, include relevant historical information regarding previous methods and procedures used or tested by OSHA, along with any informative information from the literature. In the Sampling Procedure and Analytical Procedure sections, describe the materials and procedures used for performing sampling and analysis. In the Validation section, describe the results from the validation tests performed and include a description of the testing procedures. For the Estimation of Measurement Uncertainty, list the sampling and analytical uncertainty component values. Include comments to ensure clarity on how values were determined, the combined uncertainty value, and the expanded uncertainty value with the coverage factor.

Present experimentally derived data with appropriate significant figures. Report percentages to one decimal place, unless the value is less than 1%, then report two or more decimal places as technically appropriate. Report LOQ, RL, combined uncertainty, and expanded uncertainty using two significant figures.

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