Method Validation: Performance-Based Approach

Module 8

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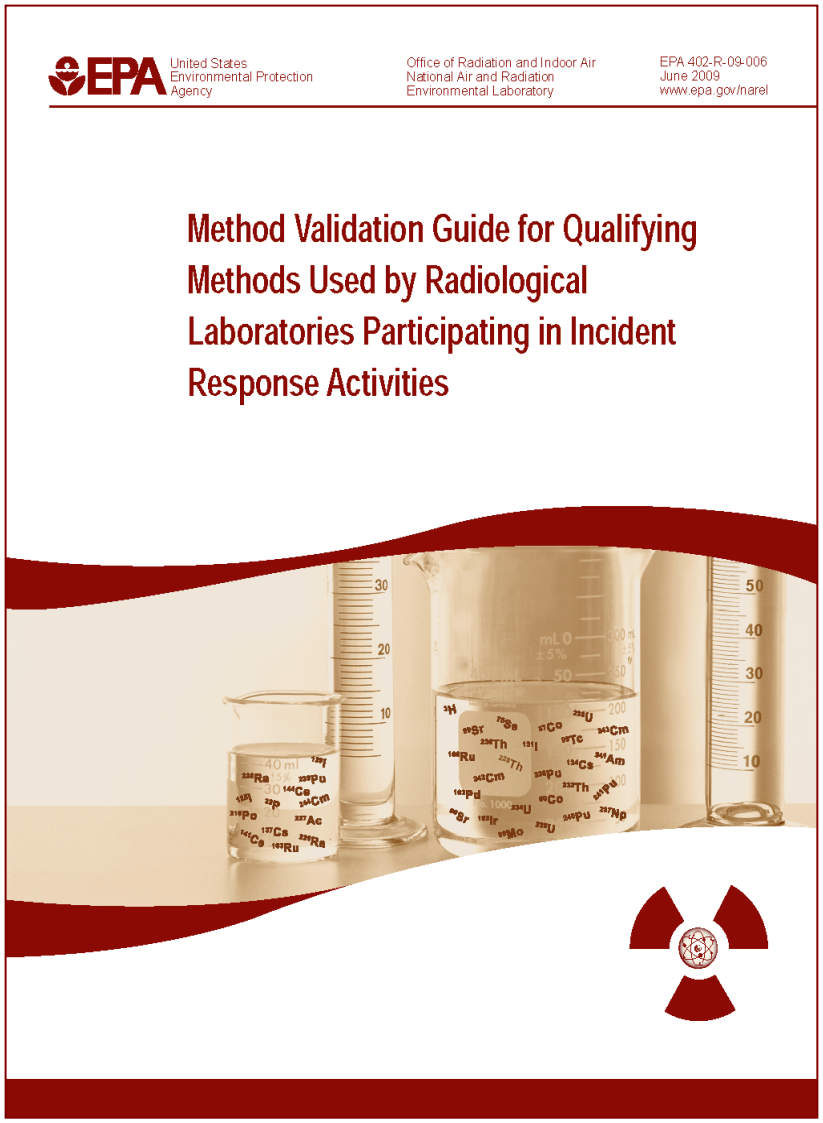
EMS

Method Selection and Validation

- Part I concepts and information were prepared for **Project Managers**
- Chapter 6 is **different** from the rest of Part I
  - Concepts and information prepared for
  - Radioanalytical Specialists, Technical Evaluation Committee members, Project Managers and
  - Laboratory Managers and staff
- Both audiences need to understand the material to be prepared to successfully implement
  - Performance-based method selection
  - Method validation

Method Validation Guide



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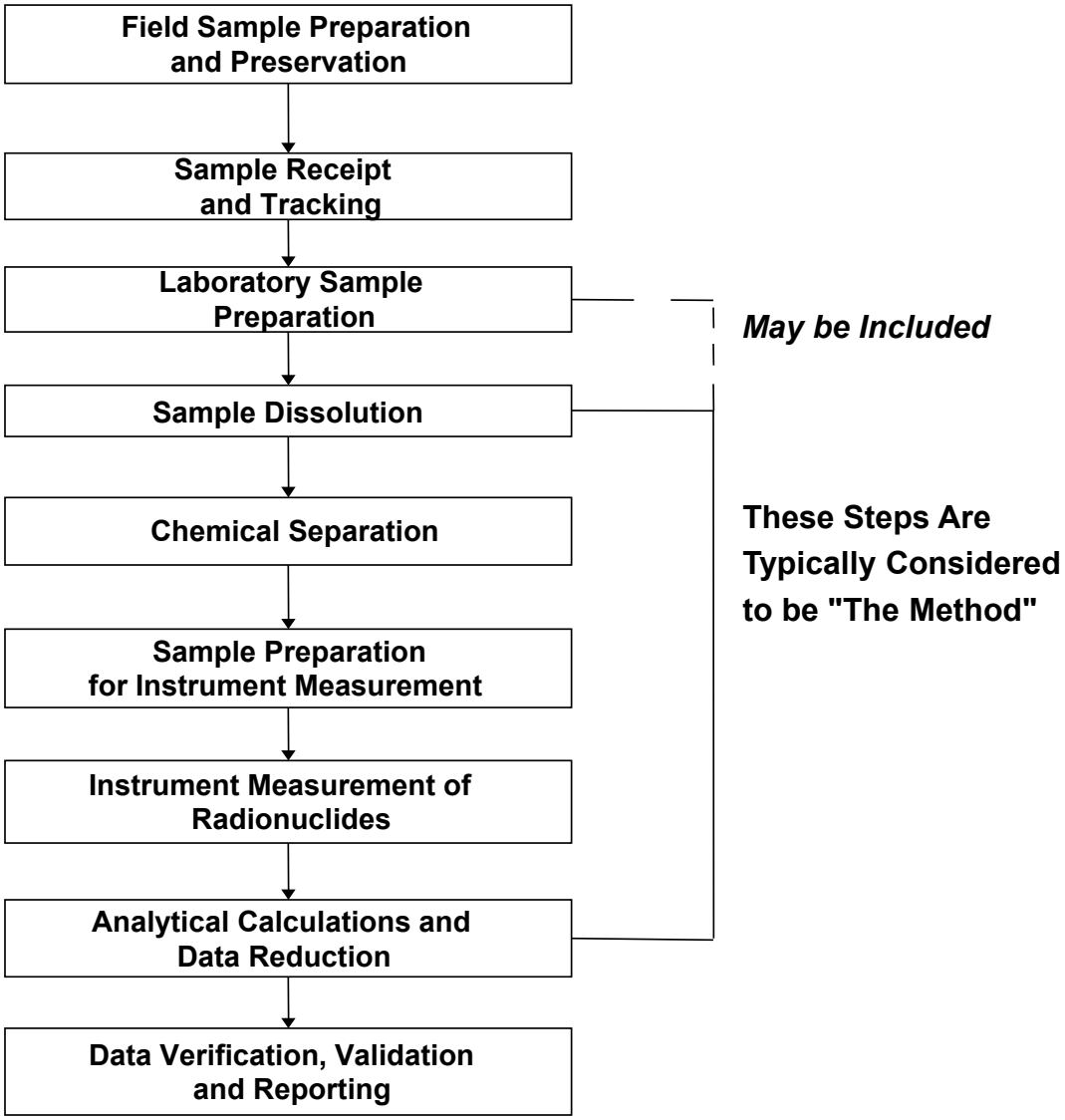
Method Definition (6.2)

A “radioanalytical method” or “laboratory method” is a set of written procedures that includes “all physical, chemical, and radiometric processes conducted at a laboratory in order to provide an analytical result.”

MARLAP Analytical Process



Prescribed-Method Approach

- Projects often prescribe methods in their SOW including:
  - **Promulgated Methods** required by regulation such as Safe Drinking Water Act (SDWA) or Clean Water Act (CWA)
  - **Voluntary Consensus Standards Body Methods**- recognized *standard methods*
- These methods *should* have undergone validation
  - In every case, check the scope and applicability and the method performance sections--is there sufficient information to show that the method will meet MQOs?
- In the end, all methods should be validated prior to using them to analyze project samples.

Performance-Based Approach To Method Selection

The selection of a validated method based on the demonstrated capability to meet defined quality and performance criteria (MQOs) when it is implemented together as part of a properly implemented QA program.

The selected method must reliably produce appropriate and technically defensible results under the conditions used for program samples.

Method Selection

- MARLAP Key Parameters – MQOs
  - Most important parameter is required method uncertainty (u_{MR}) at a specified concentration

MARLAP Recommends…

Performance-based approach to method selection (6.3-6.5):

- Laboratory proposes method(s)
- Project Manager (or TEC) evaluates the method proposed by the laboratory based on
  - Method validation documentation submitted by the laboratory
  - Laboratory performance of method-validation PT samples
- Upon contract award the APSs/MQOs and method are incorporated into a specific project work plan for the laboratory

Performance-Based Approach to Method Selection
The Project's Perspective (MARLAP 6.5)

- **Matrix and analyte identification** (radionuclide) (6.5.1)
- **Process knowledge** (6.5.2)
  - Consider potential chemical and radionuclide interferences
- **Radiological holding** and **turnaround times** (6.5.3)
- **Unique process specifications** (6.5.4)
- **MQOs** (6.5.5) -- $\mathbf{u_{MR}}$ preferred.
  - **MDA/MDC** or **MQC**
  - **Concentration range**, **method specificity** and **ruggedness**
  - **Bias considerations** (6.5.5)
- Operational aspects

Performance-Based Approach To Method Selection The Laboratory's Perspective

- The laboratory needs to consider:
  - APSs & MQOs
  - Methods available for nuclide/matrix
  - Method validation status
  - Availability of qualified staff
  - Production schedule & number of samples
  - Sufficient instruments and support equipment available and calibrated
  - Radiological holding and sample turnaround times

Project Manager:

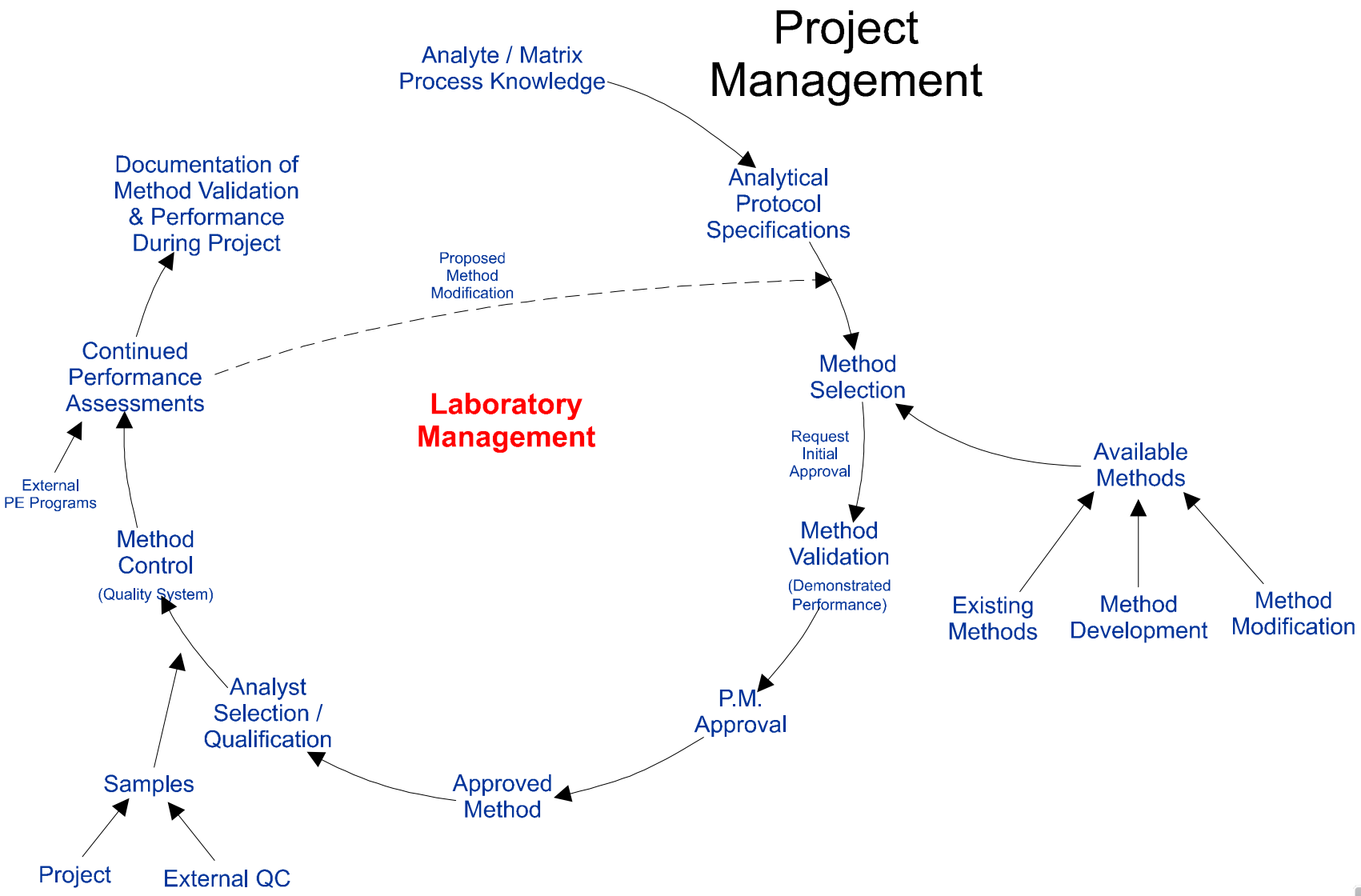
- Reviews documentation and PE program performance
- Evaluates response to other performance/production requirements
- If possible, compares submitted methods to other existing or known methods
- Evaluates response to other performance/production requirements

Continued…

Project Manager(Continued):

- Makes decision to send pre-award, site-specific proficiency testing matrix samples
- Makes decision to perform pre-award, onsite laboratory, or desk audit
- From additional information, makes list of capable laboratories (technical basis only)
- Laboratory selection (Contracting Officer)

Method Application Life Cycle



Method Validation

Project Method Validation

- Process demonstrating that the radioanalytical method selected for a particular radionuclide in a given matrix is capable of providing analytical results to meet the project's MQOs and other requirements in the APS

General Method Validation

- Is the laboratory's internal method validation process that demonstrates a method's performance will meet default quality performance requirements established for detection and quantification, especially precision and bias requirements

IUPAC: Harmonized Guidelines for Single-Laboratory Validation of Methods of Analysis. (Pure Appl. Chem., 74:5, pp. 835-855) available at http://publications.iupac.org/pac/74/5/0835/index.html

EURACHEM: *The Fitness for Purpose of Analytical Methods, A Laboratory Guide to Method Validation and Related Topics* (ISBN 0-948926-12-0). Available at: https://www.eurachem.org/index.php.

Project Method Validation

Laboratory Initiation

- Accomplished by the laboratory by processing internal, external PT, or Method Validation Reference Material (MVRM) samples according to the validation level specified by the Project Manager or Technical Evaluation Committee (TEC)

Project Manager Initiation (Optional)

- Accomplished by the Project Manager sending PT samples to the laboratory

Project Method Validation Protocol Parameters (6.6.2)

Parameters for PT sample specifications, including interferents are ascertained from the DQOs & process knowledge and documented in the APS

- MQOs for each analyte/matrix
- Defined method validation level (Slide 21)
- Analytes, testing range and interferents
- Matrix for testing
- Defined sample preservation

- Additional data testing criteria such as acceptable range for chemical/radiotracer yield and method bias (if applicable

Continued…

Tiered Approach to Method Validation (6.6.3)

- MARLAP uses a tiered approach to method validation
  - Different levels of rigor may be needed to validate methods
- Level of validation is established during project planning
  - Depends on the degree of confidence in the method's performance to produce results consistent with the required method uncertainty
  - Depends on the extent of experience with the method, specificity, and ruggedness
- The Project Manager is responsible for communicating the required level(s) of method validation in the SOW

Tiered Project Method Validation Approach

Validation Level	Application	Sample Type*	Acceptance Criteria§	Levels† (Concen.)	Replicates
A (Without Additional Validation)	Existing Validated Method	—	Method Previously Validated (By One of the Validation Levels B through E)	—	—
B	Same or Similar Matrix	Internal PT	Measured Value Within ±2.8 u_{MR} or ±2.8 φ_{MR} of Known Value	3	3
C	Similar Matrix/New Application	Internal or External PT	Measured Value Within ±2.9 u_{MR} or ±2.9 φ_{MR} of Known Value	3	5
D	Newly Developed or Adapted Method	Internal or External PT	Measured Value Within ±3.0 u_{MR} or ±3.0 φ_{MR} of Known Value	3	7
E	Newly Developed or Adapted Method	MVRM Samples	Measured Value Within ±3.0 u_{MR} or ±3.0 φ_{MR} of Known Value	3	7

Tiered Project Method Validation Approach
Notes on the Table

- *The **number of samples*** required varies by level from 3-7
- ***Concentration Range*** should bracket the expected analyte concentration range especially the action level
- ***Acceptance Criteria*** target a false rejection rate of 5%. The number of samples vary depending on the total number of validation samples required (degrees of freedom)
- ***Important -- Every validation sample*** must satisfy the acceptance limit!
- Include 5 appropriate blanks (not a test level) to estimate the absolute bias of the method
  - The test for absolute bias is presented in MARLAP Attachment 6A.

Method Validation Project Situations

- Existing Methods Requiring No Additional Validation (6.6.3.1)
- Use of a Validated Method for Similar Matrices (6.6.3.2)
- New Application of a Validated Method (6.6.3.3)
- Newly Developed or Adapted Methods (6.6.3.4)

Stop the recording and read Attachment C of the ^{90}Sr APS in the Module 8 handout

- **Level A Validation**
  - Method previously has been validated (Levels B – E)
  - Matrix and analytes of new project sufficiently similar to past samples analyzed by a lab's SOP
  - Project Manager assumes additional validation is unwarranted

Consider!!

Level A requires that the laboratory is using a method that was previously validated for similar work.
Without some degree of validation, there is no assurance that the lab can meet the same standards and quality of earlier

Examples of Existing Methods Requiring Level A -- No Additional Validation (6.6.3.1)

1) **New Client Project: Evaluation of Drinking Water**

- Use EPA approved method
- Method validated previously under Level C (External PTs)
- Historical and ongoing acceptable performance in EPA Performance Evaluation Program Studies
- Method is being used continuously

2) **New Client Project: Evaluation of ^{90}Sr in Raw Milk**

- Modified an EPA approved method for ^{90}Sr in water to be used for raw milk
- Method validated previously under Level C (Internal PTs)
- Previous and ongoing acceptable performance in internal performance testing program and other client PE programs
- Method use: continuously (for other clients)

Routine Methods – No Previous Project Validation (6.6.3.2)

Level B validation

- Level B requires evaluating methods for the same or similar matrix with internal PT samples at 3 concentration levels, with 3 replicates per level
- This assumes that the lab has a method that it uses routinely for a specific radionuclide/matrix combination.
- The method, however, has had no previous *project* method validation

An Example of Routine Method, Same Matrix No Previous Project Validation (6.6.3.2)

Level B Project Method Validation- Same Matrix

New Client Project: Surveillance of ^{90}Sr in raw cow milk

- Laboratory has routine method under general validation but not used for five years
- Expected sample matrix similar to previous milk samples
- Records of past performance in a PE program or internal QA not available/

Use of Validated Methods for Similar Matrices (6.6.3.3)

- Analysis of samples that are the same as, or similar to the matrix and analyte for which a method has been developed, can be validated according to Method Validation Levels B or C
- Validation levels will provide a reasonable assurance that the method will meet the required MQOs

Use of Validated Methods for Similar Matrices (Continued)

Level B validation requires evaluating method with internal PT samples at 3 concentration levels, with 3 replicates per level

- Each result must be within ±2.8 u_{MR} or ± 2.8 φ_{MR} of known value

Level C validation requires evaluating the method with internal or external PT samples at 3 concentration levels, with 5 replicates per level.

- Each result must be within ±2.9 u_{MR} or ±2.9 φ_{MR} of the known value

An Example – Level B or C: Use of Validated Methods for Similar Matrices (6.6.3.3)

x

New Client Project: Surveillance of ^{90}Sr in raw goat milk

- Laboratory has a validated method for ^{90}Sr in cow's milk that has been used routinely for the past eight years
- Expected sample matrix similar to cow's milk but analyte concentration expected to be higher than milk from cows in the same area
- Expected sample size is smaller but this is only a concern for reprocessing a backup sample
- Use of samples drawn from composited client goat milk with spikes is one option for method validation
  - The laboratory will use one portion of the composite to internally prepare spiked test samples.
  - Another portion of the composite used as an unspiked sample to determine the inherent ^{90}Sr in the samples

An Example -- Level B or C Project Method Validation: Similar or Slightly Different Matrix (6.6.3.3)

New Client Project: Analysis of Water with High Dissolved Solids

- **The laboratory has a gross alpha/beta method for drinking waters with low dissolved solids content using a gas proportional counter**
  - Method applicable for dissolved solids on a planchet of less than 120 mg.
  - Gross alpha and beta self absorption curves applicable from 10 to 120 mg.
- **Method is modified to eliminate counting problems encountered with high dissolved solid content**
  - Steps in front end of method to determine dissolved solid content and reduce size of aliquant taken to process.

For slight changes in matrices, Validation Level B is typically required.

New Application of a Validated Method (6.6.3.4)

New applications include:

- Dissimilar matrices
- Chemical speciation of the analyte or possible other chemical interference
- Analyte, chemical, or radiometric interferences
- Complete solubilization of the analyte and sample matrix
- Differences in analyte or sample-matrix heterogeneity

New Application of a Validated Method (continued)

Level C validation requires evaluating the method with internal or external PT samples at 3 concentration levels, with 5 replicates per level

- For lowest spike (1 pCi/L), each result must be within 2.9 u_{MR} or 1.45 pCi/L of the known value (2.9×0.5 pCi/L)
  - The acceptance range for the 1.00 pCi/L samples, is from -0.45 to 2.45 pCi/L.
- For the spike levels greater than the action level, results must be within 2.9 φ_{MR} or 18% of known (2.9 × 6.25%)
  - The acceptance range for the 10.0 pCi/L samples, is from 8.2 to 11.8 pCi/L.
  - For the 20.0 pCi/L samples the acceptable range is from 16.4 to 23.6 pCi/L.

Example of Level C Method Validation for a New Application of a Validated Method (6.6.3.4)

New Client Project: Surveillance of ^{90}Sr in raw cow's milk

- Laboratory has a method for ^{90}Sr in drinking water that was modified to be similar to U.S. Public Health Service method for ^{90}Sr in milk by ion exchange
- New method has undergone general method validation
- Method has been used in the analysis of PT samples from a commercial PE program with success

Project Manager requests Method Validation Level C with external PT samples from a selected commercial source supplier

Example Level C Method Validation for ^{90}Sr

- Lab has modified its ^{90}Sr method for water to be applicable for milk
- It will use internal PT samples prepared from fresh milk:
  - 5 milk samples spiked with ^{90}Sr at 3 pCi/L;
  - 5 milk samples spiked at 9 pCi/L;
  - 5 milk samples spiked at 25 pCi/L
- For lowest spike (3 pCi/L), each result must be within 2.9 u_{MR} of the known value: $\pm 2.9 \times 0.5$ pCi/L = ±1.45 pCi/L;
- For the two higher spike levels, results must be within 2.9 φ_{MR} of the known value: $\pm 2.9 \times 6.25\%$ = ± 18% of known;
  - for the mid level spike (9 pCi/L) this is ± 1.6 pCi/L of known;
  - for the upper level spike (25 pCi/L) this is ±4.5 pCi/L of known

Newly Developed or Adapted Methods (6.6.3.5)

- New method developed by laboratory not previously validated by laboratory
  - Published method (literature or nationally recognized standard)
  - Adaptation of a published method (literature or nationally recognized standard)
  - A newly developed method
- For routine or common matrices, Method Validation Level D is required
- For special project matrices, Method Validation Level E using Method Validation Reference Material (MVRM) test samples is required
- Project Manager supplies MVRM test samples

Newly Developed or Adapted Methods (6.6.3.5)

Level D validation: Internal or external PT samples at 3 concentration levels with 7 replicates per level

- Each result must be ±3.0 u_{MR} or ±3.0 φ_{MR} of known value
- For our ^{90}Sr example: the known value ±1.5 pCi/L

Level E validation: Requires MVRM samples at 3 concentration levels with 7 replicates per level

- Each result must be within ±3.0 u_{MR} or ±3.0 φ_{MR} of known value
- For our ^{90}Sr example: the known value ±19%

An Example of Level D and E Method Validation: Newly Developed Method or Adapted Methods (6.6.3.5)

New Client Project: Analysis of ^{129}I in groundwater

- Senior radiochemist and radiation spectrometrist develop new ^{129}I radiochemical method based on radiochemistry fundamentals and available nuclear instrumentation
  - Method formulation incorporates the sample size, sample preparation, chemical separations, final test sample mount and ^{129}I detection efficiency to meet APSs
  - No short-lived iodine isotopes expected
  - Low-energy photon detector will be used

Testing for Method Bias (6.6.4)

MV Acceptance Criteria Assume No Bias

Method Bias Should be Evaluated…

- Initially — Method validation process
- Continuously — Quality assurance program via batch QC

Testing for Method Bias (continued) (6.6.4)

- Relative bias refers to consistent deviation of the mean measured value of analyte to the true analyte concentration
  - Impacts decisions where concentration is the most important consideration.
  - Minimizing statistical bias is most important when making decisions at the Action Level.
- Absolute bias refers to a consistent deviation from zero in samples containing no analyte
  - Impacts measurements that are very close to background.
  - This may be the most important consideration when making decisions about the presence or absence of analyte in samples and for certain research or survey projects

Testing for Method Bias (continued) (6.6.4)

Two types of bias

- Absolute Bias:
  - Mean response at zero concentration

- Relative Bias:
  - Ratio of the change in the mean response to a change in sample analyte concentration

Testing for Method Bias Absolute Bias (6A.2)

Absolute bias test when analyte concentration= 0.0

$$|T| = \frac{|X_{avg}|}{\sqrt{s^2/N}}$$

X_{avg} = average measured value

s = experimental standard deviation

N = number of measurements

Example of Testing for Absolute Method Bias (6A.2)

- Analyte concentration = 0.0
- Data from 9 batch QC samples
- $$|T| = \frac{|X_{avg}|}{\sqrt{s^2/N}}$$

0.714	0.993
2.453	0.472
-1.159	-0.994
0.845	0.673
0.495	
$X_{avg} = 0.4991$	
$s = 1.0745$	

$$|T| = \frac{0.4991}{\sqrt{(1.0745 \times 1.0745)/9}} = \frac{0.4991}{0.3582} = 1.3935$$

$\nu_{eff} = 9 - 1 = 8$

$t_{1-\alpha/2}$ @ $(\nu_{eff}) = 2.306$ (Table G.2 in Appendix G)

$|T| < t$: 1.3935 < 2.306

… No bias is detected

Testing for Relative Method Bias: Same Radionuclide Concentration of PT Samples (6A.2)

- Bias test when analyte concentration ≠ 0.0
  - Applies to replicate PT samples (7, 5 or 3) for the validation of Required Method Uncertainty, and
  - 10 MDC verification samples

- Same radionuclide concentration / activity for all samples in a given test level
  - PT1conc = PT2conc = PT3conc ….
  - *Example* Water or soil matrix PT samples obtained by taking aliquots from a large volume test material

Testing for Relative Method Bias: Same Radionuclide Concentration of PT Samples (continued) (6A.2)

$$|T| = \frac{|X_{avg} - K|}{\sqrt{s^2/N + u^2(K)}}$$

and $\nu_{eff} = (N - 1) \times (1 + (u^2[K] / [s^2 / N])^2$

Where

X_{avg} = average measured value

s = experimental standard deviation

N = number of measurements

K = reference value

u(K) = standard uncertainty for reference value

T = experimental T-statistic

Bias is indicated when $|T| > t_{1-\alpha/2} @ (\nu_{eff})$

$t_{1-\alpha/2}$ = *t* statistic with significance level α (typical 0.05)

ν_{eff} = effective degrees of freedom

Testing for Relative Method Bias
Unequal Radionuclide Activities of PT Samples

- **Bias test when analyte concentration ≠ 0.0**
  - Applies to each Method Validation Test Level for Required Method Uncertainty compliance tests
  - Applies to MDA/MDC verification samples
- **Test samples having different radionuclide concentrations/activities for a Test Level**
  - *Example* Air filters, swipes, individually spiked water samples
    - For a Test Level; PT1Act ≠ PT2Act ≠ PT3Act ….

Testing for Relative Method Bias: Unequal Radionuclide Activities of PT Samples (continued)

A paired *t*-test is used for testing relative bias in this c

Calculate the average difference, $(\bar{D})$, between the measured value, (X_i), and the known spiked value, (K_i), for N samples of a Test Level as

$$\bar{D} = \frac{1}{N}\sum_{i=1}^{N}(X_i - K_i)$$

Calculate the standard deviation of the differences, S_D as

$$S_D = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N}(D_i - \bar{D}_i)^2}$$

Where $D_i = X_i - K_i$

We then calculate the standard error for the replicate samples as S-sub-D divided by the square root of N..

Testing for Relative Method Bias
Unequal Radionuclide Activities of PT Samples

Calculate the absolute value of the *t* statistic as

$$|T| = \frac{|\bar{D}|}{s_D/\sqrt{N}}$$

Bias is indicated when $|T| > t_{1-\alpha/2}$ @ $(N-1)$

$t_{1-\alpha/2}$ = t statistic with significance level α (typical 0.05)

N-1 = degrees of freedom

Testing for Method Bias – Summary of Results

Type of Bias	Test Level	Known Value ± CSU (k=1) (pCi)	Mean of Measurements ± Standard Deviation (pCi)	Mean Difference from Known (pCi)	Number of Measure-ments / Degrees of Freedom	Bias |T|	t_{df}	Bias Yes / No
Absolute	Blanks	0.0	0.045 ± 0.023	—	7 / 6	5.20	2.45	Yes
Relative	MDA	0.5026 ± 0.0085	0.53 ± 0.22	0.031	10 / 9	0.44	2.26	No
Relative	1	10.87 ± 0.20	10.99 ± 0.99	0.120	5 / 4	0.29	2.78	No
Relative	2 - AL	21.33 ± 0.34	20.68 ± 0.55	-0.651	5 / 4	2.45	2.78	No
Relative	3	64.94 ± 0.99	60.9 ± 1.6	-4.08	5 / 4	5.95	2.78	Yes

Probability of Failing MV Acceptance Because of Bias

Given:

- AL = 100 pCi/L
- u_{MR} = 10 pCi/L at or below the AL
- φ_{MR} = 0.10 of test value at or above AL
- Our acceptance bounds require sample results must fall within 30 pCi/L of the known value at or below the AL or 30% of known value at or above AL

Probability of Failing Method Validation Because of Bias
A Single Sample Result

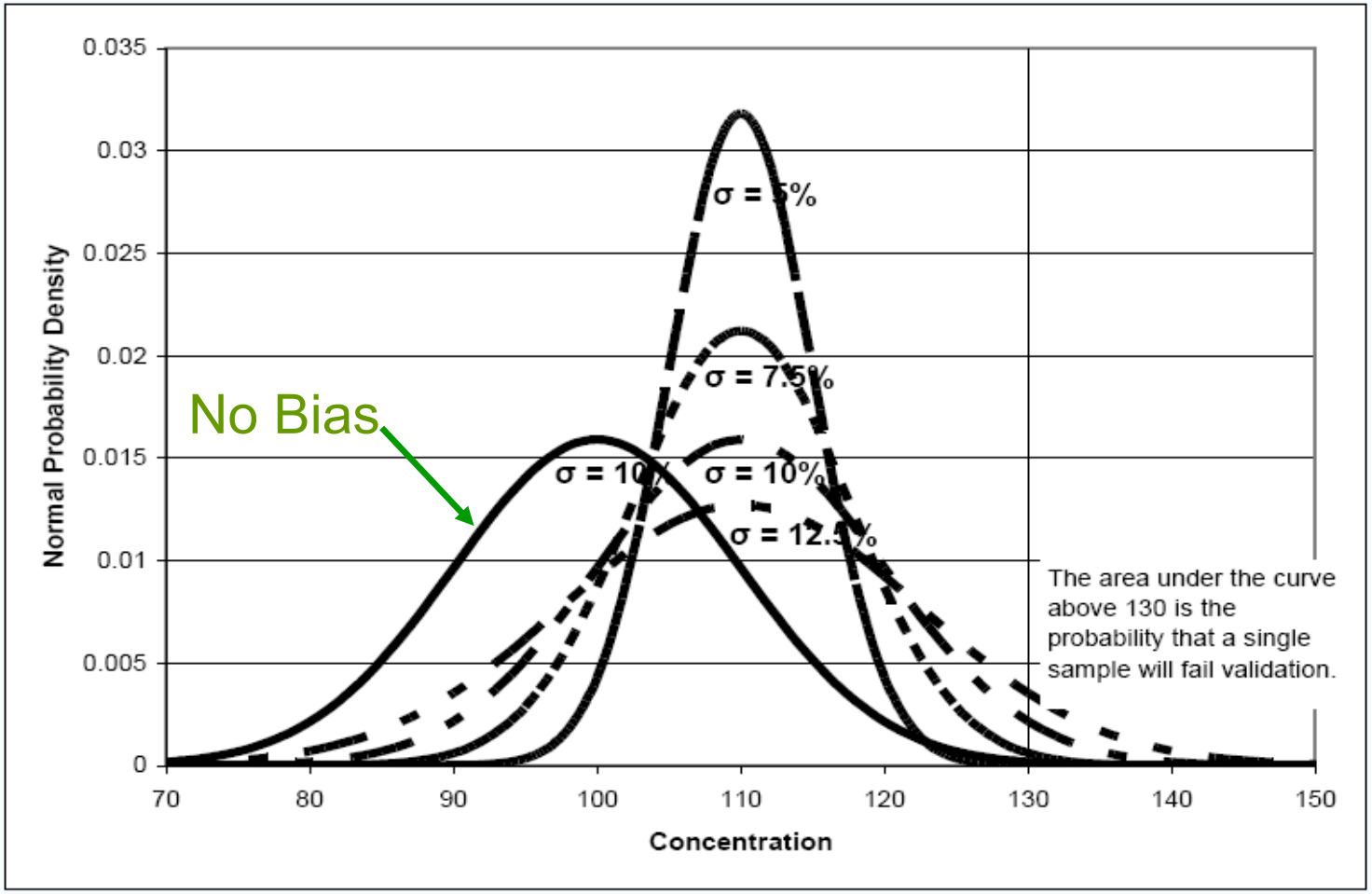
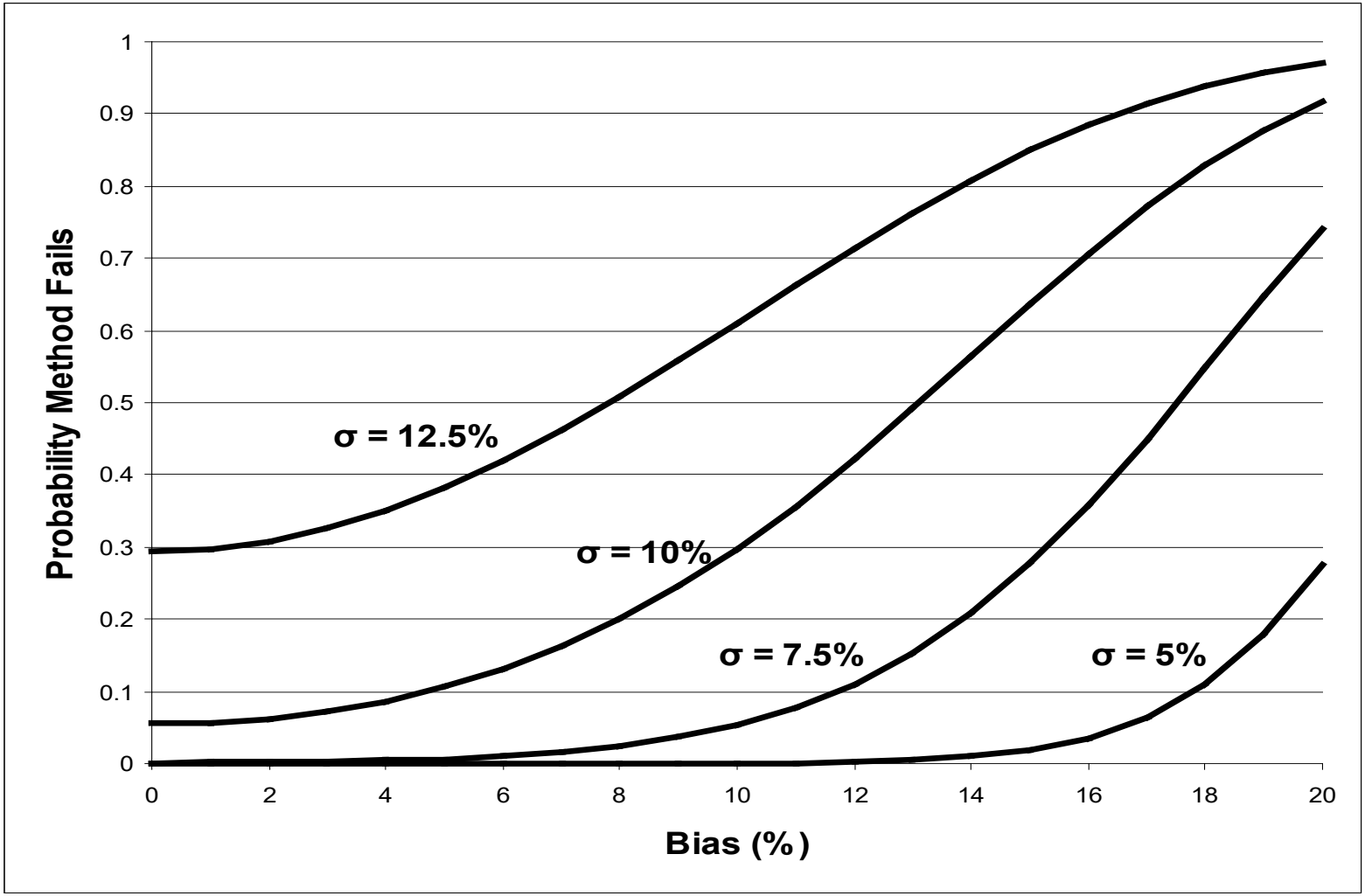


Figure 1 Probability of a validation sample failing at test level 100 with and without bias at various values of the method standard deviation.

Probability of Failing MV Acceptance Because of Bias



Protocol for Verifying the Required MDC - Method Validation (Application of MARLAP 20.4.2.5)

- Process seven blank samples using the method and the same analytical parameters that will be used for project samples.
- From the seven blank sample net results, calculate the estimated *Critical Net Concentration* (Critical Value – Section 20.18 & Equation 20.14).

Sample ID	Concentration (pCi/g)	CSU (1σ pCi/g)
B1	0.095	0.059
B2	-0.068	0.068
B3	0.140	0.099
B4	0.045	0.044
B5	0.059	0.071
B6	0.021	0.092
B7	-0.027	0.042
Mean	**0.038**	
Standard Deviation	**0.070**	
$t_{1-a}(n-1)$	1.94	
Critical Net Concentration	**0.14**	

Protocol for Verifying the Required MDC – Method Validation Application of MARLAP Section 20.4.2.5

- Process the ten replicate samples spiked at the required MDC for the radionuclide.
- Of the ten spiked samples, determine the number (Y) of sample results at or below the estimated *Critical Net Concentration*.
- $Y \leq 2$, the method tested at the required MDC meets the required MDC specification.
- If $Y > 2$, the method tested at the required MDC does not meet the required MDC specification.

Sample ID	Concentration (pCi/g)	CSU (1σ pCi/g)	Test Result ≤ CL_{NC}
M1	0.192	0.014	N
M2	0.144	0.012	N
M3	0.255	0.019	N
M4	0.161	0.013	N
M5	0.148	0.013	N
M6	0.229	0.018	N
M7	0.193	0.018	N
M8	0.164	0.018	N
M9	0.190	0.013	N
M10	0.124	0.016	Y
Mean	**0.180**		
Standard Deviation	**0.040**		
Relative Standard Deviation	**22%**		
CL_{NC} (pCi/L)	0.14		
Number of results > CL_{NC}	9		
Number of results ≤ CL_{NC}	1		
Acceptable maximum values ≤ CL_{NC}	2		
Evaluation	**PASS**		

Method Validation Documentation (6.6.5)

When laboratory conducts method validation

- All records supporting method validation, PT sample preparation and verification, and analytical data supporting processing, measurement, and data reduction, and the evaluation of method validation results.

When Project Manager conducts method validation (PT samples sent to laboratory)

- Appropriate technical representative should retain all records dealing with applicable method validation, PT sample preparation and certification, level of validation, results, and evaluations

MARLAP Recommends…

- MARLAP recommends
  - Performance-based approach for method selection
  - SOW containing the MQOs and analytical process requirements provided to the laboratory
  - SOW includes specifications for the action level and required method uncertainty (u_{MR}) for the analyte concentration at the action level for each combination of analyte and matrix
  - Method undergoes some basic general validation prior to project method validation

Continued…

MARLAP Recommends…
(Continued)

- MARLAP recommends
  - Methods applied to a specific project should undergo validation for that specific application
  - As each new project is implemented, the methods used in the analysis of the samples undergo some level of validation. It is the Project Manager's responsibility to assess the level of method validation necessary
  - Tiered approach for project method validation

Method Validation Exercises

- Take time to carefully look over the *Example Method Validation Review Form* on the following slide or page 6 of the Module 8 handout.
- Find the following items:
  - Proposed Method; Nuclide; Matrix; Action Level; Method Validation Level; Required Method Uncertainty; Required Relative Method Uncertainty
  - What are the units for the Required Method Uncertainty and Required Relative Method Uncertainty?
  - What are the three test level concentrations? Are they greater than or less than or equal to the action level concentration?
  - Can you reproduce the acceptance criteria and the acceptance ranges for the three test levels?
  - How many unacceptable results are permitted before the method fails to meet acceptance criteria?
- Does this method meet the acceptance criteria?

Sr-90 Example Method Validation Data Review Form

EXAMPLE METHOD VALIDATION REVIEW FORM

Laboratory: **XYZ Laboratory** *Proposed Method:* **W34 Radiochemistry with Gas Proportional Counting**

Nuclide: **Sr-90** *Matrix*: **Milk** *Action Level*: **8 pCi/L**

Method Validation Level: **MARLAP Level C**

Required Method Uncertainty, u_{MR}: **0.5 pCi/L** at or below the Action Level

Required Relative Method Uncertainty, φ_{MR}: **6.25 %** (at or) above the Action Level

Acceptance Criteria:

Test Level 1: known value ± [**2.9** × (φ_{MR} × known value)] = **25.00** ± **4.53** pCi/L (± **18.1**%)

Test Level 2: known value ± [**2.9** × u_{MR}] = **8.00** ± **1.45** pCi/L

Test Level 3: known value ± **[2.9** × u_{MR}] = **3.00** ± **1.45 pCi / L**

Data Evaluation

Trial #	Test Level 1 Acceptable Range 20.5 – 29.5 pCi/L			Test Level 2 Acceptable Range 6.55 – 9.45 pCi/L			Test Level 3 Acceptable Range 1.50 – 4.50 pCi/L		
	Measured ± 1σ** pCi/L	Δ pCi/L	Accepted Y/N	Measured ± 1σ** pCi/L	Δ pCi/L	Accepted Y/N	Measured ± 1σ** pCi/L	Δ pCi/L	Accepted Y/N
1	29.1 ± 1.7	+4.1	Y	8.23 ± 0.48	+0.23	Y	3.81 ± 0.29	+0.81	Y
2	24.1 ± 1.2	-0.9	Y	9.37 ± 0.53	+1.37	Y	2.23 ± 0.16	-0.77	Y
3	21.7 ± 1.3	-3.3	Y	7.80 ± 0.45	-0.20	Y	2.76 ± 0.22	-0.24	Y
4	26.6 ± 1.6	+1.6	Y	8.34 ± 0.51	+0.34	Y	3.41 ± 0.25	+0.41	Y
5	25.2 ± 1.4	+0.2	Y	7.25 ± 0.44	-0.75	Y	3.00 ± 0.23	0.00	Y

*** 1σ -- Combined Standard Uncertainty, k=1 (one standard deviation)*

Rounding of acceptable range limited by uncertainty of reported result

Example Project Method Validation
Gamma Spectrometry Method for ^{241}Am in Ground Water

- Take time to carefully look over pages 7 and 8 of the Module 8 handout.
- Page 7 addresses validation requirements for ^{241}Am, and contains information on how our laboratory has proceeded. Page 8 is a (short) procedure.
- Using the information on pages 7 and 8, complete the Method Validation Review form on page 9 of the hand-out.
  - Does the method satisfy the project's MQOs?
- When you are done (and not before then!), check your answers on page 16 of the handout.

Example Project Method Validation
Alpha Spectrometry Method for ^{241}Am in Ground Water

- Obviously, the lab's hope that gamma spec would be an easy path forward did not work so well. The action levels may have been too low and results showed positive bias, possibly due to issues calibrating for the low-energy 59 keV line from ^{241}Am.
- Not shying away from a challenge, they undertake to use a more sensitive technique that combines radiochemical separations with alpha spectrometry measurements.
- Take time to carefully look over pages 10 through 14 of the Module 8 handout.
  - Page 10 addresses validation requirements for ^{241}Am and contains information on how our laboratory has proceeded.
  - Page 11-13 are a (short) procedure.
- Using the information on pages 10-13, complete the Method Validation Review form on page 14 of the hand-out.
- Does this method satisfy the project's MQOs?
- When you are done (and not before then!), check your answers on page 17 of the handout.