U.S. Department of Health & Human Services

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Elemental Analysis Manual

for Food and Related Products

The following is a section of the Elemental Analysis Manual for Food and Related Products.

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Elemental Analysis Manual

for Food and Related Products

3.6 Performance

Version 3.0 (December 2021)

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GLOSSARY and ACRONYMS

The discussions presented in this section were largely drawn from text in the EAM methods. As such, many of the details focus on specific applications. They are given, however, as examples to convey general analytical concepts that have universal significance for the various techniques. Analysts are encouraged to pull from this information to whatever extent is useful for method development research and analytical troubleshooting.

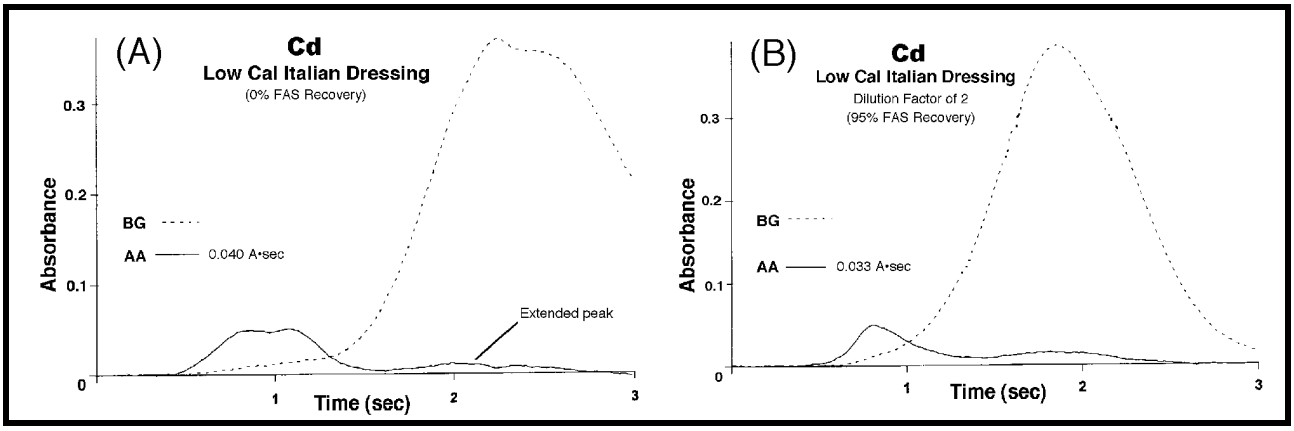
All instructions below are given for informational purposes and DO NOT SUPERSEDE any instructions given in methods - by equipment/instrument manufacturers or via a laboratory's standard operating procedures (QC, safety, program operations, etc.).

3.6.1. INSTRUMENT PERFORMANCE (GFAAS)

3.6.1.1. Interferences

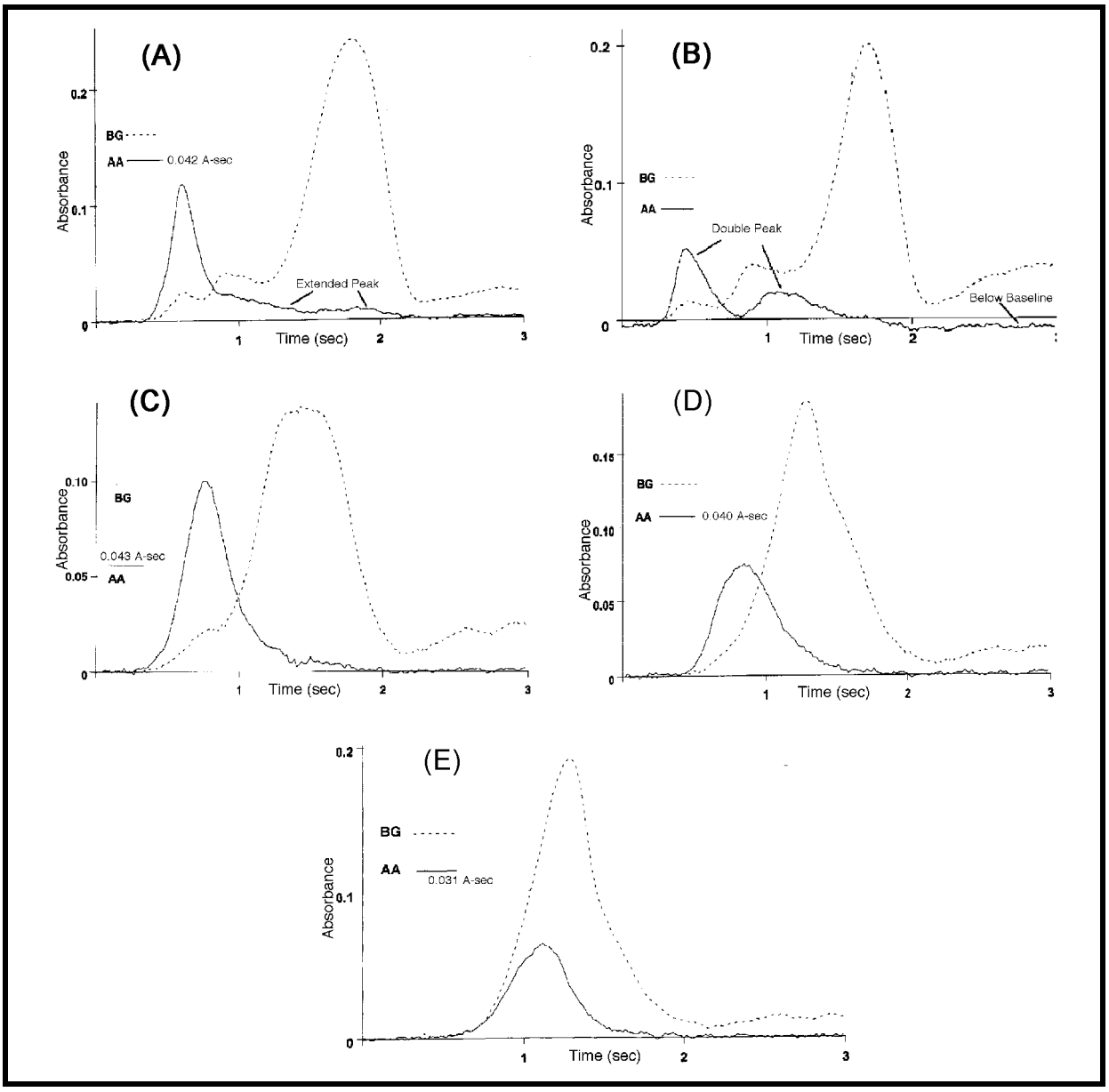
Graphite furnace atomic absorption spectrometry (GFAAS) interferences can be broadly characterized as memory, spectral, and matrix. In general, memory and spectral interferences tend to be of minor concern and relatively easy to manage whereas matrix interferences can be quite severe and challenging. Interferences are usually evidenced by poor recoveries (FAP and/or FAS) and distorted peak shapes

(3.6 Figures 1 and 2). If these occur, a matrix effect should be suspected. Regardless of the type of interference suspected, the usual practice is to dilute the analytical solution and re-analyze or use standard additions.



3.6 Figure 1. Matrix Interference with Salad Dressing: (A) Low FAS recovery, (B) Correction by diluting analytical solution. BG = Background Absorbance; AA = Atomic Absorbance.

- Memory effects typically occur when analytes are at high levels and not completely volatilized out of the graphite furnace leaving residues that cause follow up measurements to be biased high. The impact of this interference can be minimized by analyzing high analyte level samples in batches separate from those with low levels and by using a few-second clean-out step, which is especially important for high salt/mineral content foods.
- Spectral interference can result from absorption of light by an element or molecule that is not the analyte of interest or from production of light from black body radiation. Absorption by another element is rare because source lamp and absorption profile line widths are both narrow. Molecular species, however, can produce broadband absorption profiles that overlap the atomic line frequencies. The use of matrix modifiers, optimized furnace temperature programs, and Zeeman effect background correction serve to minimize this nonspecific absorption. Interference from black body emission from the hot graphite tube can be minimized by keeping atomization temperatures below that necessary to volatilize the analyte and maintaining proper furnace alignment.



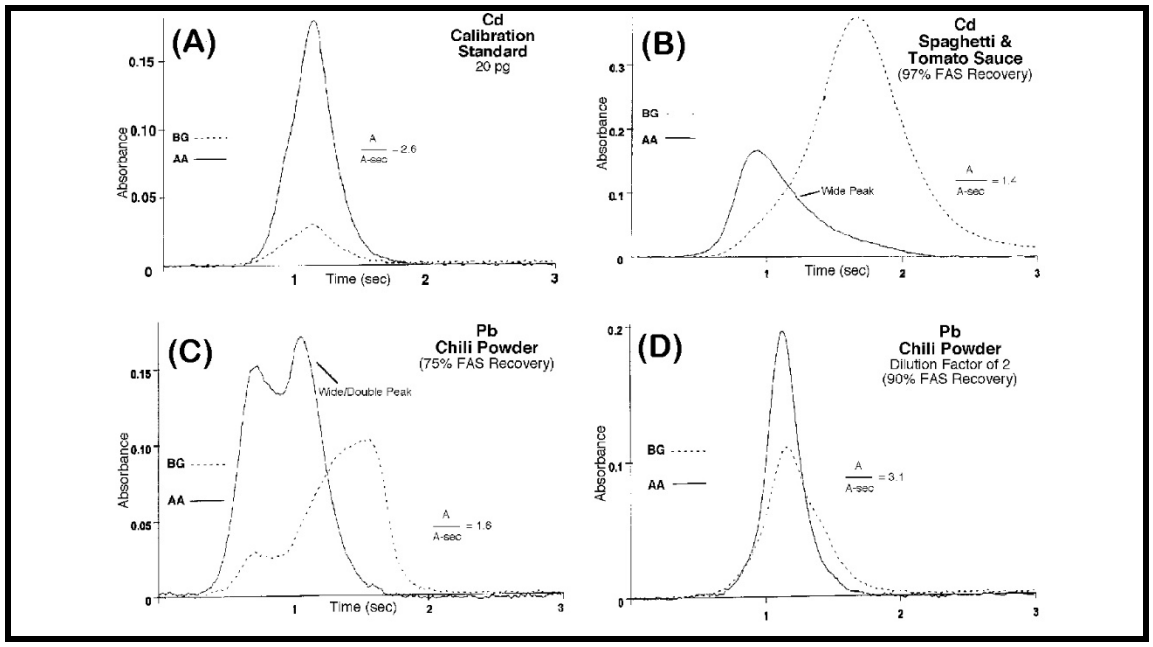
3.6 Figure 2. Dilution to Address Pb Matrix Interference (Irregular Peak Profile and Low RM & FAS Recoveries for NIST SRM Spinach SRM 1570 and 400 pg fortification): (A) DF=2, 42% RM Recovery, (B) DF 2, 0% FAS Recovery, (C) DF 3, 75% RM Recovery and 21% FAS Recovery, (D) DF 4, 102% RM Recovery and 97% FAS Recovery, (E) DF 5, 101% RM Recovery and 95% FAS Recovery. BG = Background Absorbance; AA = Atomic Absorbance.

- Matrix interference results when a sample's matrix components inhibit formation of free analyte atoms or contribute to pre-atomization volatilization of analyte during the furnace program's atomization step. This can be particularly challenging for high salt/mineral content foods such as salad dressings, pickles, cheese, processed meats, mustard, ketchup etc. Matrix interferences can be minimized by using platform atomization (instead of tube wall atomization), which provides a

more constant temperature environment that is conducive to the formation of free analyte atoms. The use of 5% hydrogen in the argon gas during the dry and char steps is also useful because it reduces interference from high levels of chloride [1].

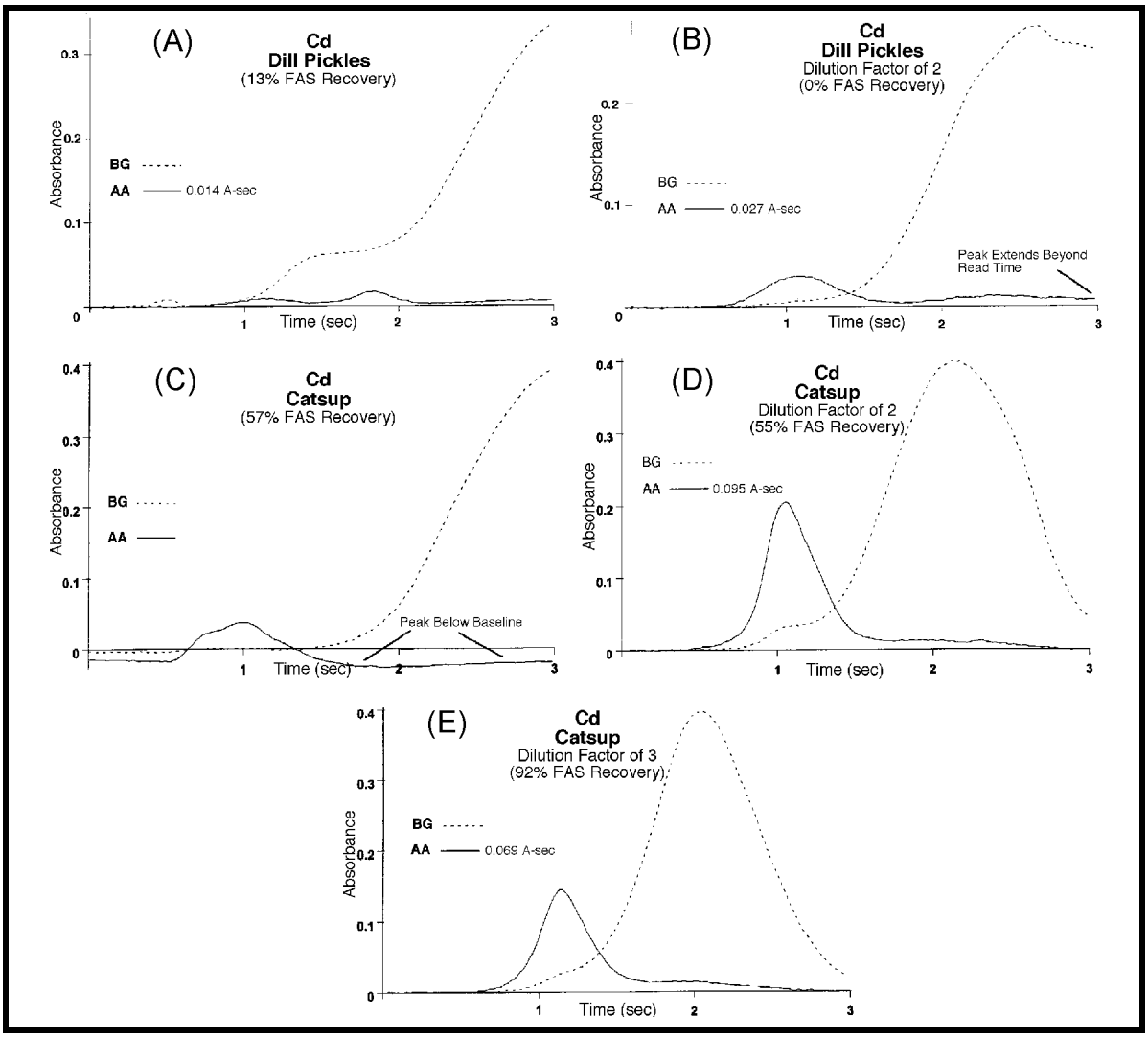
3.6.1.2. Peak Profile

Peak profile (shape of absorbance vs. time graph) is used to evaluate the quality of the analyte atomization. Peak to area ratios (H/A) are particularly useful for this. Spectra should therefore always be examined and compared with standard solution peaks to watch for irregular profiles (3.6 Figure 3A). Often, verification of no problematic irregularities can be accomplished simply via observation on an instrument display.



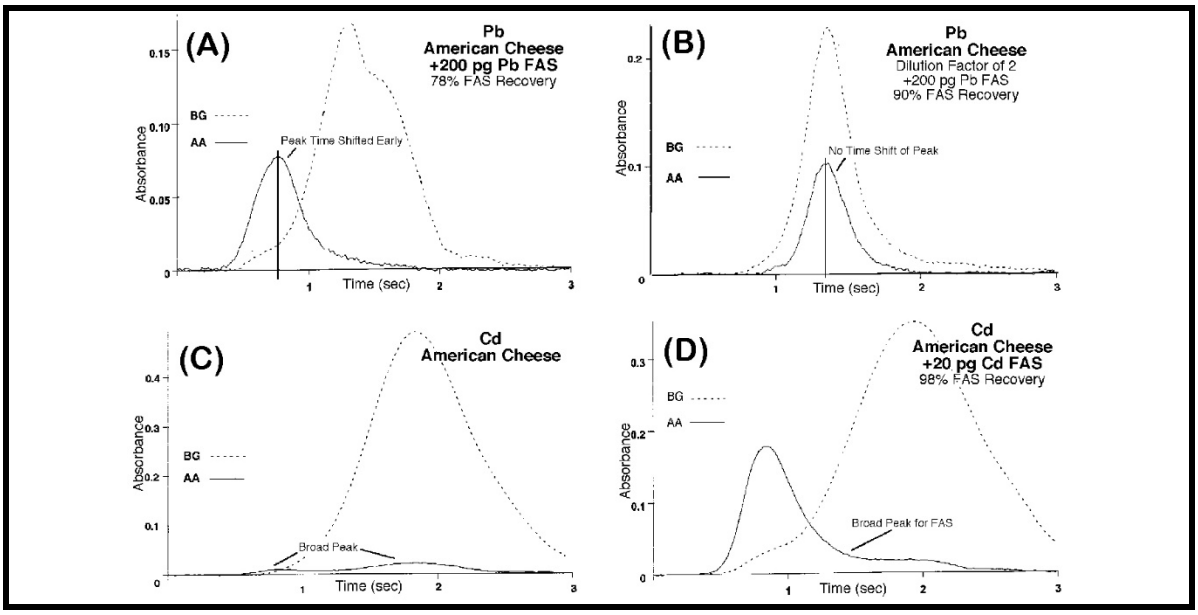
3.6 Figure 3. Peak Profiles (Matrix Interference - Wide Peaks): (A) Calibration standard, ideal profile, (B) Excessively wide peak, (C) Wide and doublet, low FAS Recovery, (D) Correction via dilution. BG = Background Absorbance; AA = Atomic Absorbance.

Standard solution profiles should be very close to the manufacturer's 'ideal peak' examples (for the particular setup of instrument, furnace, tube, and elements). Peak tails should return to the baseline before the end of the integration/read step (3.6 Figure 4A & B). Small amounts of peak broadening (e.g., H/A values in the 80-95% range relative to standard solutions) is, however, common and may indicate slow release of analytes that still remain in the tube. This can be accounted for by lengthening the read step (e.g., 3-4 sec instead of 2-3 sec). This adjustment is appropriate since furnace programs are usually optimized using a standard solution (no matrix effect).



3.6 Figure 4. Peak Profiles (Matrix Interference - Tail Extension and Pre-atomization Analyte Loss): (A) & (B) Peak tail does not return to baseline before end of integration/read step, (C) Pre-atomization loss indicated by absorbance less than zero at start and end of read step, (D) & (E) Correction of pre-atomization loss by dilution. BG = Background Absorbance; AA = Atomic Absorbance.

More serious irregularities are indicated for peaks that are excessively broadened (low H/A; 3.6 Figure 3B), occur in multiplets (3.6 Figure 2B & C), and/or have shifted peak appearance time (3.6 Figure 4A & B). American cheese, for example, usually exhibits low recoveries due to high levels of salt and/or minerals (*i.e.*, phosphate) which hinder rapid atomization of Cd and Pb. This results in low H/As (3.6 Figure 5C & D) which can be as much as 40-60% lower relative to standard solutions. A 0.8 g analytical portion of American cheese, for example, will typically have a 75% percent FAS Pb recovery. Correspondingly, the standard addition curve slope will be ~75% of the slope of a check solution that has a matrix of just nitric acid.



3.6 Figure 5. Peak Profiles (Matrix Interference - Salt/Mineral Causing Time Shifted Peaks): (A & B) Peak time shift and correction by dilution, (C) Broad peak due to high phosphate level, (D) Low FAS recovery due to high level(s) of mineral element(s). BG = Background Absorbance; AA = Atomic Absorbance.

Negative absorbances at the beginning of the read cycle and at the end where the peak's tail dips below the baseline (3.6 Figure 4C-E) can result from pre-atomization analyte loss during the char step (e.g., with high-salt foods) causing results to be biased low. This can occur even when using a matrix modifier and a conservative char temperature.

3.6.1.3. Instrument Setup

- Clean optical windows and replace if absorbance is >50% of manufacturer's specification for new windows.
- Inspect tube and platform (replace if necessary). A tube/platform will last between 200-800 firings depending on instrument manufacturer, atomization temperature, and sample type. Laboratory records will be useful for predicting when replacement will be needed. Replace if m_o has increased 10-15%, when peak profiles have degraded (longer tails, doubled peaks, wider peaks), or when laboratory records indicate tube is approaching the end of its performance lifetime (i.e., replace if performance is expected to degrade during an analytical run).
- Check optical alignment of furnace and alignment of autosampler tip.
- After≥30 minutes instrument warm-up, record lamp energy (should be ≥90% of expected).

3.6.1.4. Pre-standardization Checks

Analyze a standard solution that results in a 0.05–0.1 A-sec characteristic mass (m_o; EAM §3.2.1). Typically, instrument sensitivity (m_o) needs to be within 20% of the laboratory average (for the conditions used) and stability is ≤5% RSD (n ≥5 analyses).

3.6.1.5. Standardization Verification

Standardization should be verified initially then periodically during an analytical run and at its end.

- Analyze ICS and standard blank immediately following instrument standardization. Typically, ICS recovery must be 100 ± 5% of laboratory average and blank <ASDL.
- For continuing standardization verification (monitoring for instrumental drift), an ICS is usually analyzed at a 10% frequency (one out of every ten analyses) and at end of analytical run. Control limits are typically 100 ± 10%.

3.6.1.6. Analysis Checks

- Solution measurements are based on the mean of ≥2 injections (from the same autosampler cup).
- Typically (for absorbance ≥0.012 A-sec), precision must be ≤7% RSD or RPD and the standard curve correlation coefficient (r) ≥0.998 (≥0.995 for standard addition).
- All analysis solutions (including standard additions) must be within the LDR.
- Examine the peak profile (shape) of each analytical solution. The profiles of the standard solutions should be very close to the manufacturer's example of an ideal peak
- Use the blank to verify absence of carry-over of mercury(II) ion from previous solutions.
- Problems are usually associated with one or more of the solutions and evidenced in the standard curve (A-sec vs. concentration). New solutions and re-standardization will be needed.
- There are limitations to the amount of matrix effect correctable by standard addition.

3.6.2. INSTRUMENT PERFORMANCE (CV-GFAAS)

3.6.2.1. Interferences (Hg Example)

- Mercury contamination tends to be ubiquitous in reagents, laboratory supplies, and (as vapor) in a laboratory's air.
- All laboratory ware (containers, pipette tips, etc.) and reagents need to be checked, possibly cleaned using ultra-pure acid.
- Store laboratory ware and reagents in sealed secondary containment (to minimize absorption of mercury vapor). Ideally, this will be done as close in time as reasonably possible to the time of use.
- If stannous chloride reducing solution is used, it needs to be purged with argon to remove mercury contamination.
- Spectral interferences due to direct line overlap of other elements are rare in atomic absorption and are further minimized by the vapor generation step in which mercury, but not other elements, is reduced to atomic vapor.

3.6.2.2. Instrument Setup

- Warm-up as directed by manufacturer. Electronics and detector may require ≥3 hours for stability (absence of drift) and the Hg lamp may require ≥30 minutes.

- Inspect peristaltic pump tubing (replace if it has flat or worn spots).
- Start gas and liquid flows (ensure transfer through uptake tubing, gas-liquid separator, and drain tubing).
- Condition new tubing for 30-60 minutes (pump acid at a level equal to that used during analyses).
- Inspect peak profiles and calculate an initial instrument sensitivity and the RSD for replicates of a high concentration standard solution.
- Measure pump speed (revolutions/minute) and solution uptake rate (mL/minute, e.g., using a graduated cylinder and stopwatch).
- Compare all observations and values with historical findings to confirm they are consistent and acceptable for the method (adjust operating conditions if necessary).

3.6.2.3. Pre-standardization Checks

Analyze a middle-range standard solution and verify that instrument sensitivity (Â) is acceptable (e.g., within 20% of manufacturer specification). Stability should be ≤2% RSD (n ≥5 analyses).

3.6.2.4. Standardization verification

- Immediately after standardization, analyze the low and high concentration standard solutions and standard blank. Standard solution recoveries must be 95-105% and blank must be <ASDL.
- For continuing standardization verification (monitoring for instrumental drift), analyze an ICS (usually a middle-range standard solution) at a 10% frequency (i.e., one out of every ten analyses) and at end of analytical run. Control limits are typically 100 ± 10%.

3.6.2.5. Analysis Checks

- Measurements are usually based on the means of ≥2 injections (from the same autosampler cup).
- Absorbance precision (≥0.012 A-sec) will have a QC requirement such as ≤7% RSD (or RPD).
- The standard curve correlation coefficient (r) will have a QC requirement such as ≥0.998.
- All analysis solutions (including standard additions) must be within the LDR.
- Examine the peak profile (shape) of each analytical solution. The profiles of the standard solutions should be very close to the manufacturer's example of an ideal peak
- Use the blank to verify absence of analyte carry-over from previous solutions.
- Problems arising from problematic standard solutions will usually be evidenced in the standard curve.

3.6.3. INSTRUMENT PERFORMANCE (ICP-OES)

3.6.3.1. Interferences

- Interference effects must be evaluated for each instrument [2].

- Spectral interferences are caused by background emission from continuous or recombination phenomena, stray light from line emission of high concentration elements, overlap of a spectral line from another element, or unresolved overlap of molecular band spectra. Background emission is usually subtracted for most analytical emission lines.
- Spectral scans (wavelength verses intensity) in analyte wavelength region may indicate when alternate emission lines are desirable because of severe spectral interference. They will also show whether the most appropriate estimate of background emission is provided by an interpolation from measurements on one or both sides of the analyte peak. Locations selected for background intensity measurements will be determined by the complexity of spectrum adjacent to a wavelength peak. Locations used for routine measurement must be free of off-line spectral interference (inter-element or molecular) or adequately corrected to reflect the same change in background intensity as occurs at the wavelength peak.
- Spectral overlap may be avoided by using alternate wavelengths or can be compensated for by correcting for inter-element contributions, which involves measuring interfering elements. Extensive information on interferences at various wavelengths and resolutions is available in Boumans' Tables [3] and Winge's Atlas [4]. Users may apply inter-element correction factors determined on their instruments within tested concentration ranges to compensate (off-line or on-line) for effects of interfering elements. When inter-element corrections constitute a major portion of an emission signal, accuracy may be greatly reduced. For the element levels typically found in foods, spectral overlap is not likely [3, 4, 5] except for phosphorus, calcium, iron, zinc, aluminum and titanium. These elements should be included in the analyte list even if quantitative results are not needed so that inter-element corrections can be applied.
- Scan on either side adjacent to the analytical wavelength to determine appropriate location for off-line background correction and record apparent emission intensity from all other method analytes. On-line and off-line spectral interference effects must be determined and documented for all method analytes and corrections performed on all analyses. Tests to determine spectral interference must be done using analyte concentrations that will adequately describe interference. Expansion of the scan's scaling may be necessary to observe the interference or ascertain its absence. For most elements, 100 mg/kg single element solutions are sufficient although higher concentrations may be necessary for some mineral elements (e.g., calcium). Failure to correct for spectral interference can result in false positive or false negative results. Uncorrected interfering peaks occurring on or very close to the analyte peak can result in false-positives or positive bias. Uncorrected interfering peaks occurring on or very close to a background correction wavelength can cause negative bias or even negative results.
- Physical interferences are effects associated with sample nebulization and transport processes. Changes in viscosity and surface tension can cause significant inaccuracies, especially in analytical solutions containing high dissolved solids or high acid concentrations. Physical interferences can be reduced by diluting the analytical solution. Chemical interferences include molecular-compound formation, ionization effects, and solute-vaporization effects. Normally, these effects are not significant with ICP-OES. If observed, they can be minimized by careful selection of operating conditions, matrix matching, and using method of standard-additions. Chemical interferences are highly dependent on matrix type and specific analyte element determined.

- Memory interferences occur when analytes from a previously measured analytical solution contribute to analyte signals currently being measured in an analytical solution. Memory effects can result from analyte deposition on nebulizer uptake tubing or from build-up of material in the plasma torch and spray chamber. The site where these effects occur is element dependent and can be minimized by flushing with a standard blank between analytical solutions. Monitoring for memory interferences is performed during an analytical run and suitable rinse times are to be established to control their affect on analyte measurements. Rinse times necessary for a particular element must be determined before analysis. Determination of a sufficient rinse time may be achieved by aspirating a standard solution containing elements corresponding to either the upper end of their LDRs or concentrations ten times those usually encountered. A normal aspiration time should be used, followed by analysis of the standard blank at designated intervals. The length of time required to reduce an analyte's signal to within a factor of two of the ASDLs should be used as the rinse time if more than the minimum 60 sec is required. Until required rinse time is established, a 60 sec rinse period is recommended between analytical solutions and standards. If memory interference is suspected, analytical solutions should be re-analyzed using a longer rinse period.

3.6.3.2. Instrument Setup

Safety Note: Inductively coupled plasmas emit ultraviolet radiation and must be viewed with proper eye protection.

- Each laboratory must determine optimum instrument parameters for radio frequency (RF) power, view height, argon flow rates and sample uptake rate.
- Small changes in RF power, view height and argon flow rates can greatly affect instrument performance and inter-element correction factors.
- Inspect sample introduction system including nebulizer, torch, injector tube and uptake tubing for salt deposits and dirt that would restrict solution flow and affect instrument performance. Inspection frequency will depend on work load and analytical solution composition. Inspect system at each use and clean as needed.
- Allow instrument to become thermally stable before standardization and analyses. This usually requires at least 20 to 30 minutes of operation.
- After instrument warm-up, perform optical profiling. Optical profiling is performed with a built-in mercury lamp, a 2 mg/kg Mn solution, or a procedure recommended by instrument manufacturer.
- For sequential type ICP-AES instruments, perform wavelength calibration (according to manufacturer's instruction).

3.6.3.3. Pre-standardization Checks

Check instrument sensitivity and short-term precision before standardizing. Analyze (≥5 integrations) one of the standard solutions (or a separate solution made for this check). Monitor the emission counts (or emission ratio) of a selected element (*e.g.*, Mn at 2 mg/kg does not need to be an element of interest).

The emission count mean should be within 20% of the laboratory's historical mean and the RSD should be <5%. Failure of either of these usually indicates a solution introduction problem. Correct before proceeding.

3.6.3.4. Standardization Verification

- After standardization, verifications are performed periodically during analytical run and at the end.
- Typically verifications are on a n=10 sample frequency.
- Measure an ICS and a standard blank (n ≥5 separate analyses with normal autosampler rinse in between and the blank immediately after ICS).
- ICS recovery should initially be 100 ± 5% of expected value then meet the method's QC specification (e.g., <10%) to verify lack of instrument drift.
- Standard blank must be less than the ASDL.
- Relative to the laboratory's records, IDLs should be within 3 times the standard deviation of the laboratory's average and the blank should confirm no carry over according to method requirements.
- If an ICS check is out of control and it was prepared from the fortification solution, the FAP may need to be re-prepared.

3.6.3.5. Analysis Checks

- Precision is verified using RSDs (e.g., ≤5% for analytes above ASQL).
- When control limits are not met, methods usually require re-analysis then (if still out of control), diagnosis, correction, and re-standardization.
- Measurements are typically based on the means of ≥3 replicate integrations.
- Levels must be within the LDR.
- Standardization correlation coefficients (r) usually must be ≥0.998.
- If possible, measurement results should be based on multiple wavelengths and agree to within ±10%
- Common problems are with the instrument, a matrix interference, the sample introduction system, or a physical interference with the analytical solution. Flushing the sample introduction system for several minutes and diluting the analytical solution by a factor of 2 may circumvent some types of problems.
- Perform a wavelength scan (emission count intensity verses wavelength) for each analytical solution to check for spectral interference. Depending on instrument software, these scans can be incorporated into the analytical run or performed separately. A standard solution scan can be overlaid with the analytical solution scan (element should be comparable to that in the analytical solution). Interfering or otherwise unresolved broad or multiplet peaks may result in a positive bias. Peaks in the baseline background areas may result in a negative bias. Background correction points must be in an area(s) free from other peaks.

3.6.4. INSTRUMENT PERFORMANCE (ICP-MS)

3.6.4.1. Interferences

Several types of interferences are associated with inductively coupled plasma-mass spectrometry (ICP-MS). Instrument operators must be familiar with the various interferences, the means of detecting interferences and the ways to eliminate or minimize them. Typical quadrupole-based instruments are not able to resolve interfering lines that are less than one nominal mass unit such as ^{75}As (mass 74.9216) and $^{40}Ar^{35}Cl$ (mass 74.9312).

- Elemental isobaric interference occurs when a singly charged non-analyte-element ion has the same nominal mass-to-charge ratio as the analyte isotope (e.g., ^{114}Cd and ^{114}Sn). Recommended isotopes for measurements will ideally be free from this interference.
- Doubly charged species isobaric interference occurs when a doubly charged species has an interfering mass-to-charge ratio. For example, the nominal ratio for $^{150}Sm^{++}$ and $^{150}Nd^{++}$ matches ^{75}As. This type of interference can be minimized by tuning the instrument but correction factors may still be needed to prevent a positive bias.
- Polyatomic isobaric interference occurs when molecular species have an interfering mass-to-charge ratio. These ions form in the plasma, interface or reaction cell. The sources for these molecular ions are the plasma (Ar), the atmosphere (C, O, N, CO_2), the matrix (e.g., H_2O).

> *^{75}As - Example interferences are $^{40}Ar^{35}Cl$ (due to Cl in high-salt processed foods or when HCl is added to help stabilize Hg) and $^{40}Ca^{35}Cl$ (due to Ca is in dairy products).*
>
> *^{111}Cd - A possible interference is $^{95}Mo^{16}O$ but it should be negligible because Mo levels are typically low in food and proper tuning will minimize oxide formation.*
>
> *Pb & Hg should not be affected for most food and dietary supplements (by virtue of their higher atomic mass and no possible double-charged interference.*

- Matrix interference results from analytical solution properties such as high dissolved solids, which can affect nebulizer operation, make deposits on the interface cones, and suppress ionization efficiency [especially for elements with <9 eV ionization potential (IP)]. Response factors will therefore differ from those for the standards.

> *Matrix effect is a common cause of poor FAS and FAP recoveries.*
>
> *Cone deposits lead to instrument drift.*
>
> *Lighter elements can have a "space charge effect" where they are said to be "knocked around" and pass through ion lenses less efficiently.*
>
> *Ideally, analytical solutions will have <0.2% or <2,000 mg/kg dissolved solids.*
>
> *Internal standards can not compensate for all matrix effects but some compensation is possible - for ionization efficiency suppression if an analyte if the internal standard has an element with a similar IP and/or for space charge effect if it has similar mass.*
>
> *Internal standard isotope suppression is likely the result of a matrix effect. Dilution is recommended if an internal standard signal differs by more than 40% from the calibration blank.*

- Memory effect interference occurs when an element is not fully rinsed out of the sample introduction system between analyses and is most pronounced for high element levels. Rinse time must therefore be anticipated to rinse out the highest levels expected. Analysis of a blank immediately after the highest-level standard solution confirms if the rinse time is long enough. Mercury is especially prone to memory effects (the highest Hg standard should be ≤1 µg/kg).

3.6.4.2. Instrument Setup

Use proper eye protection as inductively coupled plasmas emit ultraviolet radiation during operation.

- Inspect sample introduction system, including nebulizer, torch, pump tubes and sampler cone. Sample introduction system inspection frequency will depend on work load and analytical solution composition but at minimum at each use (or daily if round-the-clock operation) and especially if high salt/mineral samples are being analyzed. Clean as needed (e.g., when the cone has a deposit).
- Allow instrument to become thermally stable before tuning and standardization and analyses (usually >20 minutes of operation).
- Enter information into autosampler sequence table plus any correction factors needed.
- *Optimum instrument parameters will be laboratory and instrument specific - including radio frequency (RF) power, sampling depth, argon flow rates, collision cell gas flow rate, lens voltages and sample uptake rate.*
- *Instrument performance is greatly affected even with small changes in RF power, sampling depth and argon flow rates.*

3.6.4.3. Pre-standardization Checks

Verify that instrument sensitivity and short-term precision are satisfactory. Failure of either of these checks is usually the result of a solution introduction problem (correct before standardizing).

- After tuning and while still aspirating the tune solution, run the "Tune Report".
- Verify that sensitivity, oxide level, double charged species, peak axis and peak height meet laboratory or manufacturer's specifications.
- Analyze a midlevel standard solution and verify that the RSD is acceptable for the laboratory QC requirements (e.g., ≤5%).

3.6.4.4. Standardization Verification

Standardize the instrument, verify IDL and standardization initially, then repeat instrument standardization verification during and after the analytical run.

- Standard curve correlation coefficients (r) are usually required to be ≥0.998. Although failure could be due to a number of reasons, usually the cause lies with one or more standard solutions and/or the standard blank. A problem with one or two solutions would likely be evident in the display of the standard curve (intensity vs. concentration). Diagnose, correct, and re-standardize. The autosampler may have also been sent to the wrong location.

- IDL is verified by analyzing the standard blank. This typically involves ≥5 separate analyses with normal autosampler rinse in between and IDLs should be within 3 times the standard deviation of the laboratory's normally obtained IDL values.
- Standardization is verified initially by analyzing the ICS and the standard blank immediately following. ICS recovery typically needs to be 100 ± 5% of expected value. The standard blank analysis verifies absence of carry over. Results for the standard blank must be less than the ASDL. If either of these conditions is not met, diagnose, correct, and re-standardize.

> *If an ICS check is out of control and it was prepared from the fortification solution, the FAP may need to be re-prepared.*

- Continuing standardization verifications are performed throughout the analytical run and typically included on a n=10 sample frequency. An ICS and a standard blank are both measured (n ≥5 separate analyses with normal autosampler rinse in between and the blank immediately after ICS). ICS recovery should initially be 100 ± 5% of expected value then meet the method's QC specification (e.g., <10%) to verify lack of instrument drift. Standard blank must be less than the ASDL. Relative to the laboratory's records, IDLs should be within 3 times the standard deviation of the laboratory's average and the blank should confirm no carry over according to method requirements.

3.6.4.5. Analysis Checks

All measurement results of analytical solutions, diluted analytical solutions, standard solutions, and quality control solutions should be based on the mean of 3 replicate integrations.

- Precision (of replicate integrations) is usually required to be ≤7% RSD (if above ASQL) for all analytical solutions with re-analysis if the limit is not met. If the repeat analysis is still out of control, then suspect instrument problem or matrix interference and diagnose, correct, and re-analyze. There may be either a problem with the sample introduction system or a physical interference with the analytical solution. Flushing the sample introduction system for several minutes and diluting analytical solution by a factor of 2 may resolve the problem.
- If standard addition is used, the correlation coefficient (r) must be ≥0.995.

3.6.5. METHOD PERFORMANCE

3.6.5.1. Reference Material (RM)

RMs are used to assess accuracy. For each element of interest, each run should have at least one RM with an established value for that element at a concentration above LOQ. To evaluate results, use of z-scores (§3.5.3) is preferred. For simplicity, however, it is not unusual for control limit recoveries to be required to fall within the RM certificate's stated uncertainties (at 95% confidence level) or 100 ± 20%, whichever is greater. The latter is overly restrictive but the criteria will nevertheless usually be met.

- If three or more RMs are analyzed then usually the recovery results must meet the control limit for only two thirds of the RMs.
- If RM recovery fails, all of a batch's analytical solutions can be re-analyzed but if RM recovery fails again, then repeat digestion and analysis is required.

- When appropriate RMs are unavailable, other quality control measures may be used to judge acceptance of batch analytical results (e.g., FAP recovery, FMB recovery).
- Failing an RM control limit should be highly unusual because a laboratory's experience analyzing a RM should establish predictable results.
- When a new RM is investigated, it is best treated initially as an unknown. If recovery discrepancies exist, investigate and decide whether it should be used as a laboratory's control material for judging batch quality.
- In-house RMs with established values are acceptable.
- To the extent practical, RM matrices should be similar to the sample matrices.
- RM selection is subject to availability.
- When necessary, non-certified element levels may be used - if the laboratory has established acceptance criteria.

3.6.5.2. Fortified Analytical Portion (FAP)

FAP results are used to demonstrate QC with recovery criteria typically at 100 ± 20%. Poor recoveries indicate problems such as analyte loss during preparation, physical/transport interference, spectral interference, etc.

- FAP recoveries involve processing two replicate portions - an unfortified analytical portion (UAP) and a FAP, which is fortified with each analyte before digestion.
- Typically, up to ~1 g fortification solution is added and analyte levels should be increased 100-200% relative to expected.
- For foods with low or unknown analyte levels, fortify to achieve approximately midpoint of LDR.
- In general, an FAP should be analyzed for each food type but the diversity of food types precludes this from happening with every analysis run. Routinely, each run should include at least one FAP.
- If FAP recovery is unacceptable, re-analyze the FAP solution. If FAP recovery fails again then examine the other QC information (e.g., RMs, FMBs) to determine whether there is an isolated anomaly with the FAP or if the entire batch is in question.
- FAP recovery may be outside of the control criteria but nonetheless acceptable due to high measurement imprecision when the analyte level is low.

3.6.5.3. Fortified Analytical Solution (FAS)

FAS results provide QC that primarily assesses matrix-induced interference. QC typically requires recovery to be 100 ± 10%.

When out of control, the FAS would typically be diluted by a factor of 2 or more and be re-analyzed to further evaluate a matrix effect.

- The instrument's software and autosampler set-up can be set to perform FAS fortification, analysis (with recovery check), dilution, and even automatic re-analysis, if needed.

- If FAS recovery is ≥50%, the analytical solution could alternatively be analyzed via standard additions.

3.6.5.4. Fortified Method Blank (FMB)

Although usually an optional QC step, FMB results verify accuracy of the fortification procedure (without matrix effects) and can be used to identify problems such as pipet malfunctions and dilution errors. QC typically requires recovery to be 100 ± 10%. Out of control is usually due to a problem with the fortification solution or the blank so another FMB would need to be prepared and analyzed.

3.6.5.5. Laboratory MBK (MBK_L)

MBK_L is a laboratory mean (often called a "running average") established using MBK results accumulated from many independent analyses over extended periods (i.e., months). It represents the expected blank analyte level during routine analyses and is therefore subtracted from all analytical solutions results.

- MBK_L is determined for each analyte-method-instrument combination.
- During an analysis run, results for MBKs included with a batch of samples are compared to MBK_L.
- Initially, MBK_L is the mean for ≥5 independently prepared MBKs (unfortified) but over time, the number of MBKs used will increase.
- Trends (increasing or decreasing values) should be watched for to monitor for contamination or decreasing blank levels (that would require changing the MBK_L value).

3.6.5.6. Laboratory MBK Critical Value (MBK_C)

MBK_C is used to judge the quality of MBKs analyzed with each batch of samples, MBK_C is calculated using 3.6 Equation 1.

$$MBK_C = MBK_L + (2s) \qquad \text{3.6 Equation 1}$$

where, s is the standard deviation of the MBKs used to establish MBK_L.

3.6.5.7. Method Blank (MBK)

For an analysis run, MBK results are used to assess contamination from the laboratory environment and reagents and are compared to MBK_C. For a batch (or 'run'), MBK results are acceptable when at least two-thirds of them are ≤MBK_C. Individual MBKs can be above MBK_C but it should be uncommon for a batch's MBKs to be out of control. The more frequently MBKs exceed MBK_C, the more attention should be directed to identifying and correcting the cause of contamination or to consider reestablishing MBK_L and MBK_C.

3.6.6. HISTORY

EAM 3.6 Table 1. History

Version	Revisions Made	Effective Date
1.0	*Instrument Performance*	June 2008
2.0	Renamed to *Performance* with *Instrument Performance* becoming a subsection along with *Method Performance Checks* (formerly 4.0.2); converted to PDF for web posting.	September 2014
3.0	Updated; added *History* section.	December 2021

References

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