The Abdus Salam
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Workshop on Understanding and Evaluating Radioanalytical Measurement Uncertainty

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Stability of the Analytical System - Part II

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Understanding and Evaluating Radioanalytical Measurement Uncertainty

Stability of the analytical system

Part 2- Quality Control

A. Shakhashiro

8–16 November 2007ICTP, Trieste, Italy

IAEA

Atoms for Peace: The First Half Century

1957–2007

QC mechanism

Analytical results								
Nuclide	S-1-1		S1-2		S1-3		S1-4	
	Bq/kg	Unc	Bq/kg	Unc	Bq/kg	Unc	Bq/kg	Unc
Pb-210	78.4	3	64.0	3	70.4	4	74.5	3
Am-241	70.6	0.6	68.8	0.6	68.0	0.6	68.8	0.6
Cd-109	278.0	4	262.1	4	264.9	4	267	4
Cs-134	73.5	2	70.7	2	66.5	1.5	70.1	2
Cs-137	84.2	0.5	81.0	0.5	75.3	0.6	80.5	0.5
Mn-54	77.9	0.6	74.5	0.6	70.0	0.4	74.5	0.6
Zn-65	41.5	0.6	40.4	0.6	38.1	0.5	41.1	0.6
Co-60	100.3	0.6	95.7	0.6	91.8	0.8	96.6	0.6

Mean	STD	Rel. STD		
Bq.kg				u (%)
71.8	6.17	8.6%		4.2%
69.0	1.09	1.6%		0.9%
267.9	7.01	2.6%		1.5%
70.2	2.89	4.1%		2.8%
80.3	3.69	4.6%		0.6%
74.2	3.22	4.3%		0.8%
40.3	1.50	3.7%		1.5%
96.1	3.51	3.7%		0.6%

QC mechanism

Activities implemented before, during and after the analysis of a batch of samples aiming at:

- **Checking the conformity to the acceptance criteria,**
- **Validating analytical results,**
- **Assuring that the analytical process is under statistical control,**

QC mechanism

Activities implemented before starting the analysis:

- Trackability (samples, chemicals, instruments…)
- Traceability (balances, pipettes, temperature…..)
- Acceptance criteria,
- Reference materials, in-house reference materials, QC materials,
- Plan the sequence of QC elements to be used,
- Plan statistical tools to be used for QC data analysis (control charts)

QC mechanism elements

- Blank / Background
- Control sample
- Duplicate analysis
- Replicate analysis
- Certified Reference Material
- Spike sample
- Participation in PT

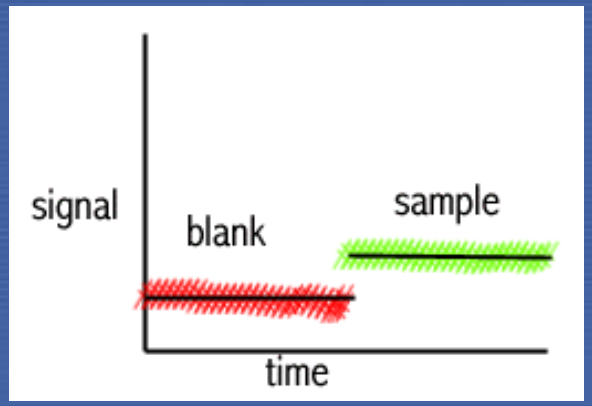
Blank / background

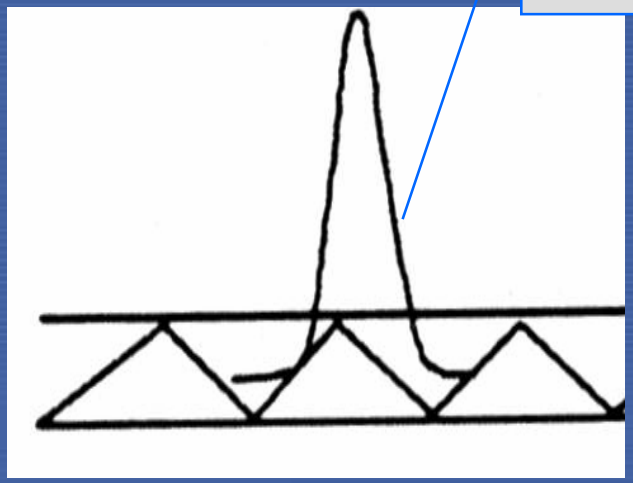
- **What is it?**
- **What for?**

The signal which is attributed to all parameters expect the analyte.

To check for any contamination in the system or in the reagents
To avoid any unexpected sources of uncertainty

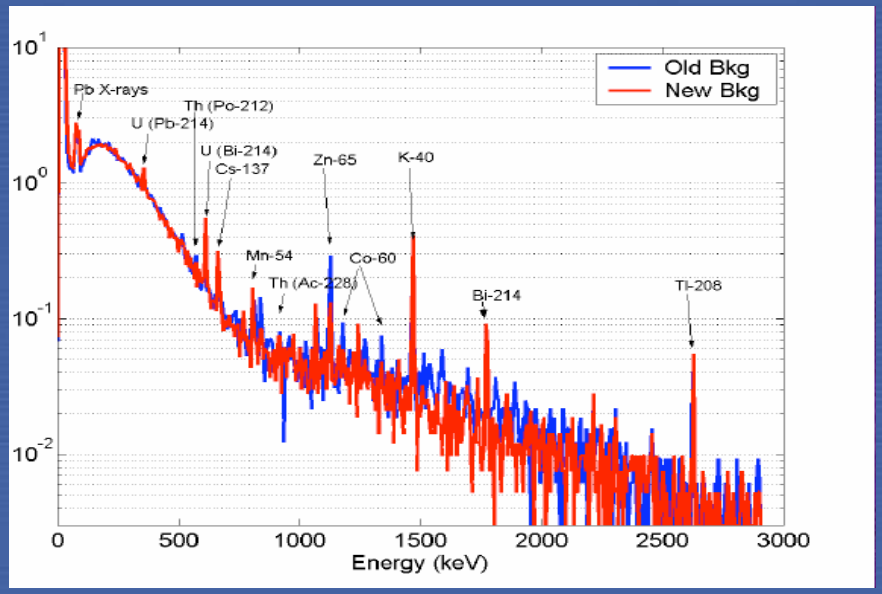
Signal/Noise=2-3





Blank / background

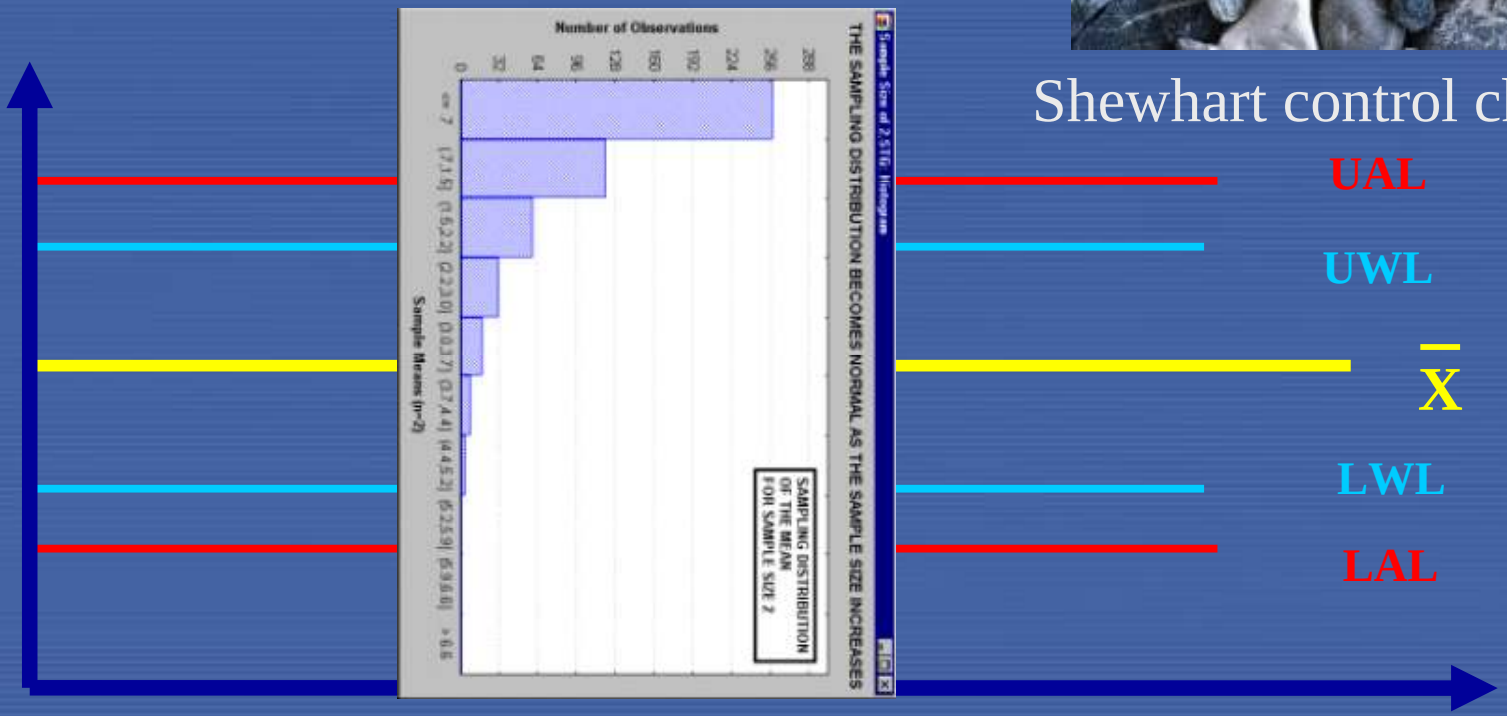
- To check the stability of the blank / background



Control sample

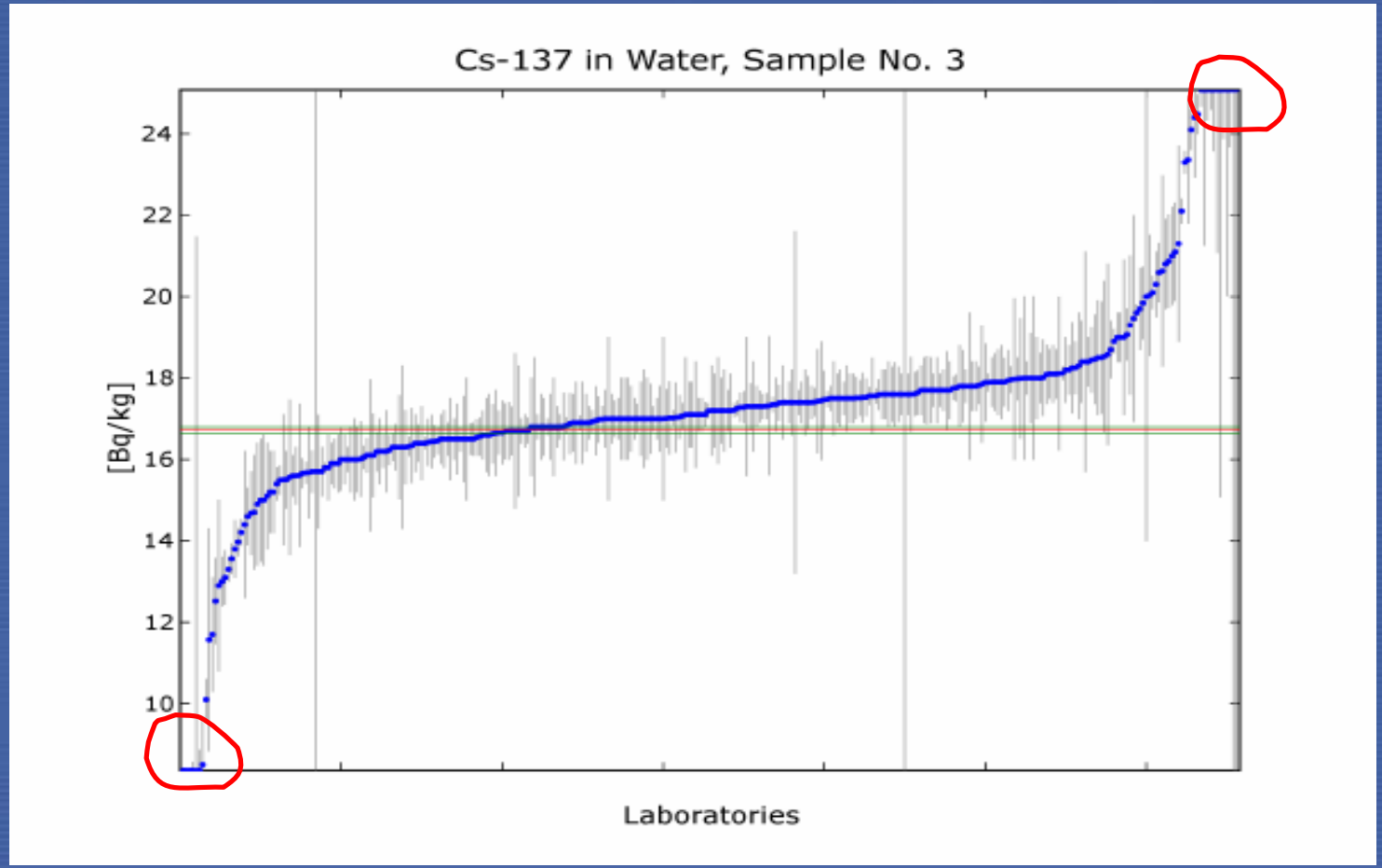
- **What is it?** Stable, homogenised, well characterized material
- **What for?** To monitor the performance of the analytical system (precision, trueness)

Shewhart control chart

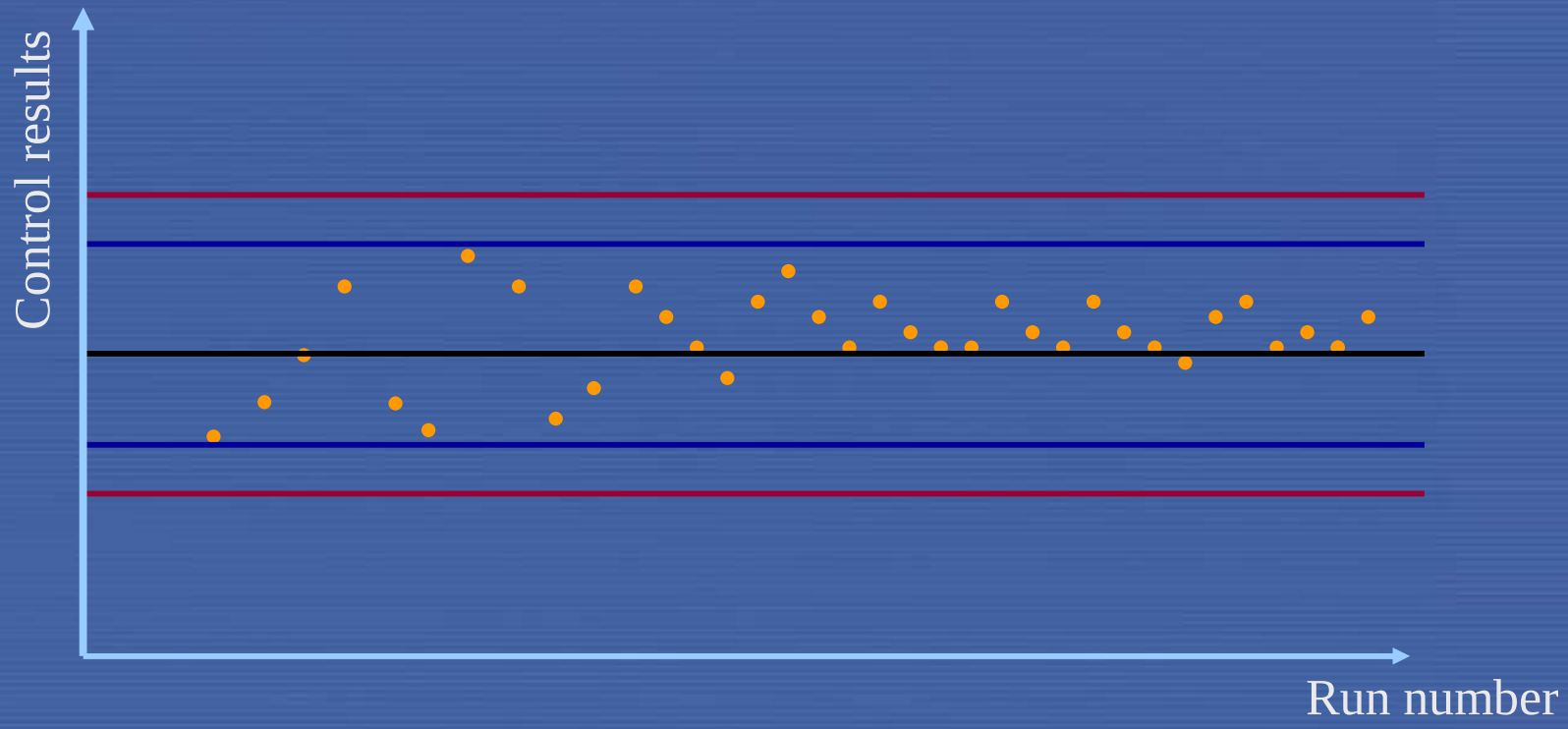


Control sample

IAEA-CU-2006-03 world wide open PT

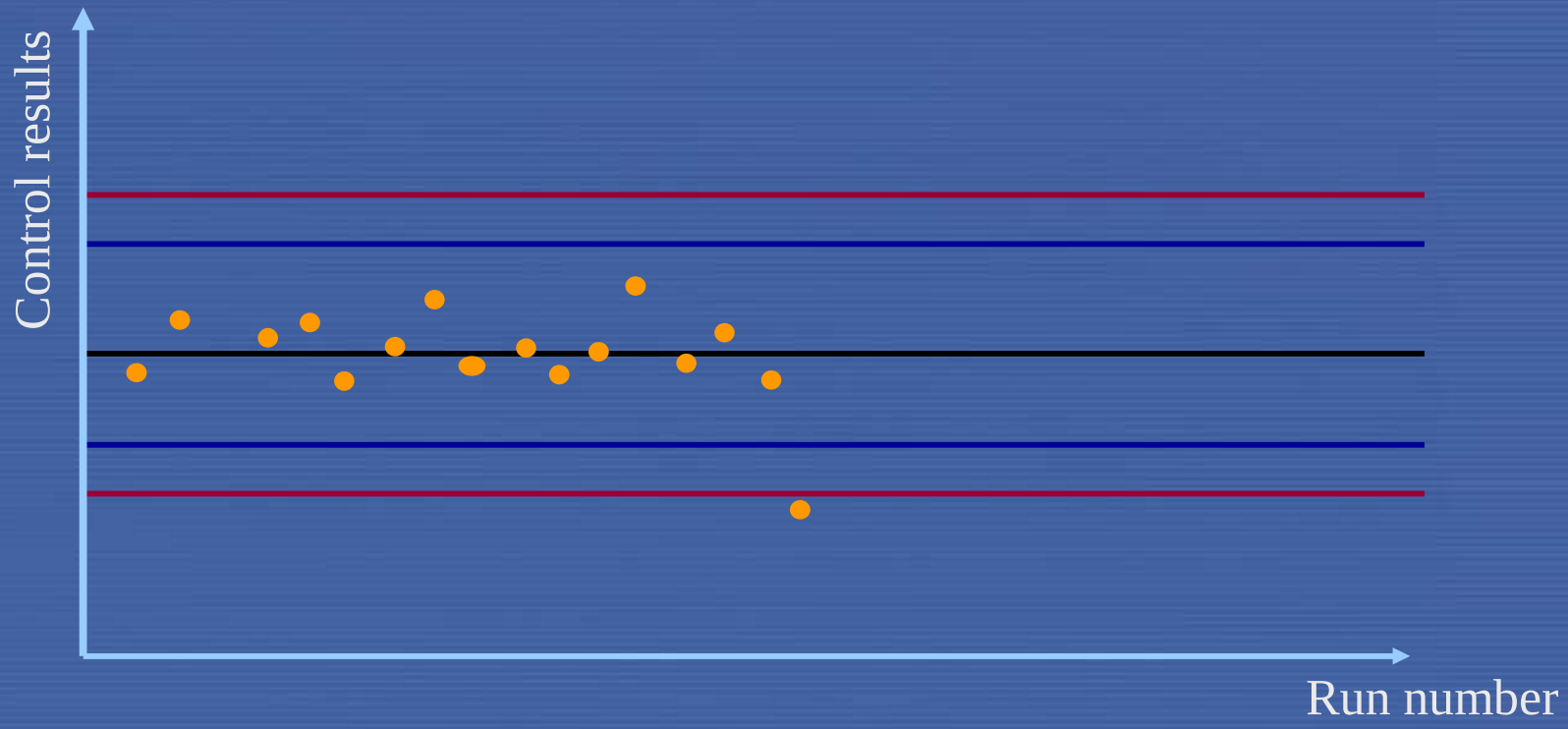


Control sample



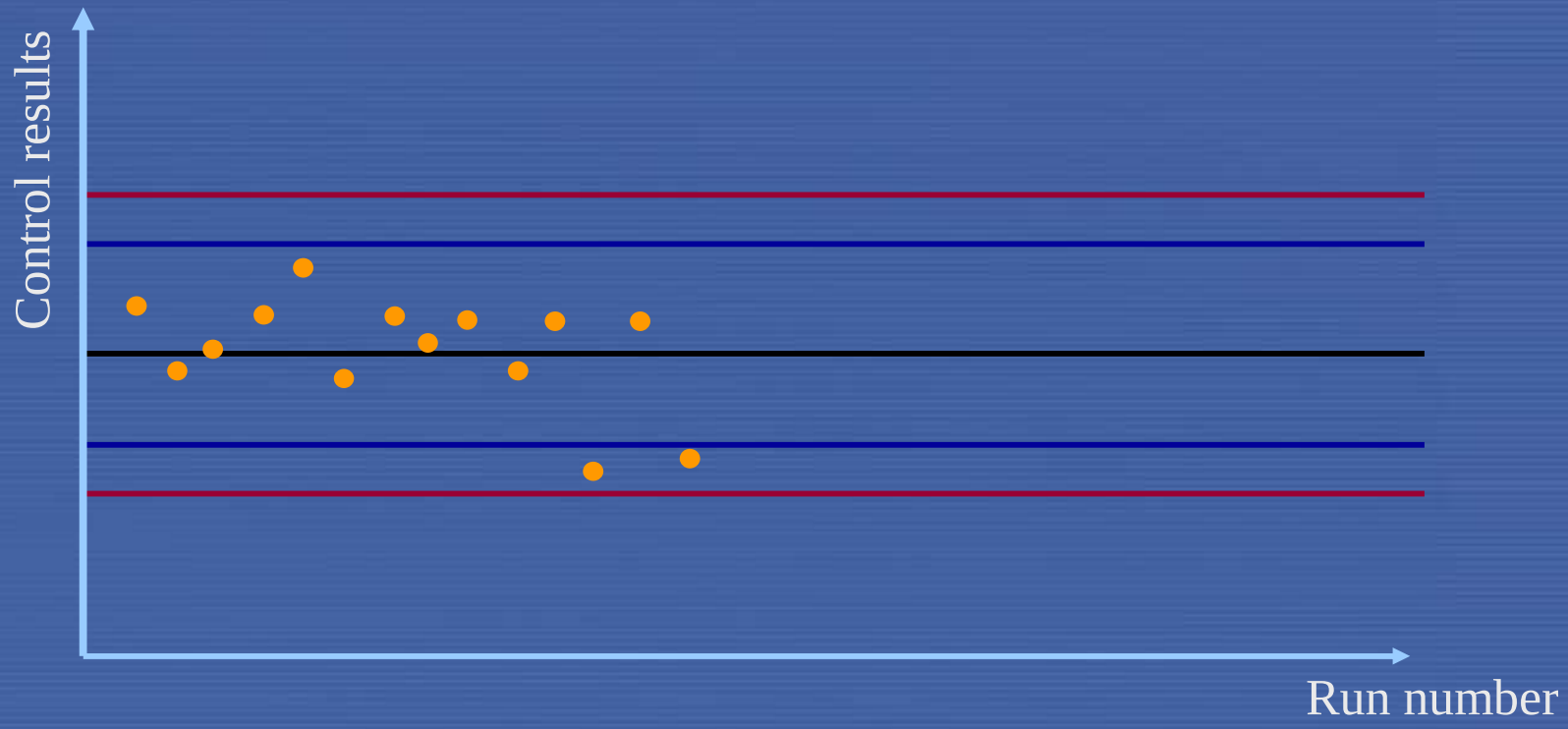
Control sample

One point at the action limit line



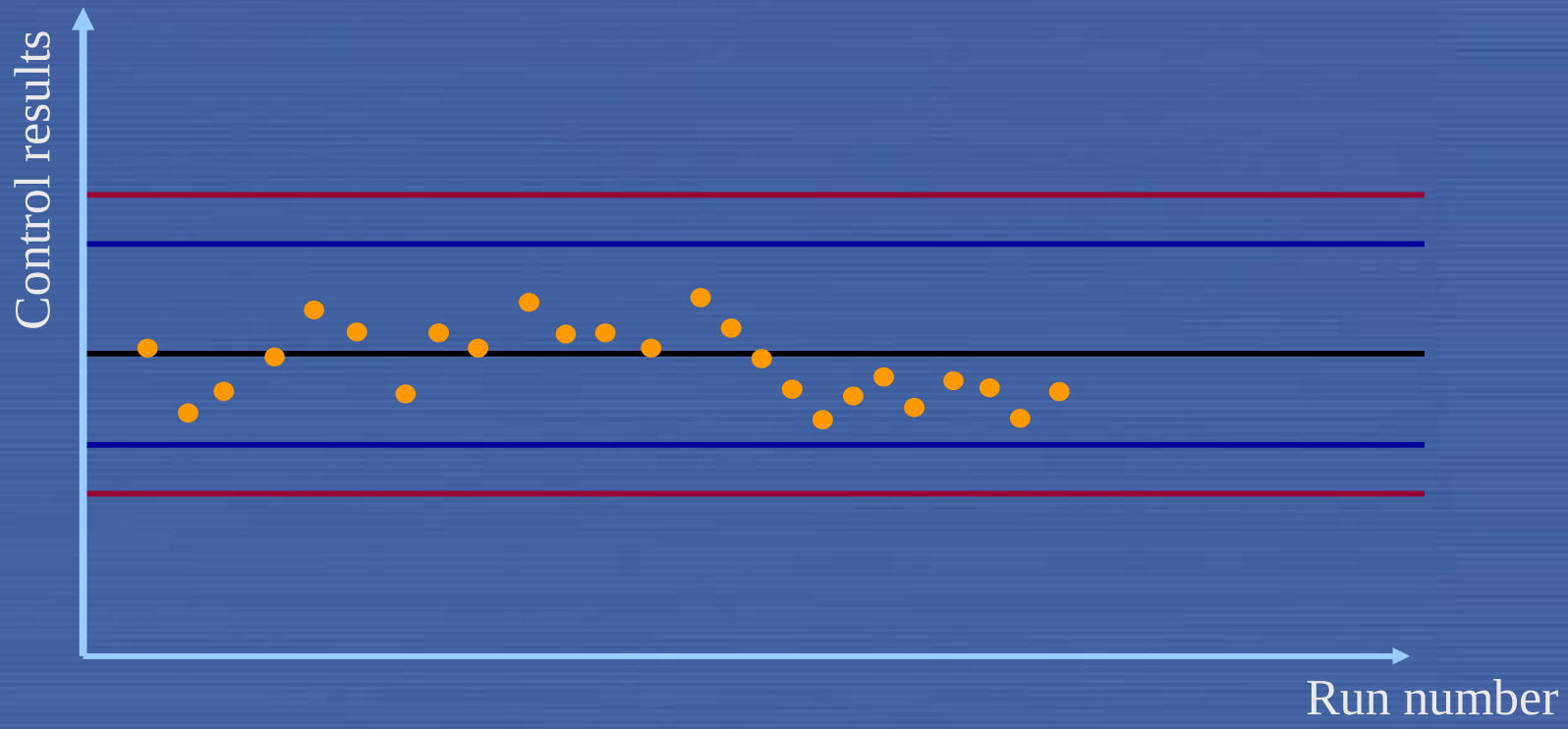
Control sample

2 points of 3 are out of lower warning limit line



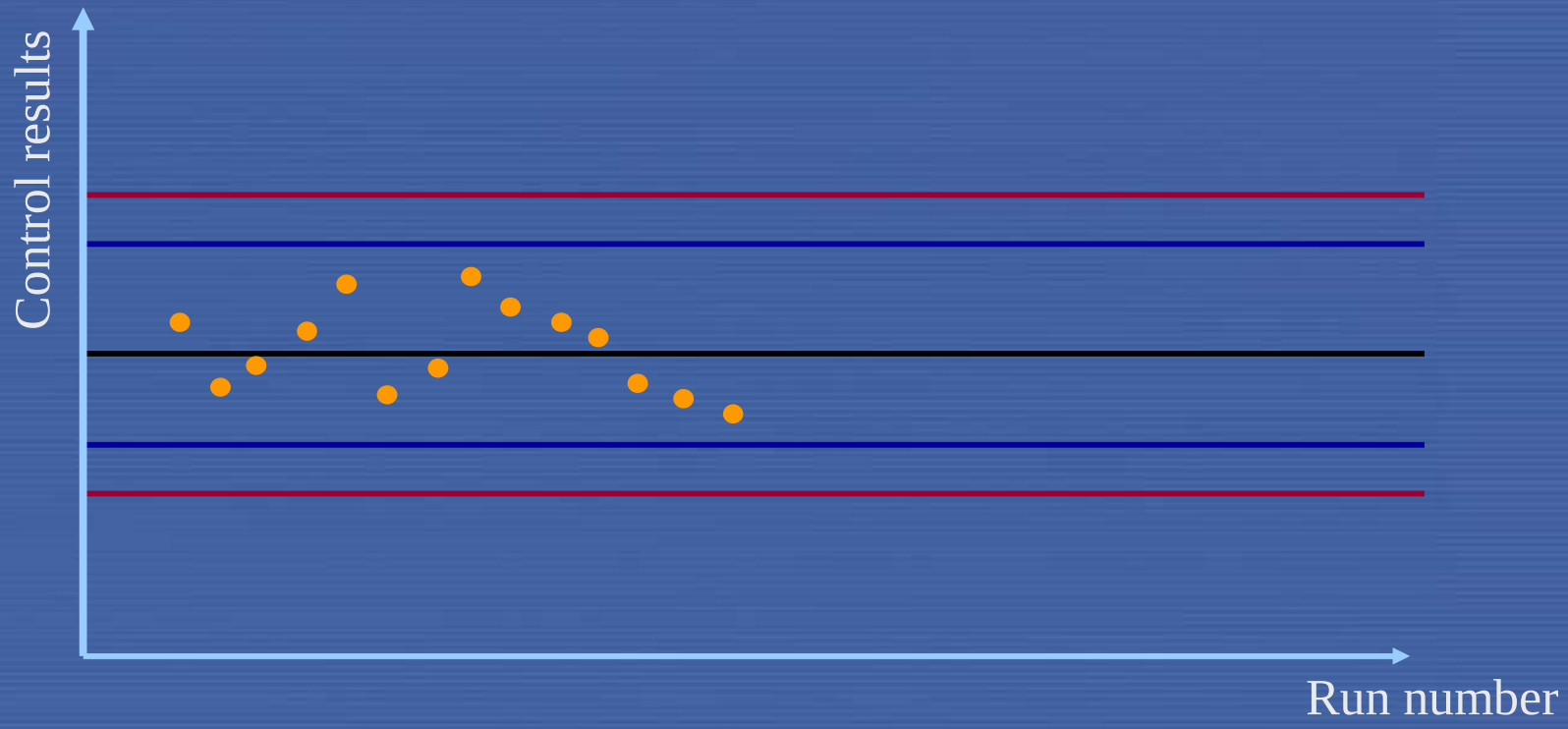
Control sample

10 consecutive points at the same side of the central line



Control sample

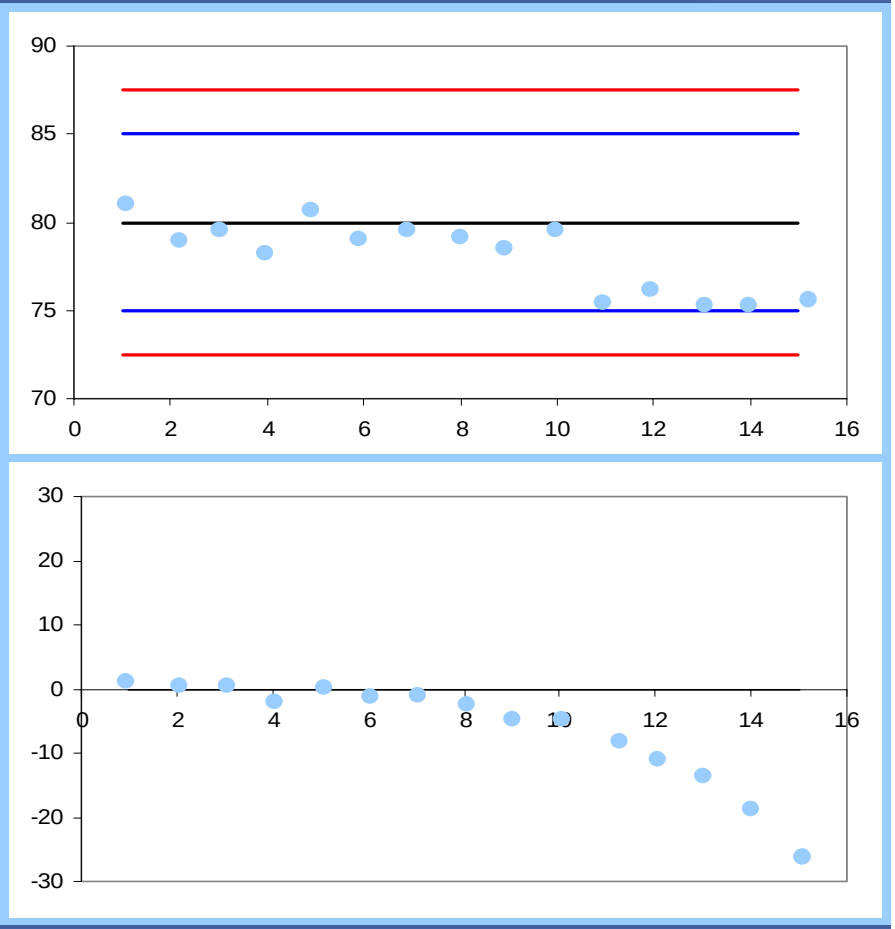
7 consecutive points have a distribution ascending or descending pattern



Control sample

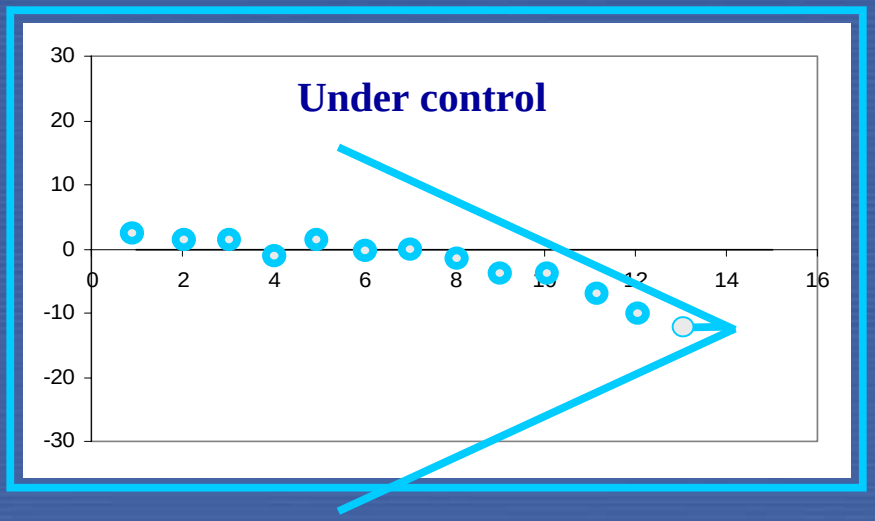
CUSUM chart

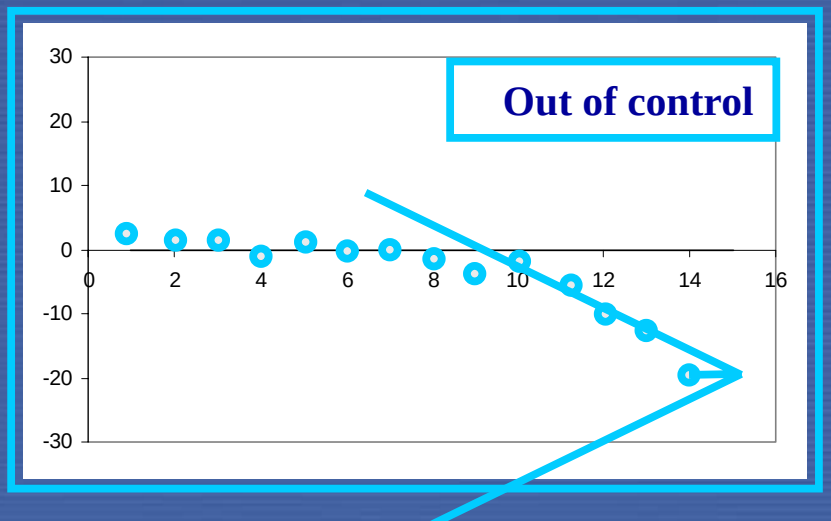
MV = 80	s = 2.5		
Nr.	X	X-MV	Cusum
1	82	+2	+2
2	79	-1	+1
3	80	0	+1
4	78	-2	-1
5	82	+2	+1
6	79	-1	0
7	80	0	0
8	79	-1	-1
9	78	-2	-3
10	80	0	-3
11	76	-4	-7
12	77	-3	-10
13	76	-4	-14
14	76	-4	-18
15	75	-5	-23

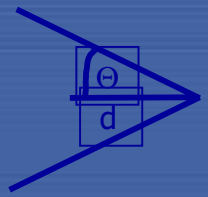


Control sample

- **Use V mask to check for out of control situation**







- **Choose d and Θ so that:**
  - **Min of false outliers observed when system under control**
  - **Can detect the out of control situation.**

Control sample

Advantages of CUSUM charts:

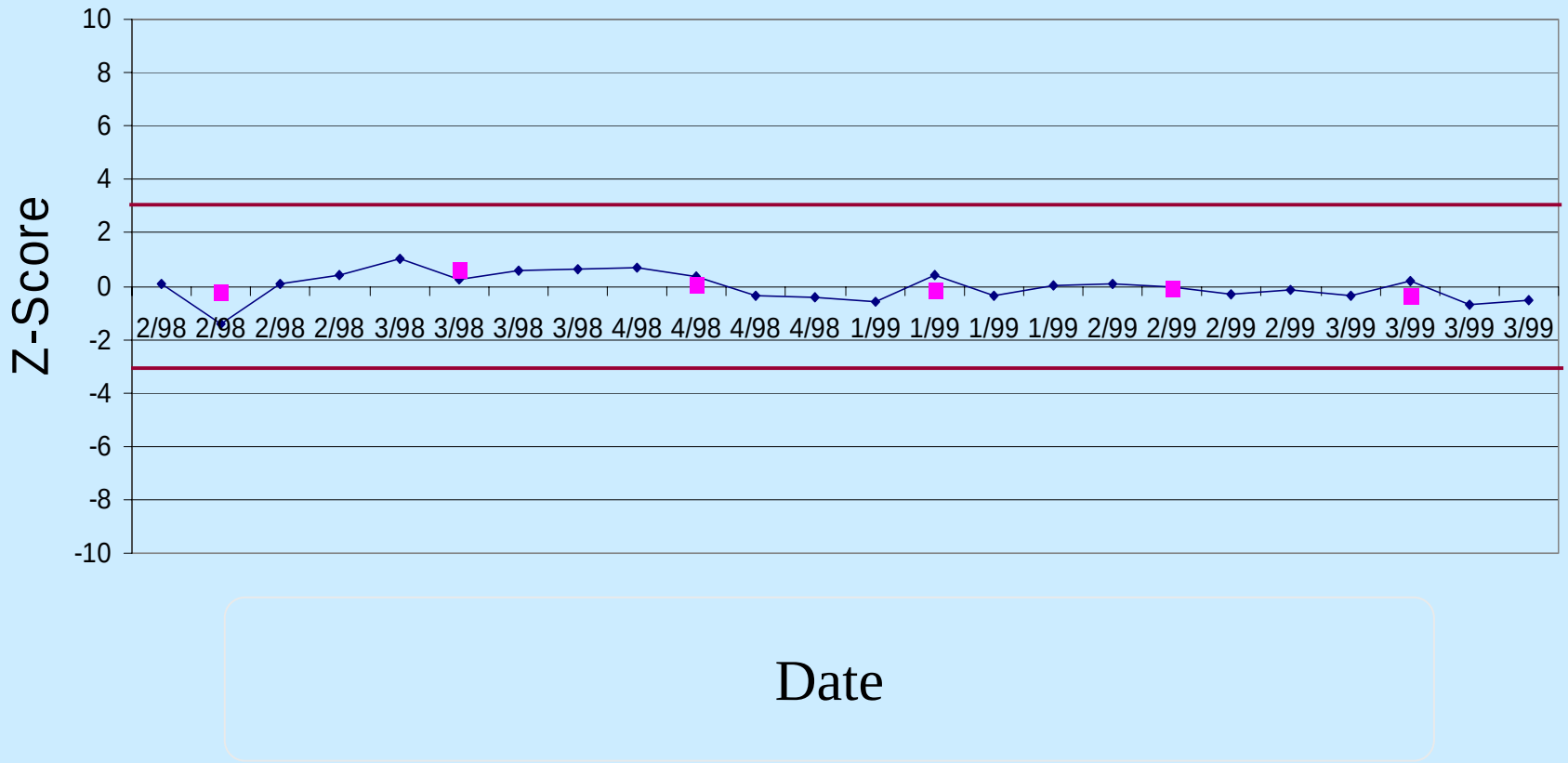
- **More clear when the process is out of control**
- **Needs less data to observe out of control situation**
- **The magnitude of the change can be estimated from the slope of the line.**

Z-score chart:

- Central line equal to zero
- Upper and lower warning limits equal to ± 2 STD
- Upper and lower action limits equal to ± 3 STD

$$\text{Z-score} = (X - \overline{X})/\text{STD}$$

Control sample



Control sample

Group exercise 1: (Five groups 20 Minutes)

A control samples was used to demonstrate the stability of ^{90}Sr determination, create Shewhart control chart and Z-score chart to monitor the data, comment the charts.

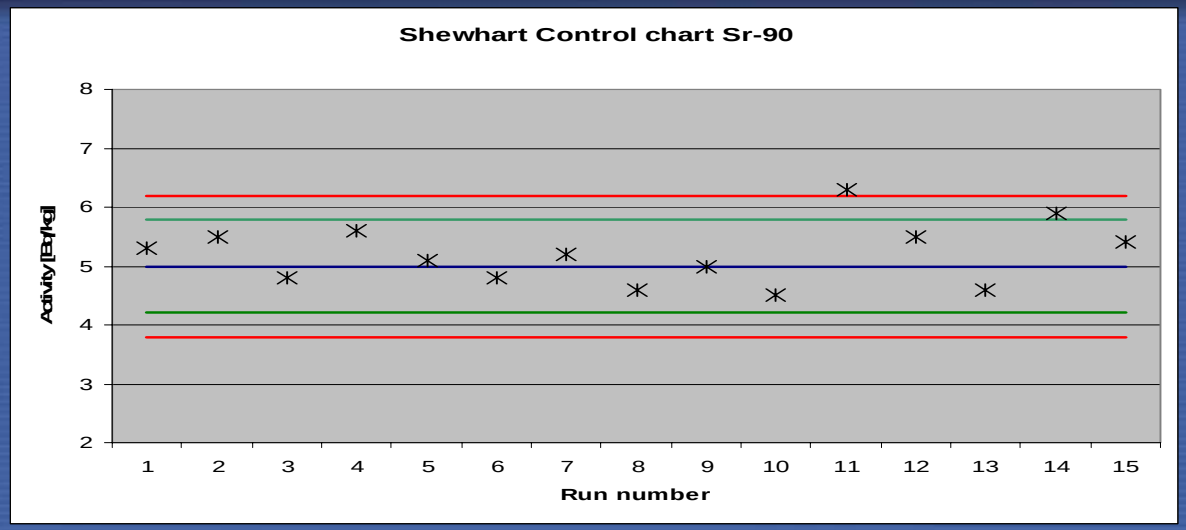
Mean value of ^{90}Sr: 5.0 $Bq.kg^{-1}$, Standard deviation: 0.4 $Bq.kg^{-1}$

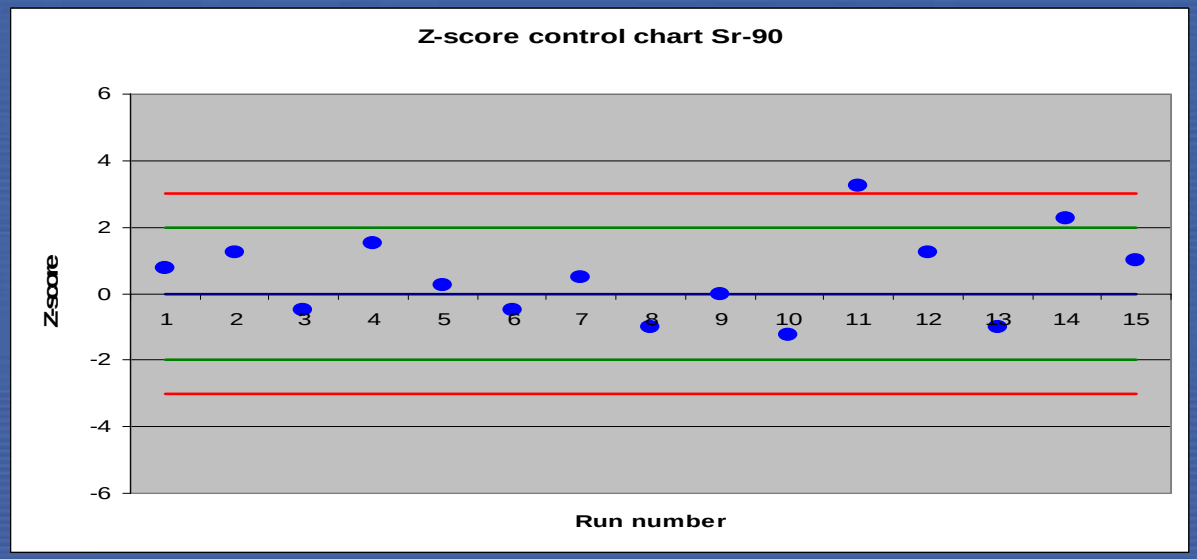
Run #	Measurement results
1	5.3
2	5.5
3	4.8
4	5.6
5	5.1

Run #	Measurement results
6	4.8
7	5.2
8	4.6
9	5.0
10	4.5

Run #	Measurement results
11	6.3
12	5.5
13	4.6
14	5.9
15	5.4

Control sample





Duplicate and replicate analysis

- Blank or Background
- Control sample
- Duplicate analysis
- Replicate analysis
- Certified Reference Materia
- Spike sample
- Participation in PT

The same sample is analysed in duplicate in repeatability conditions

The same sample is analysed in duplicate in reproducibility conditions

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Duplicate and replicate analysis

- Blank or Background
- Control sample
- Duplicate analysis
- Replicate analysis
- Certified Reference Material
- Spike sample
- Participation in PT

$$|d| < 2\sqrt{2} \times S_r$$

$$S_r = \sqrt{\sum_{I=1}^{I=n} (X_I - \bar{X})^2 / (n-1)}$$

$$|d| < 2\sqrt{2} \times S_R$$

$$S_R = \sqrt{\sum_{I=1}^{I=n} (X_I - \bar{X})^2 / (n-1)}$$

Use of Reference Materials

- Blank or Background
- Control sample
- Duplicate analysis
- Replicate analysis
- Certified Reference Material
- Spike sample
- Participation in PT

Use of Reference Materials

Main use of matrix CRMs:

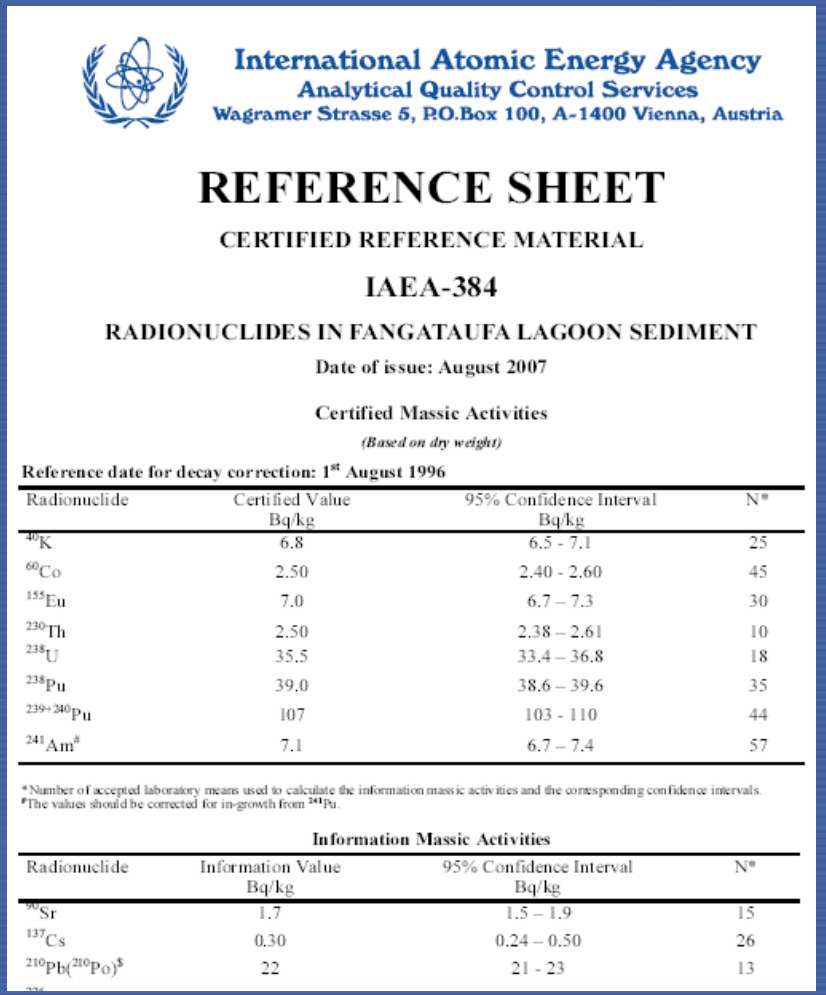
Comparison of measurement result with certified value, evaluate the method trueness.

- usually, U_{CRM} is given on certificates and must be transformed in u_{CRM}
- measurement uncertainty should be known. standard deviation of results can be used as (very!) rough estimate

Use of Reference materials

Notes on the use of RM (1)

- **Distinction between certified (recommended) and non certified (information) values**
- **Minimum sample intake**
- **Measurement method used**



International Atomic Energy Agency
Analytical Quality Control Services
Wagramer Strasse 5, P.O.Box 100, A-1400 Vienna, Austria

REFERENCE SHEET

CERTIFIED REFERENCE MATERIAL

IAEA-384

RADIONUCLIDES IN FANGATAUFA LAGOON SEDIMENT

Date of issue: August 2007

Certified Massic Activities

(Based on dry weight)

Reference date for decay correction: 1st August 1996

Radionuclide	Certified Value Bq/kg	95% Confidence Interval Bq/kg	N*
^{40}K	6.8	6.5 - 7.1	25
^{60}Co	2.50	2.40 - 2.60	45
^{155}Eu	7.0	6.7 – 7.3	30
^{230}Th	2.50	2.38 – 2.61	10
^{238}U	35.5	33.4 – 36.8	18
^{238}Pu	39.0	38.6 – 39.6	35
$^{239+240}Pu$	107	103 - 110	44
$^{241}Am^{\#}$	7.1	6.7 – 7.4	57

*Number of accepted laboratory means used to calculate the information massic activities and the corresponding confidence intervals.
#The values should be corrected for in-growth from ^{241}Pu.

Information Massic Activities

Radionuclide	Information Value Bq/kg	95% Confidence Interval Bq/kg	N*
^{90}Sr	1.7	1.5 – 1.9	15
^{137}Cs	0.30	0.24 – 0.50	26
$^{210}Pb(^{210}Po)^{\$}$	22	21 - 23	13

Use of Reference materials

Notes on the use of RM (2)

- **Moisture correction,**
- **Moisture determination procedure,**
- **Same method as for certification must be used,**
- **Storage of opened materials should not be done,**

Dry weight determination: The average moisture content of the lyophilized sample after bottling, determined by drying several aliquots in an oven at 80 °C to constant weight (1-2 days), was found to be approximately 1.3%. Since the moisture content can vary with ambient humidity and temperature, it is recommended that the water content should be checked prior to analysis and that all results should be reported on a dry-weight basis

Notes on the use of RM (3)

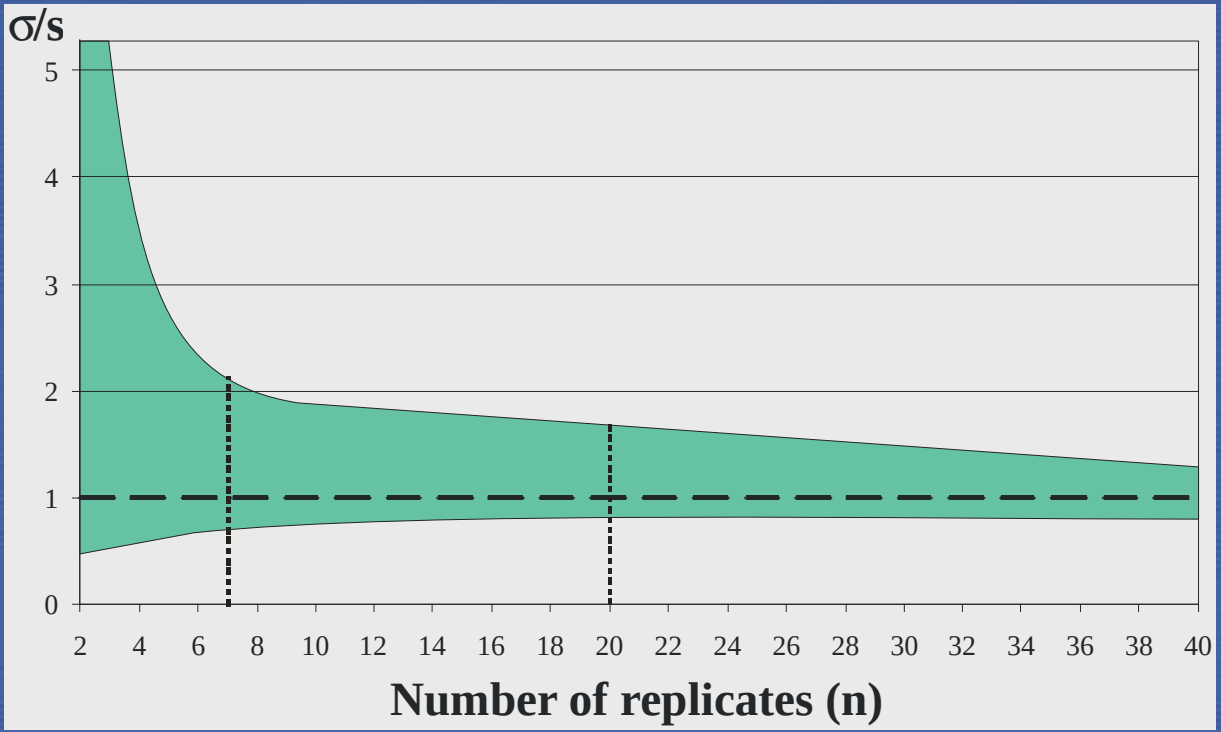
- **Matrix Match**
- **Analyte or value level Match**
- **As close as possible to real samples**
- **As comparable as possible to real samples**
- **Homogeneity**
- **Segregation**

Notes on the use of RM (4)

- **Uncertainty fits for the purpose**
- **Stability during the shipment and shelf life**
- **Storage conditions:**
  - **Secure area, environmental conditions, stock**
  - **A procedure for RM management in the lab.**
  - **Master list, Trackability records**
  - **Designated responsible for RM in the Lab.**
  - **Not to be used for every day QC**

Notes on the use of RM (5)

Number of required replicates



Data evaluation (1)

I analyzed the RM several times, how do I locate a single outlier?

Dixon test or Grubbs test (G') for single outlier

How do I locate a pair of outliers in a set of experimental results?

Grubbs test (G'' and G''') for outlying pairs

Data evaluation (2)

Dixon test

The results must be ranked in order of magnitude. The appropriate ratios are calculated and the largest value of these is compared with the tabulated critical value at either the 95% or 99% significance level.

*Note: The Dixon test criterion varies depending on the size of the sample **n**.*

$$for \quad 3 \le n \le 7 \qquad D_{lowest} = \frac{x_2 - x_1}{x_n - x_1} \qquad D_{highest} = \frac{x_n - x_{n-1}}{x_n - x_1}$$

$$for \quad 8 \le n \le 12 \qquad D_{lowest} = \frac{x_2 - x_1}{x_{n-1} - x_1} \qquad D_{highest} = \frac{x_n - x_{n-1}}{x_n - x_2}$$

$$for \quad 13 \le n \le 40 \qquad D_{lowest} = \frac{x_3 - x_1}{x_{n-2} - x_1} \qquad D_{highest} = \frac{x_n - x_{n-2}}{x_n - x_3}$$

Data evaluation (3)

Group exercise 2: 20 min,

Outliers testing: Dixon Test

Analysis results of 7 independent determinations of Cs-137 in a CRM gave the following figures:

8.6
8.4
8.5
8.4
9.13
8.3
8.2

Apply Dixon test and check for any outliers

Data evaluation (4)

Measures of location

- **Arithmetic mean**

$$\bar{x} = \frac{\sum_{i=1}^{n} x_i}{n}$$

If the sample is random then $\bar{x}$ is the best estimate of μ (the population mean).

- **Median**

$$\tilde{x} = \begin{cases} x_m & when \quad n \quad is \quad odd \quad 1,\ 3,\ 5,\ \ldots \\ \dfrac{x_m + x_{m+1}}{2} & when \quad n \quad is \quad even \quad 2,\ 4,\ 6,\ \ldots \end{cases}$$

where m = roundup (n/2). For symmetrical distribution the mean and median have the same value. The median is more robust, is that it is unaffected by extreme values.

- **Mode**

The value of the variable that occurs most frequently. The presence of two or more modes usually indicates a non-homogeneous data set. For a symmetrical distribution the mode usually coincides with the mean and the median.

Data evaluation (5)

Measures of dispersion (1)

- **Variance**

  Data can be classified in two forms, population and sample, according to the context used.

$$\sigma^2 = \frac{\sum_{i=1}^{n}(x_i - \mu)^2}{n}$$

Population

$$s^2 = \frac{\sum_{i=1}^{n}(x_i - \bar{x})^2}{n-1}$$

Sample

- **Standard deviation**

$$\sigma = \sqrt{\frac{\sum_{i=1}^{n}(x_i - \mu)^2}{n}}$$

Population

$$s = \sqrt{\frac{\sum_{i=1}^{n}(x_i - \bar{x})^2}{n-1}}$$

Sample

Data evaluation (6)

Measures of dispersion (2)

- **Standard deviation of the mean (standard error)**

$$s_{\bar{x}} = \frac{s}{\sqrt{n}} \qquad \left(\bar{s} \quad or \quad s_E\right)$$

The sample standard deviation of the mean is less than standard deviation of a sample because it is an estimation of the variation that would arise if repeated samples were taken from the population.

- **Range**

The difference between the highest and lowest values in a set of results. It is only useful when dealing with a very small sample size. However, it tends to convey distorted information about larger samples since the appearance of an outlier is probable.

Data evaluation (7)

Measures of dispersion (3)

- **Relative standard deviation**

$$RSD = \frac{s}{\bar{x}}$$

The measure of the spread of data in comparison to the mean of the data.

- **Coefficient of Variation**

$$CV = RSD\% = \frac{s}{\bar{x}} \times 100$$

The relative standard deviation expressed as a percentage.

Data evaluation (8)

I analyzed the RM several times, how do I evaluate the Trueness

There is essentially no evidence for a bias if the following criteria are met:

$$-2\sqrt{u_{CRM}^2 + s^2} \leq \bar{x} - \mu \leq +2\sqrt{u_{CRM}^2 + s^2}$$

where S is the precision of the method under investigation. The u_{CRM} is the standard uncertainty for the CRM.

The bias detection is limited to a minimum of twice the standard uncertainty of the certified value of the CRM.

Data evaluation (9)

Group Exercise 3, 20 Min.

Evaluate the **trueness** of a method for the determination of Co-60 in water, using a CRM sample. The mean of the replicate measurement results was 57.6 Bq kg^{-1} . The standard uncertainty was 1.17 Bq kg^{-1}. The certified value for the CRM is 60.1 Bq kg^{-1} with an expanded uncertainty of 2.5 Bq kg^{-1}. k = 2.

Is there any evidence of a bias in the determination?

$$\bar{x} - \mu = 57.6 - 60.2 = -2.5$$ and $$2 \times \sqrt{u_{CRM}^2 + s^2} = 2 \times \sqrt{\left(\frac{2.5}{2}\right)^2 + 1.17^2} = 3.42$$

$$(-3.42 \le -2.5 \le +3.42)$$

There is no evidence of a significant bias in the method.

Data evaluation (10) Case study

IAEA-375: ***RADIONUCLIDES AND TRACE ELEMENTS IN SOIL***

Cert. value for ^{241}Am: 0.13±0.02 Bq.kg^{-1} , p=95 %, n=6 labs

Results of 6 determinations are: 0.15, 0.16, 0.17, 0.18, 0.14, 0.19

The mean value: 0.165 Bq.kg^{-1}; 0.019 Bq.kg^{-1};

Is there any need for bias correction?

RM uncertainty is CI, p=95 %, df= 5 (6-1)

$t_{0.05,5}$=2.571

uRM=CI/t= 0.02/2.571=0.0078

$$u_t = \sqrt{\frac{s^2}{n} + u_{RM}^2} = \sqrt{\frac{0.019^2}{6} + 0.0078^2} = 0.011 Bq/kg$$

Even for k=2 there is no difference, NO NEED for CORRECTION

Data evaluation (11)

Comparison and Significance Testing

- **Comparing results or averages with one another**

  I used a RM using two different matrix correction method, Is there a real difference between the two sets of results?

Student t-Test (paired samples comparisons)

Student t-Test (comparison of two independent sets of data)

- Assuming equal variances

- Assuming unequal variances

Data evaluation (12)

Statistical Information Relating to Methods

What do I do if I need to evaluate the method repeatability and reproducibility?

One-way ANOVA (analyze the same sample in triplicate in different days, operators, systems)

ANOVA: s within = repeatability (sr)
s between = reproducibility

Prerequisites:

- Stability of the RM (over the whole duration)
- Homogeneity, bb, wb (substantial amount of sample)
- Commutability

Data evaluation (13)

Statistical Information Relating to Methods

Precision or spread of data

Is my new method performing to the same precision than the one previously used?

F-Test (if you have a set of data on the same material for each method)

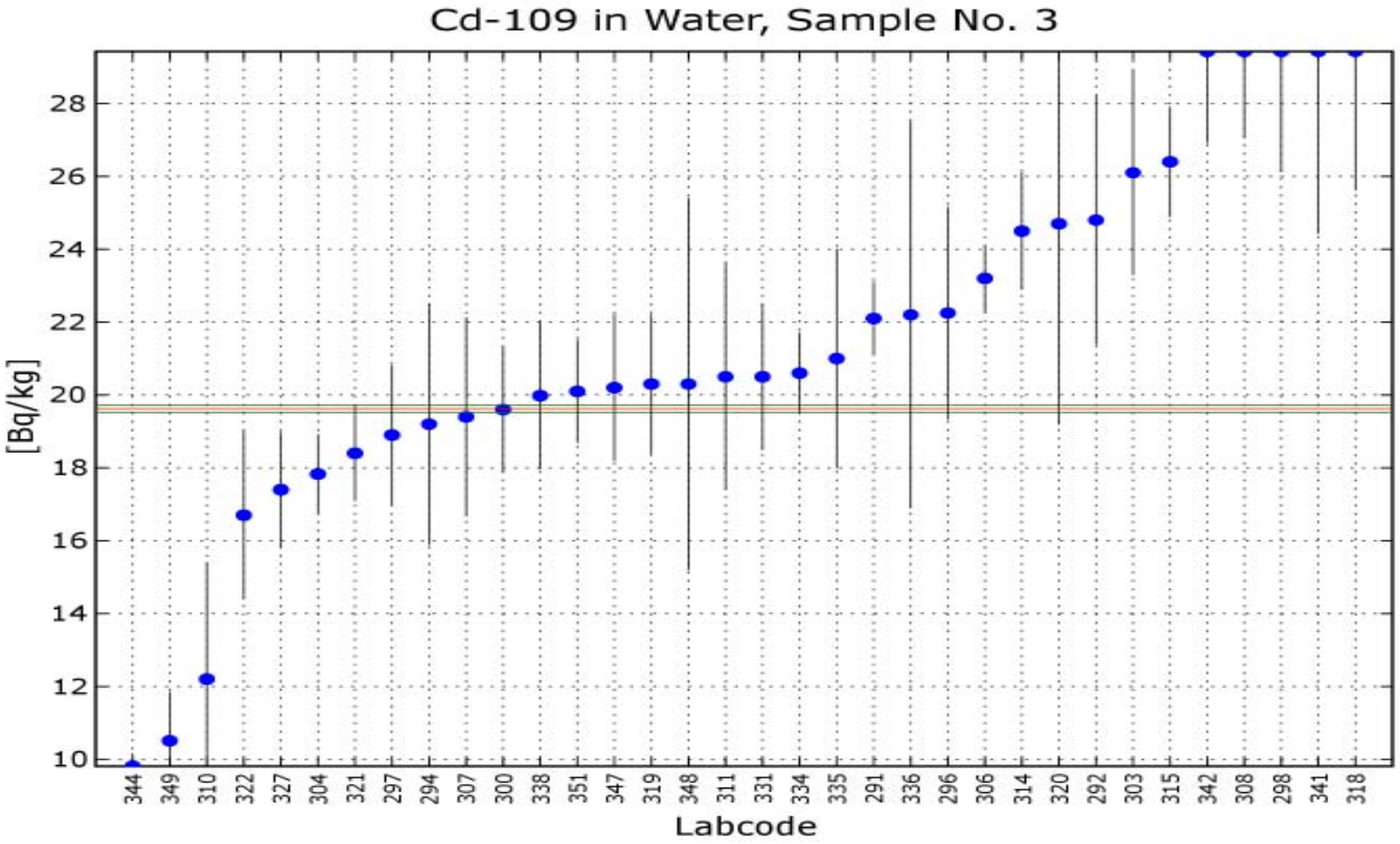
Spike sample

To check the matrix effect

To validate the applied corrections

$$\text{Recovery}(\%) = (C_{ss} - C_{us}) / C_{sa} \times 100$$

Spike sample



Participation in proficiency testing

Before participating in a PT verify

- The relevance of the organized proficiency testing scheme
- Quality of the PT
  - Sample preparation
  - Homogeneity testing
  - Stability evaluation
  - How the target values were assigned?
  - How the associated uncertainties were evaluated?
  - Scoring system,
  - Uncertainty evaluation
  - Reporting

Participation in proficiency testing

Understanding PT results

- Variations in performance is “natural”
- PT is within a complete QAS
- PT is a retroactive snapshot
- PT is not a way of method validation
- PT Provides an indication of an analytical problem
- Looking for the root cause of problem,
- Corrective actions, rechecking, monitoring
- Success for one analyte does not indicate that a laboratory is equally competent in determining an unrelated analyte
- Self scoring

Use of Method validation data in estimation uncertainty

Measurement uncertainty comprises

- **uncertainty due to repeatability (s_r)**
- **uncertainty due to reproducibility (s_R)**
- **uncertainty due to trueness (u_t)**

$$U = k\sqrt{s_r^2 + s_R^2 + u_t^2}$$

Use of Method validation data in estimation uncertainty

u_t determined from measurement of CRMs

- several replicate measurement of a CRM
- test whether significant difference
  - yes: either method revision or bias correction
  - no: estimate u_t

$$u_t = \sqrt{\frac{s_t^2}{n_t} + u_{RM}^2}$$

Finally

- Record the QC results for monitoring,
- Monitor the system stability,
- Work on the evaluation of measurement uncertainty,
- Based on QC and method validation data check your estimate of uncertainty,


THANK
YOU!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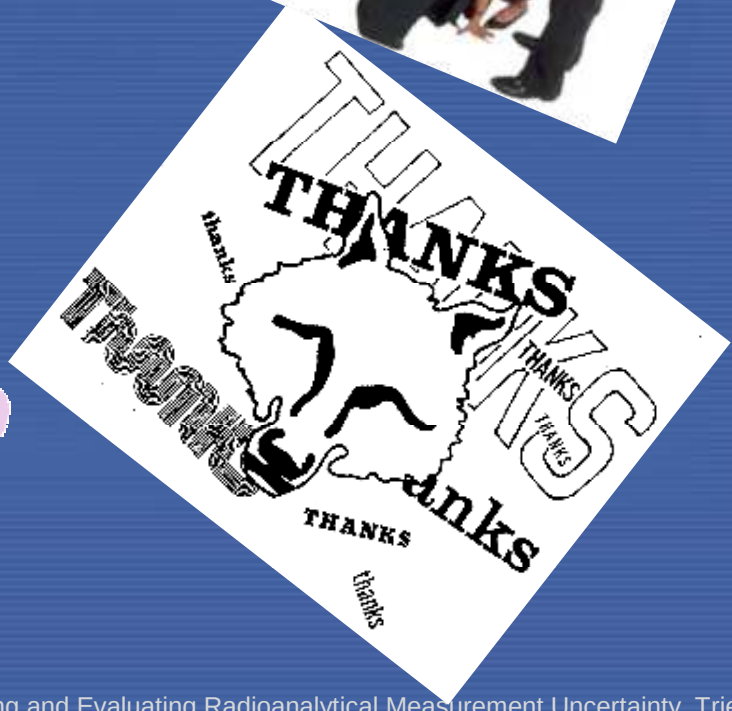
Many thanks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