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Accuracy profile: an efficient tool for a fair evaluation of analytical techniques and instruments

光 Spectroscopy Forever
Consulting and Training

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Several ages of a researcher

- When you are young, you describe what you are *currently doing*.
- When you become a big name, you are asked to define the *future*.
- One day, you are invited to speak about *history, my memories of…* (except if you remember very little or have done little worth remembering!).

☞ (*Aut tace aut loquere meliora silentio*).

Another ICP-based lecture?

My research interests have been focused on spectrochemistry of plasmas and lasers from fundamental, analytical and instrumental aspects based on the following types of plasma: i) the inductively coupled plasmas (**ICP**); ii) the microwave-induced plasmas (MIP) sustained by propagation of surface waves; iii) the hollow-cathode plasmas; and iv) the laser-produced plasmas (LPP).

Therefore, it could have been an:

Inestimable **C**reative **P**resentation to discuss about
Incredibly **C**omplex **P**roblems so as to suggest
Innovative **C**ontribution **P**ossibilities for
Informative **C**haracterization **P**rocedure so as to obtain
Interesting **C**hallenging **P**erformance of **ICP**.

Current position

- However, since I am retired from my academic duties, I can select what I wish to do, with avoiding any bureaucracy or paperwork.

☞ *Consulting and training*

Consulting and training

- Validation of method
- Calibration (strategy, optimization…)
- Limits of detection/quantitation
- Specs
- Method development
- Use of laser in atomic spectrometry (LIBS, Laser ablation).
- Microsamples.
- …..

☞ Accuracy profile

Accuracy

- Until the beginning of the 1990s, “accuracy” was the difference between experimental measurements and a true, or correct, or accepted value.
- However, there was already a trend to include not only a systematic bias but also random errors: “Accuracy may be estimated by proper evaluation of both systematic and random errors”*.

*Compendium of Analytical Nomenclature, 2nd Edition, H. Freiser and G.H. Nicolas (Eds), Blackwell, Oxford, 1987.

Accuracy

- In 1993, the ISO 3534-1 standard introduced a new term, “trueness”.
- Trueness is the closeness of agreement between the average value obtained from a large series of test results and an accepted reference value.
- Accuracy became the sum of:
  - trueness (systematic errors)
  - and precision (random errors).

Accuracy

- The most recent version of the VIM used the same approach and added some notes to emphasize the difference between accuracy and trueness, e.g. para 2.13, note 2: The term "measurement accuracy" should not be used for measurement trueness and the term measurement precision should not be used for "measurement accuracy"

Appropriate use of accuracy

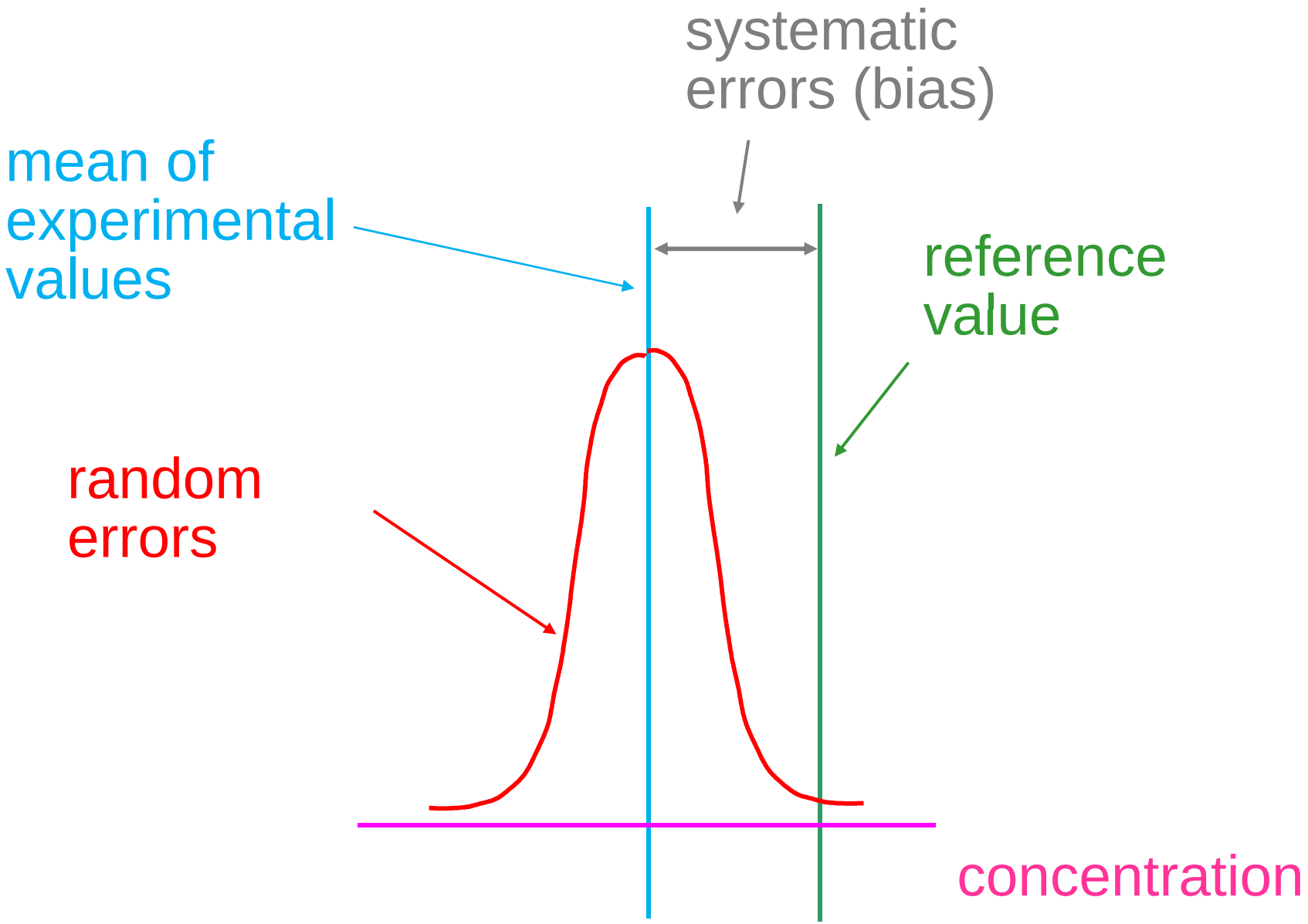
- However, a survey of publications in the field of atomic spectrometry shows that accuracy is still widely used with the former meaning, which may bring some confusion for the readers.

Trueness

- Trueness can be expressed either as a bias or as a percentage recovery. Ideally, trueness should be verified by using certified reference materials (CRMs). An alternative is the involvement in interlaboratory (round-robin) experiments.

Precision

- Precision is a broad term that includes:
  - instrumental repeatability,
  - method repeatability,
  - intermediate precision,
  - intralaboratory (internal or within-laboratory)
  - interlaboratory (between-laboratory) reproducibility.
- As intermediate precision and reproducibility imply that at least one condition is changed, it is important to clearly specify the conditions changed and unchanged, to the extent practical, as noted by the VIM.


systematic
errors (bias)
mean of
experimental
values
reference
value
random
errors
concentration

Accuracy profile

- The potential of a given method is, therefore, clearly defined by its accuracy.
- The study of accuracy over a large range of concentrations, including low levels, provides a so-called accuracy “profile”.
- From this profile, experimental tolerance intervals as a function of the concentration are obtained for the accuracy, which have to be compared with acceptability limits fixed by the analyst.

Fields of applications

- The accuracy profile method was already used mainly in the field of separation methods by estimating the bias and the intermediate precision, using several experiments per day, and repetitions over several days

References

- New advances in method validation and measurement uncertainty aimed at improving the quality of chemical data, M. Feinberg B. Boulanger, W. Dewé, Ph. Hubert, *Anal. Bioanal. Chem*., **380** (2004) 502–514.
- Harmonization of strategies for the validation of quantitative analytical procedures. A SFSTP proposal—part I, Ph. Hubert, J.-J. Nguyen-Huu, B. Boulanger, E. Chapuzet, P. Chiap, N. Cohen, P.-A. Compagnon, W. Dewé, M. Feinberg, M. Lallier, M. Laurentie, N. Mercier, G. Muzard, C. Nivet, L. Valat, *J. Pharm. Biomed. Anal*., **36** (2004) 579–586.
- Accuracy profiles from uncertainty measurements, A. Gustavo González, M. Ángeles Herrador, *Talanta* **70** (2006) 896–901.

- Harmonization of strategies for the validation of quantitative analytical procedures. A SFSTP proposal – Part II, Ph. Hubert, J.-J. Nguyen-Huu, B. Boulanger, E. Chapuzet, P. Chiap, N. Cohen, P.-A. Compagnon, W. Dewé, M. Feinberg, M. Lallier, M. Laurentie, N. Mercier, G. Muzard, C. Nivet, L. Valat, E. Rozet, *J. Pharm. Biomed. Anal.*, **45** (2007) 70–81.
- Harmonization of strategies for the validation of quantitative analytical procedures A SFSTP proposal–Part III, Ph. Hubert, J.-J. Nguyen-Huu, B. Boulanger, E. Chapuzet, N. Cohen, P.-A. Compagnon, W. Dewé, M. Feinberg, M. Laurentie, N. Mercier, G. Muzard, L. Valat, E. Rozet, *J. Pharm. Biomed. Anal.,* **45** (2007) 82–96.
- Harmonization of strategies for the validation of quantitative analytical procedures: A SFSTP proposal. Part IV. Examples of application, Ph. Hubert, J.-J. Nguyen-Huu, B. Boulanger, E. Chapuzet, N. Cohen, P.-A. Compagnon, W. Dewé, M. Feinberg, M. Laurentie, N. Mercier, G. Muzard, L. Valat, E. Rozet, *J. Pharm. Biomed. Anal.*, **48** (2008) 760–771.

Interlaboratory approach

- An alternative to within-laboratory experiments is an interlaboratory approach. Besides a possible feedback for laboratories that provided outlier results, more information can be obtained from such a testing, by adapting the accuracy profile to collaborative studies*.
- When several studies are performed with different analyte concentrations, it is possible to plot an accuracy profile that takes into account the bias of the collaborative study and the interlaboratory reproducibility, based on a large number of participating laboratories.

*Interpretation of interlaboratory validation of analytical methods based on accuracy profiles, M. Feinberg, G. Granier, J.M. Mermet, J. of the AOAC INTERNATIONAL, 93 (2010) 725-733.

Accuracy computation

- Accuracy is computed based on the standards ISO 5725-1, 5725-4 and 21748.
- This series of standards was mainly written for interlaboratory experiments, but can also be applied to within-laboratory experiments. In this case, the experimental tolerance intervals for accuracy are equal to:

tolerance intervals = reference value + bias $\pm$ *intermediate precision*

Intermediate precision

- VIM: same measurement procedure, same location, and replicate measurements on the same or similar objects over an extended period of time, (but may include other conditions involving changes).
- The intermediate precision is equal to $k_s.s_R$, k_s being a coverage factor or Mee* factor, and s_R being the standard deviation of the intermediate precision.

*R.W. Mee, β-expectation and β-content tolerance limits for balanced one-way ANOVA random model, Technometrics 26(3) (1984) 251-253.

Within- and between series

- A series consists of several determinations, typically performed within the same day. Several series are performed over several days, consecutive or not. To compute s_R, it is considered that the intermediate precision is the sum of two contributions,
  i. the within-series repeatability, s_r,
  ii. the between-series reproducibility, s_L, i.e., independent series,

$$s_R^2 = s_r^2 + s_L^2$$

Application to ICP spectrometry

i. the within-series repeatability, s_r, i.e., the same plasma ignition and standard solutions, with the possibility of recalibration to avoid drift,

ii. the between-series reproducibility, s_L, i.e., independent series, with new plasma ignition for each series, and new standard solutions.

Uncertainty on the bias

- Not only the accuracy may be deduced from the experiments but also the uncertainty on the bias. This is an important information to verify whether the degradation in the accuracy is only due to the intermediate precision or also to a significant bias.
- Actually, this is the only information that can be directly deduced from ISO 5725-4 and ISO 21748 norms.

β-factor

- The Student's coefficient, and, therefore, the degree of freedom, is involved in the computation of k_s.
- This coefficient is related to a confidence percentage β, for which an expected proportion of expected values will be within the accuracy tolerance limits. An arbitrary value of 80% is often selected, but this value does not currently correspond to any norm or recommendation*.

*A. Gustavo González, M. Ángeles Herrador, Accuracy profiles from uncertainty measurements, Talanta 70 (2006) 896–901.

Tolerance intervals and acceptability limits

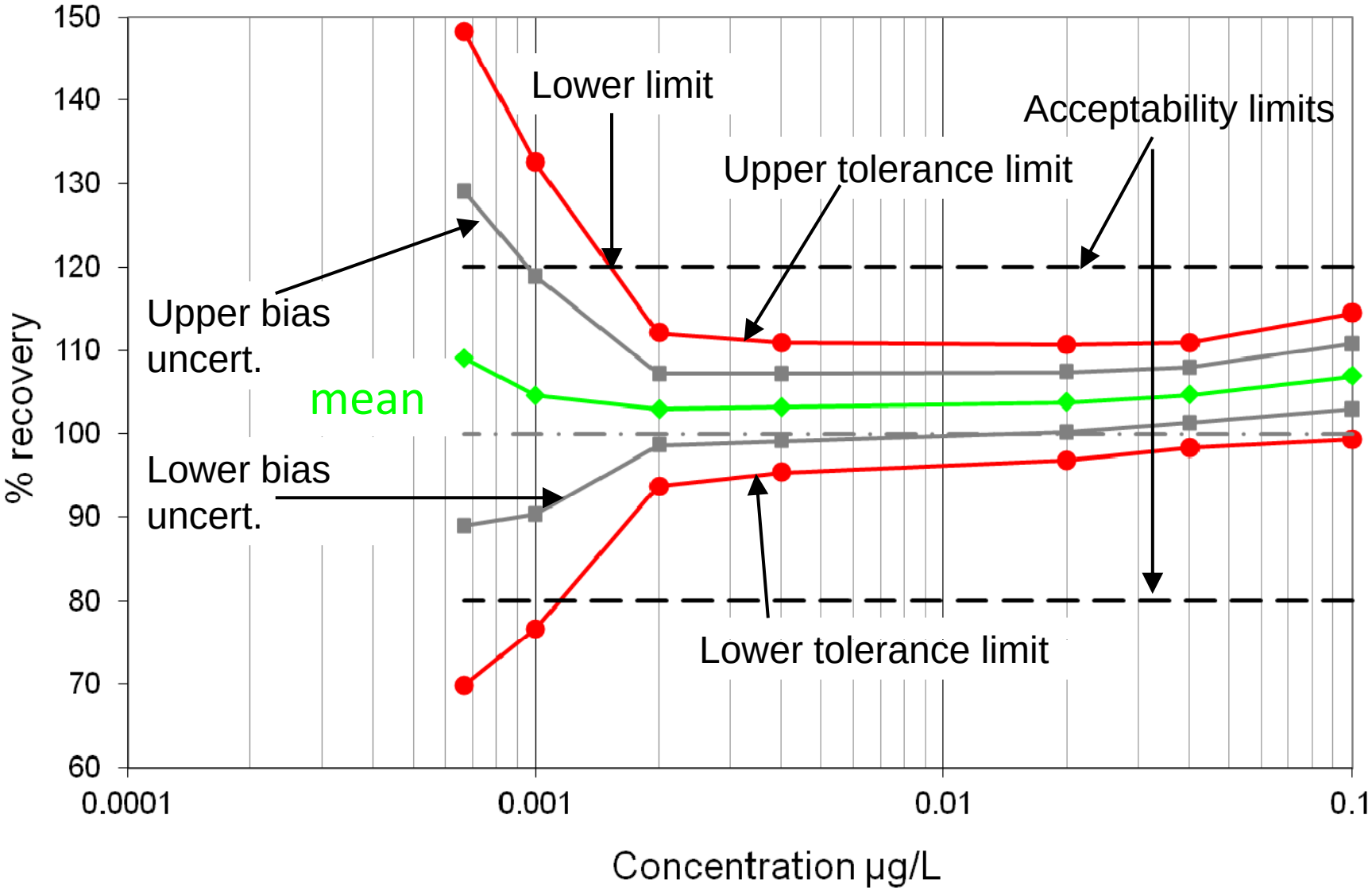
- To express the tolerance intervals, the use of the %recovery is convenient, because of the normalization to 100% :

limits expressed as a %recovery = 100*(reference value + bias $\pm k_s.s_R$)/reference value

- Acceptability limits are defined by the analyst as a function of the analytical problem, e.g., ±10 or ±20%.

☞ A method is claimed to be valid when tolerance intervals are fully included within the acceptability limits.

B in ICP-AES

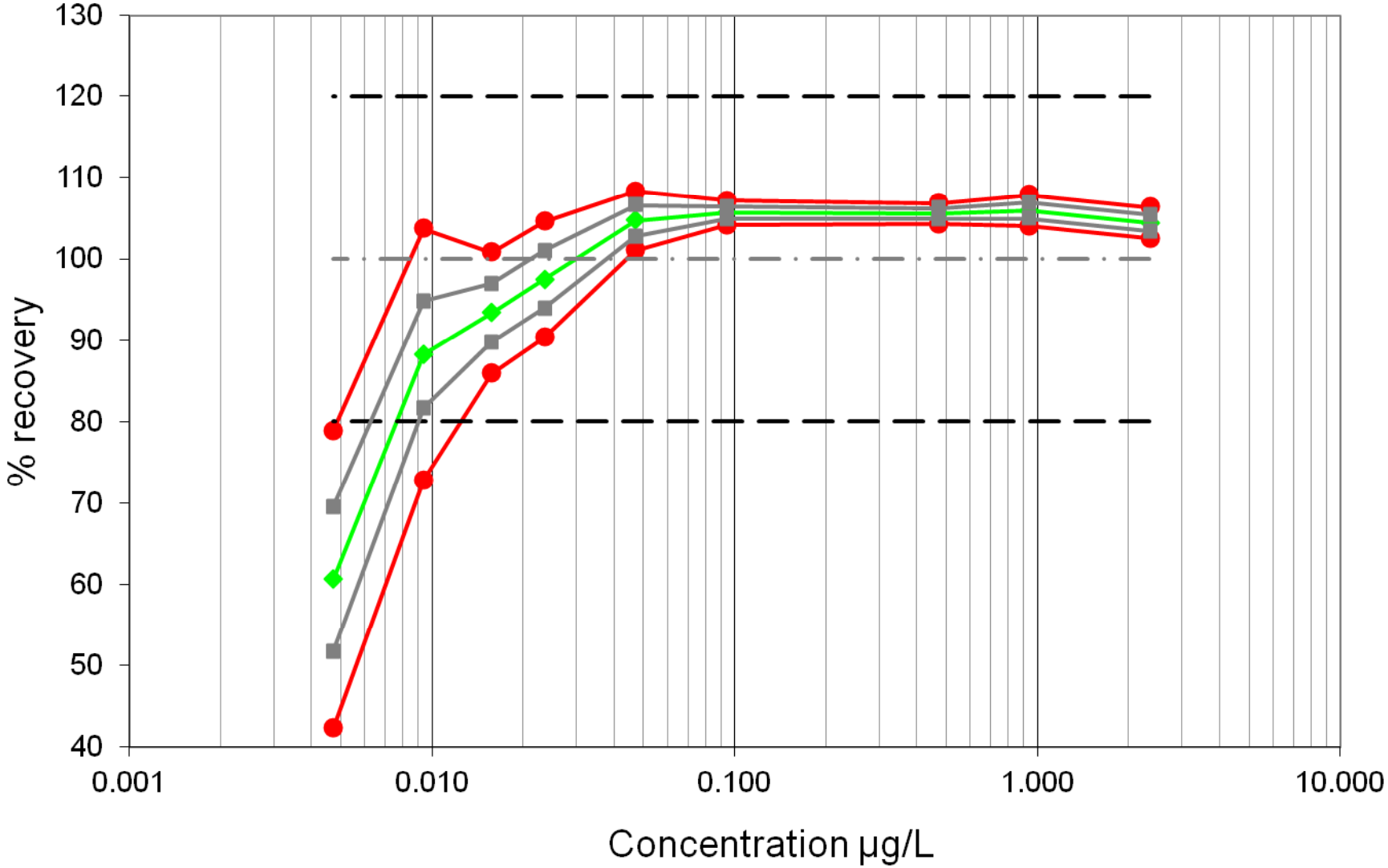

150
140
130
120
110
100
90
80
70
60
% recovery
0.0001
0.001
0.01
0.1
Concentration µg/L
Lower limit
Upper tolerance limit
Acceptability limits
Upper bias uncert.
mean
Lower bias uncert.
Lower tolerance limit

Tolerance intervals *vs*. concentration

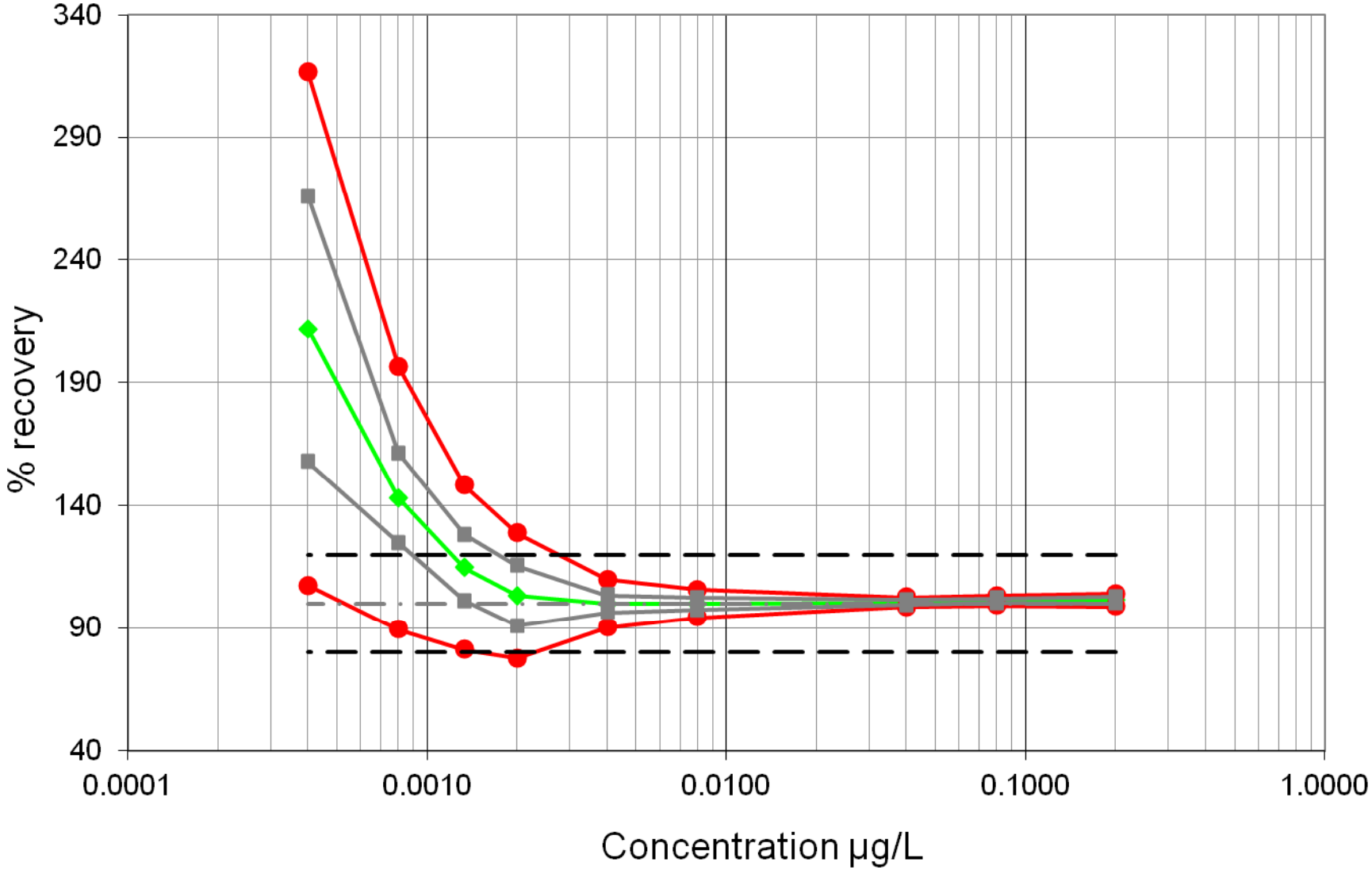
- Usually, when decreasing the concentration, the tolerance intervals become larger because of accuracy degradation, and when there is an intercept between the tolerance intervals and the acceptability limits, this defines a lower limit of quantitation truly based on both trueness and precision.
- Accuracy profile proposes, therefore, a graphical method for establishing whether the combination of precision and trueness of a given method is correctly adapted to the analytical problem within a requested analytical range.
- ☞ Note that the tolerance intervals may be asymmetrical when a significant bias is observed. In this case, the most pessimistic interval is selected.

☞*Different types of accuracy profiles*

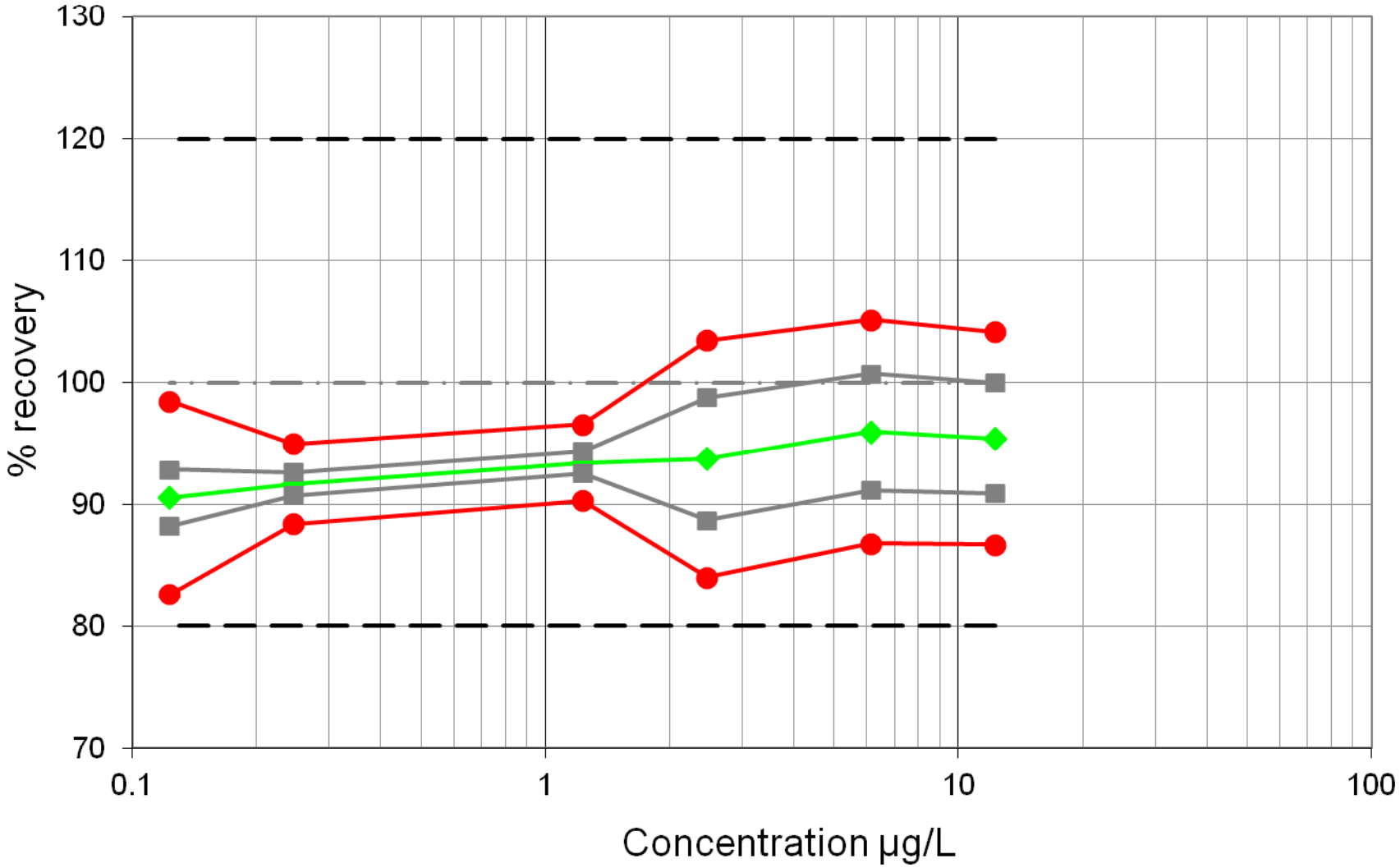
Bias degradation (Al in ICP-AES)



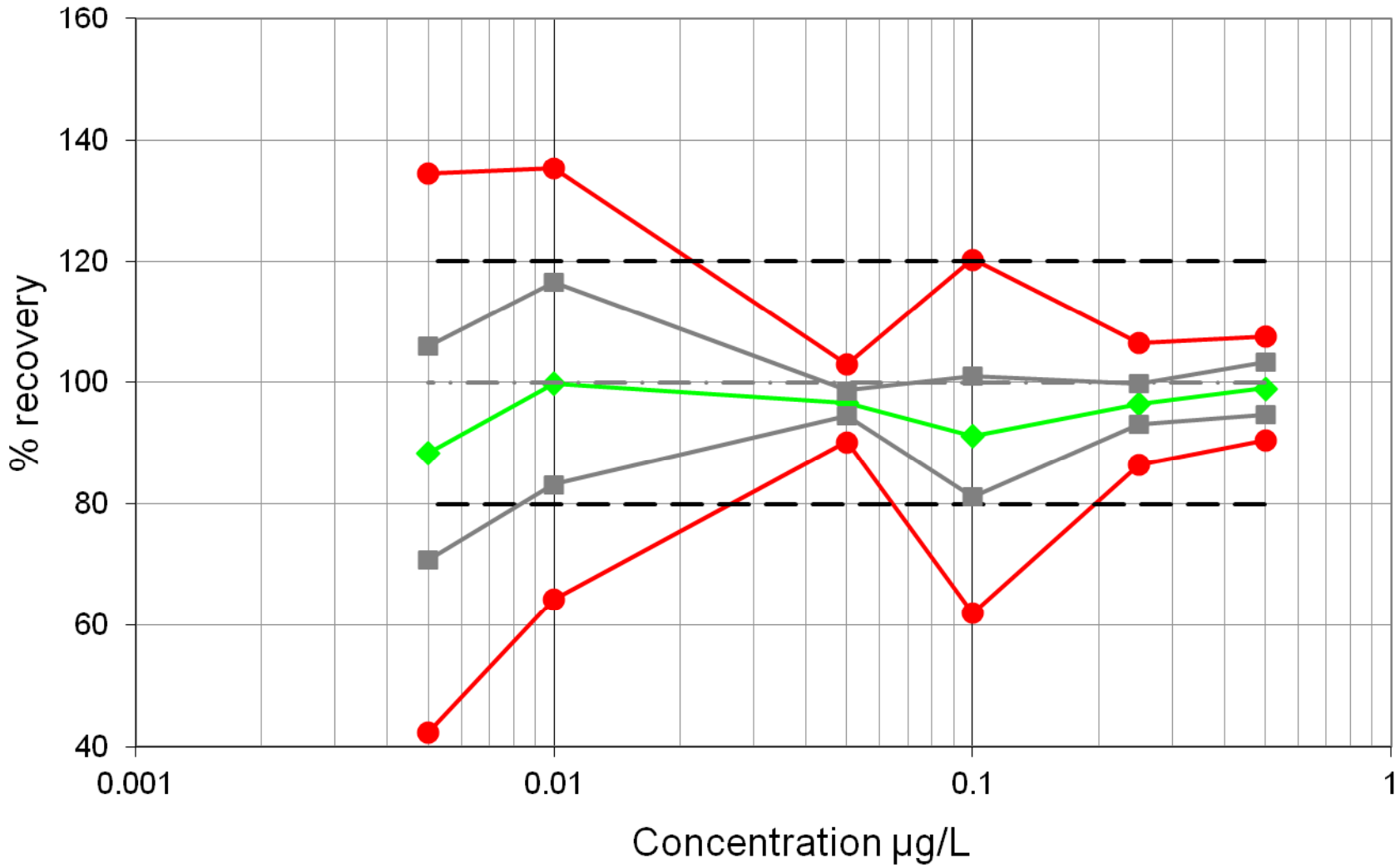
Bias degradation: Cu in ICP-AES



Systematic bias: U in ICP-AES



Erratic behavior: Na in ICP-AES



Need for a weighting procedure

- A standard linear regression favours the highest concentrations to the detriment of the lowest ones.
- A consequence is a large uncertainty associated with a significant bias for low values.
- Besides, the standard LSM assumes that the standard deviation is constant all over the concentration range, which is usually not true in atomic spectrometry.
- There is, then, a need to use a weighting procedure.

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Review

Calibration in atomic spectrometry: A tutorial review dealing with quality criteria, weighting procedures and possible curvatures

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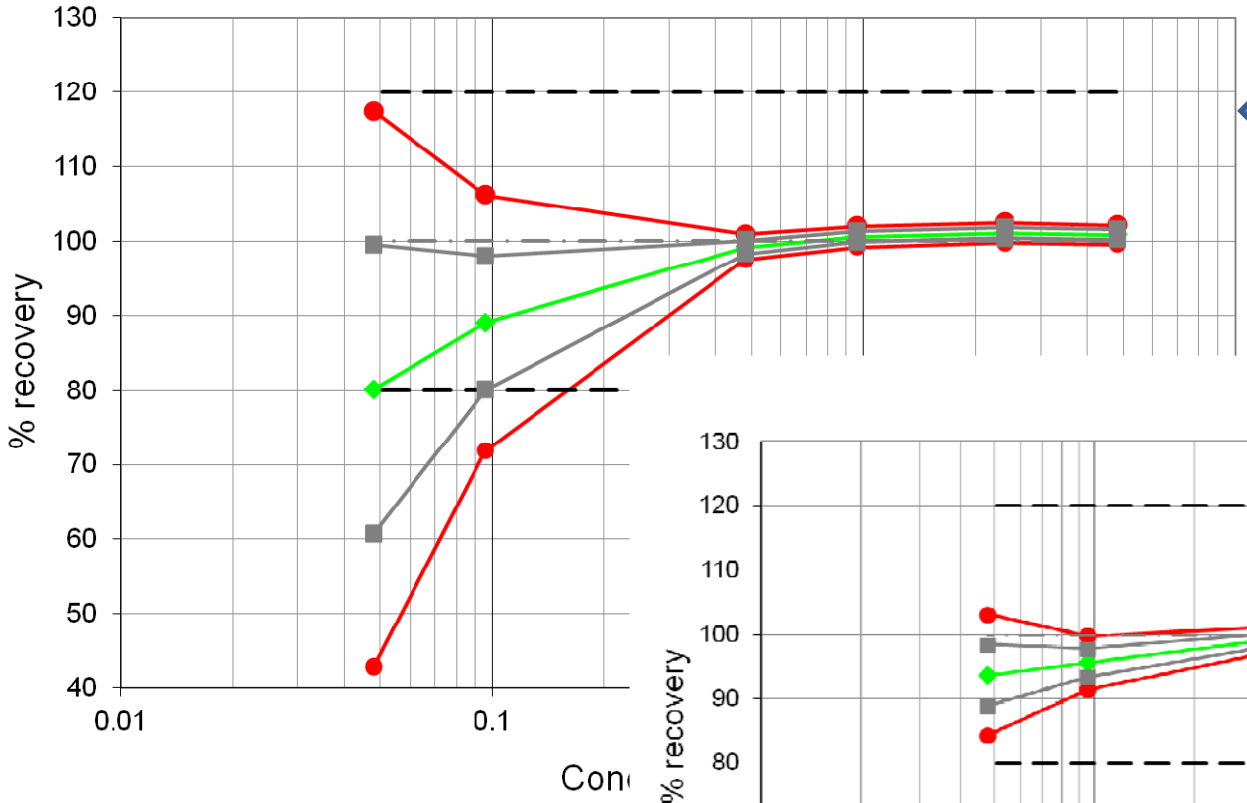
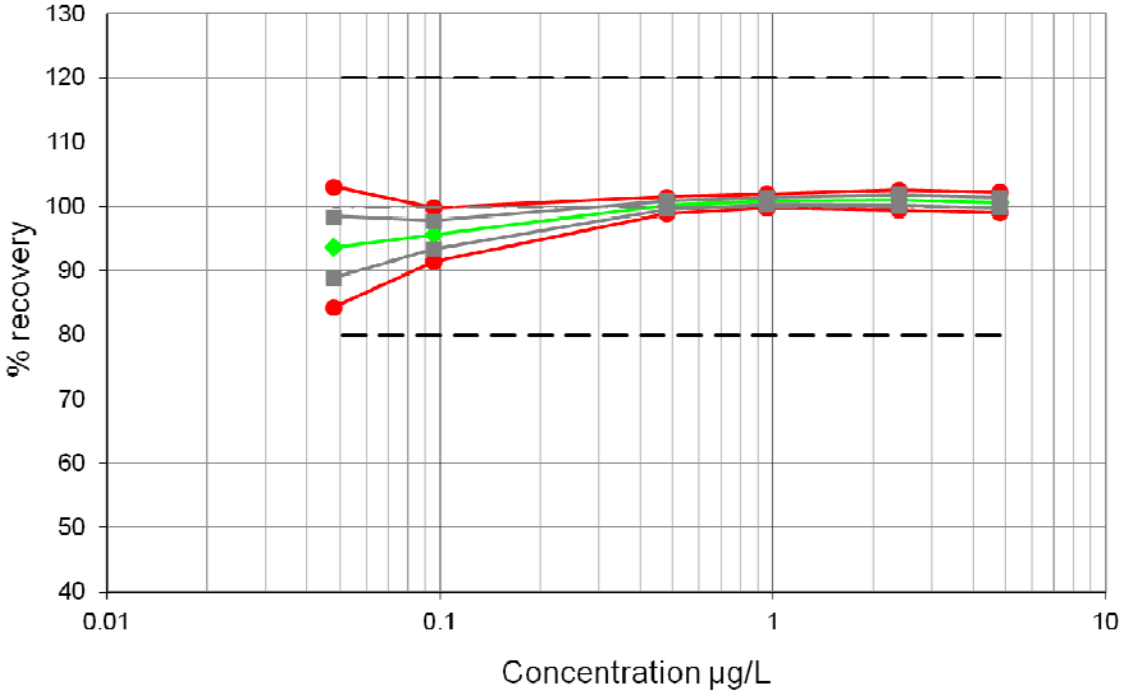
Calibration weighting : Si in ICP-AES

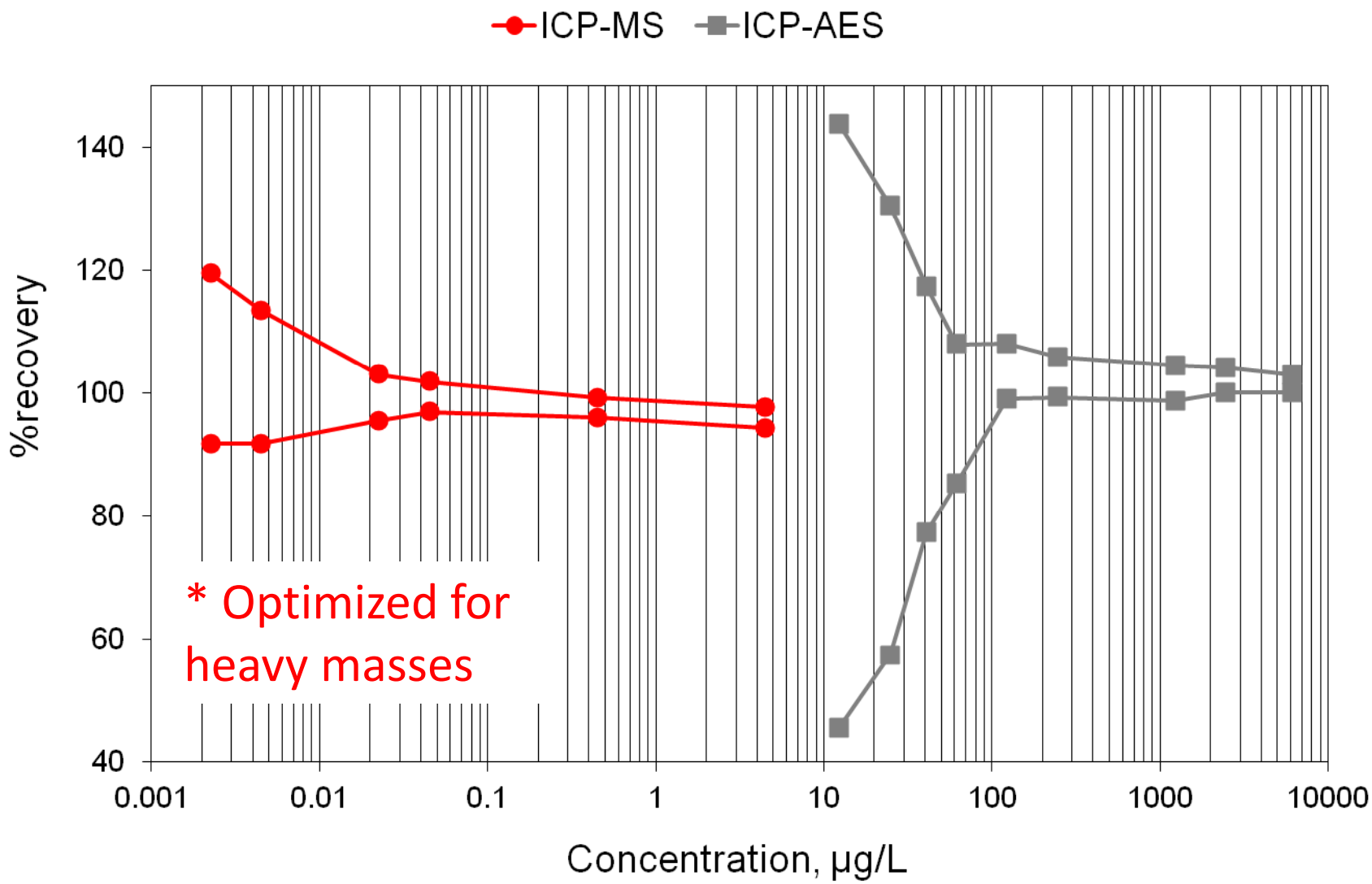


non-weighted

weighted



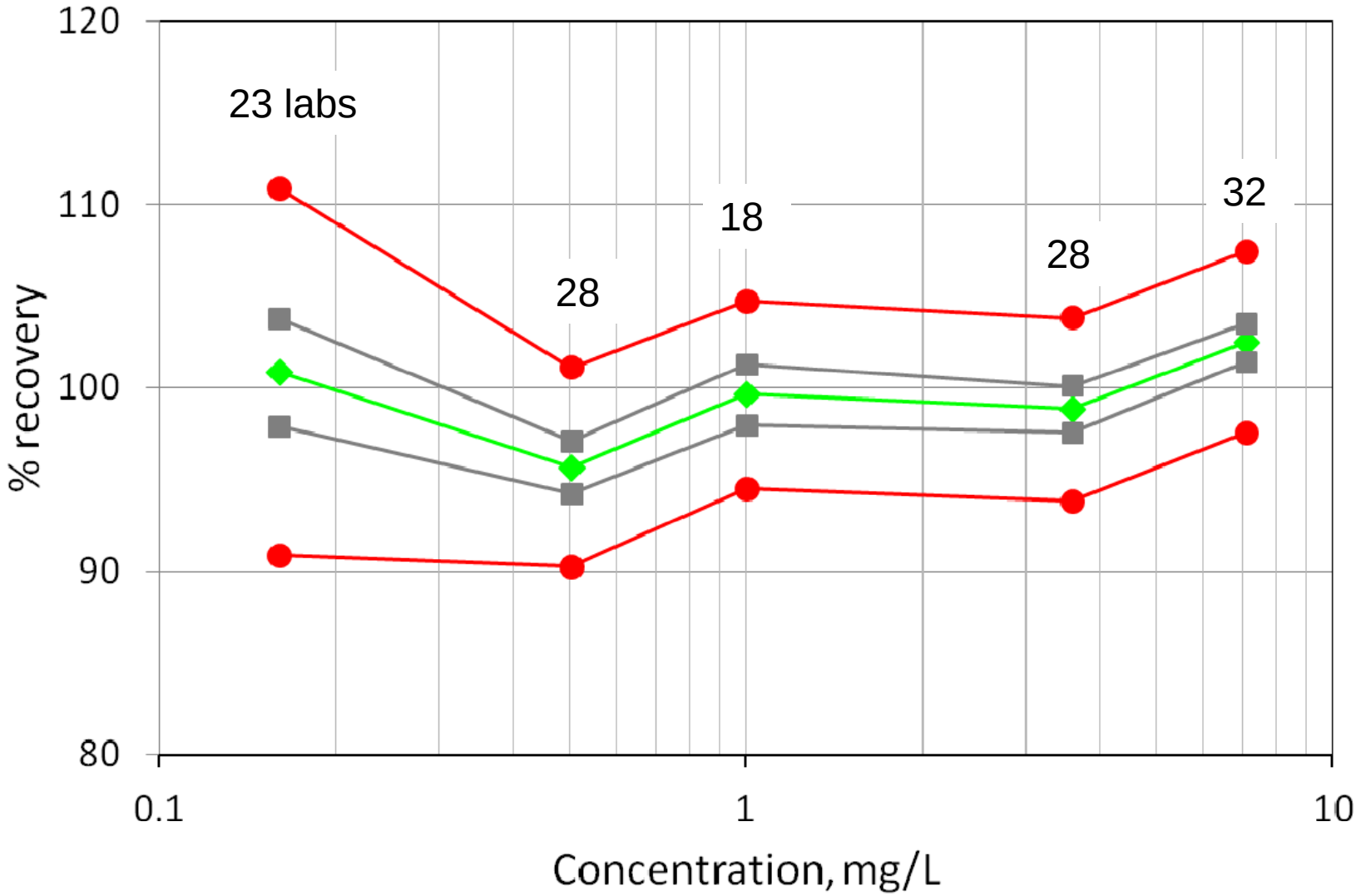
U: ICP-AES vs ICP-MS



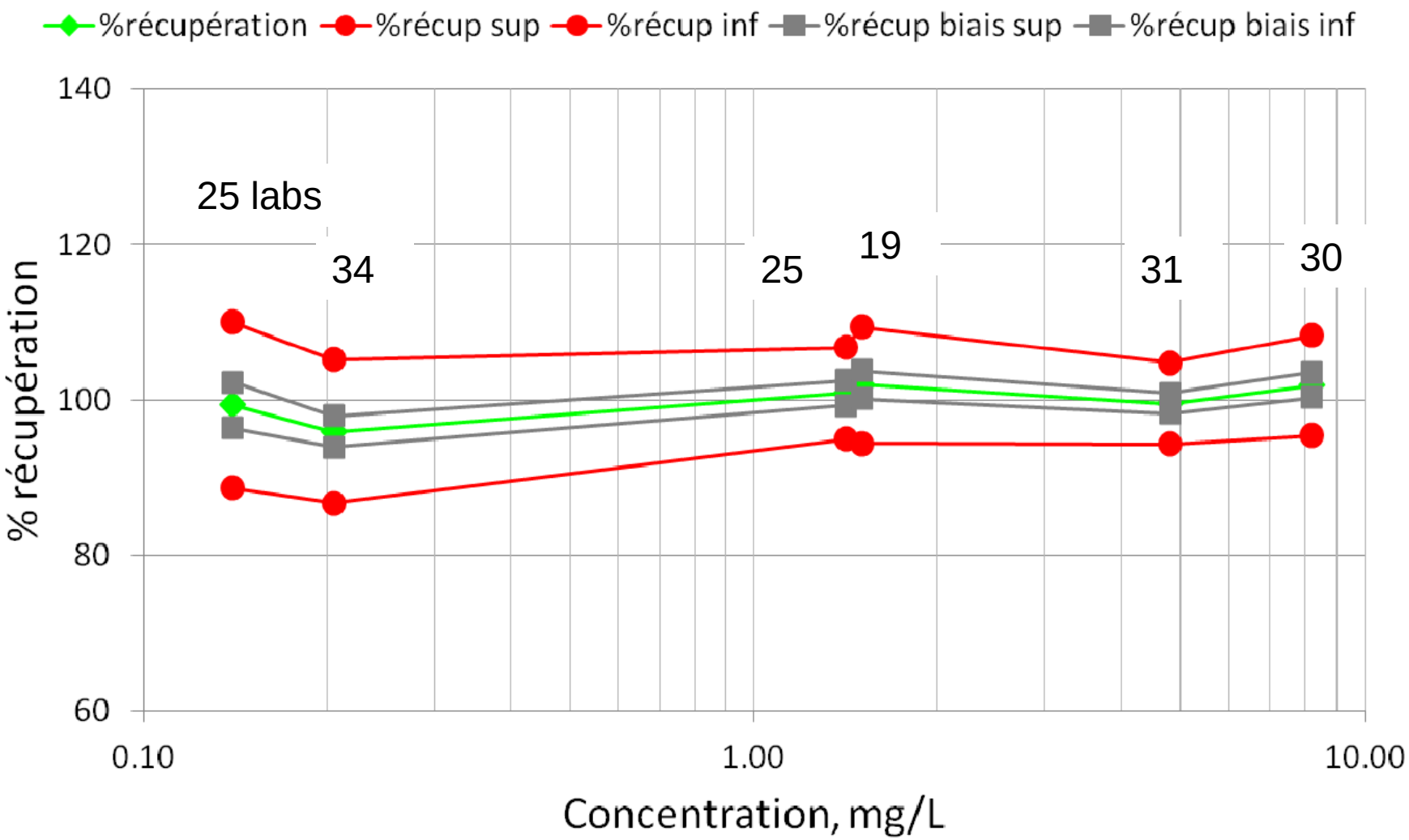
Interlaboratory experiments

- Several collaborative studies were organized by the Committee for the Establishment of Analysis Methods (CETAMA), which is part of the French Atomic Energy Commission (CEA).
- Its primary missions are to draft analysis methods, and to organize periodic round-robin campaigns to validate methods and laboratory capabilities, particularly in the field of atomic spectrometry (ICP-AES and ICP-MS).

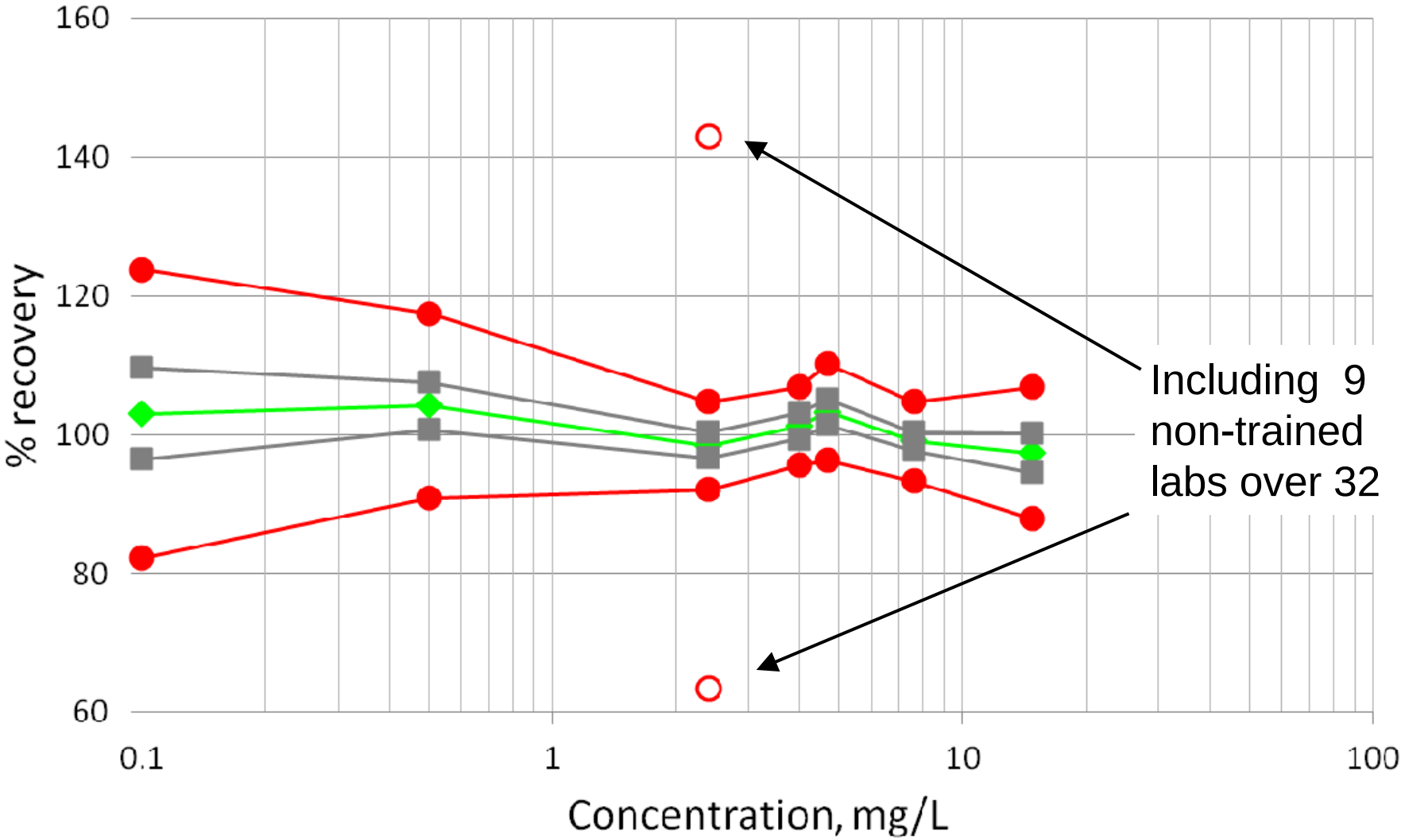
Co in ICP-AES


120
110
100
90
80
% recovery
23 labs
28
18
28
32
0.1
1
10
Concentration, mg/L

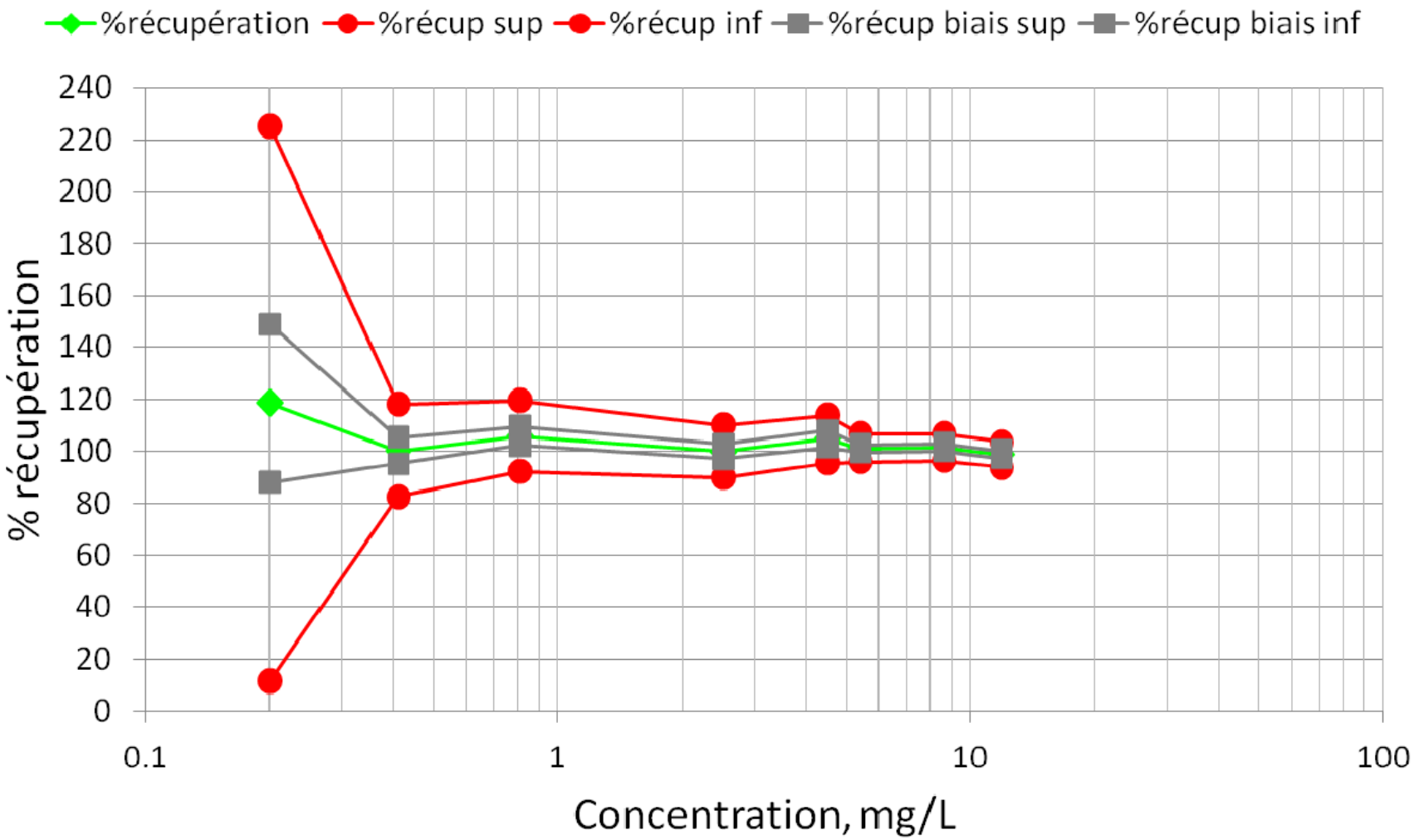
Cr in ICP-AES


%récupération
%récup sup
%récup inf
%récup biais sup
%récup biais inf
140
120
100
80
60
% récupération
25 labs
34
25
19
31
30
0.10
1.00
10.00
Concentration, mg/L

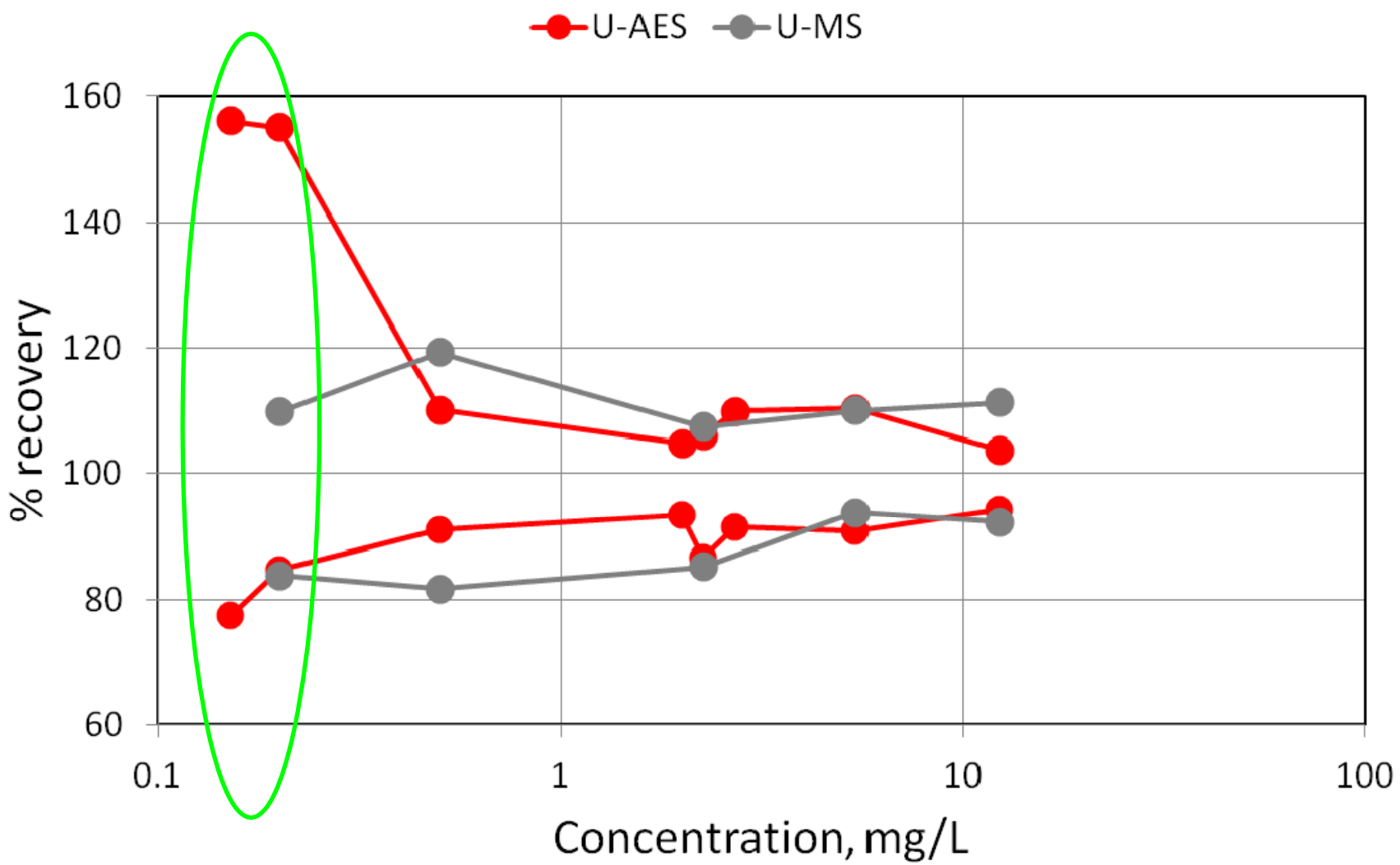
Al in ICP-AES


160
140
120
100
80
60
% recovery
0.1
1
10
100
Concentration, mg/L
Including 9
non-trained
labs over 32

B in ICP-AES


%récupération
%récup sup
%récup inf
%récup biais sup
%récup biais inf
240
220
200
180
160
140
120
100
80
60
40
20
0
% récupération
0.1
1
10
100
Concentration, mg/L

U: ICP-AES *vs* ICP-MS



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SPECTROCHIMICA ACTA PART B

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Limit of quantitation in atomic spectrometry: An unambiguous concept? ☆

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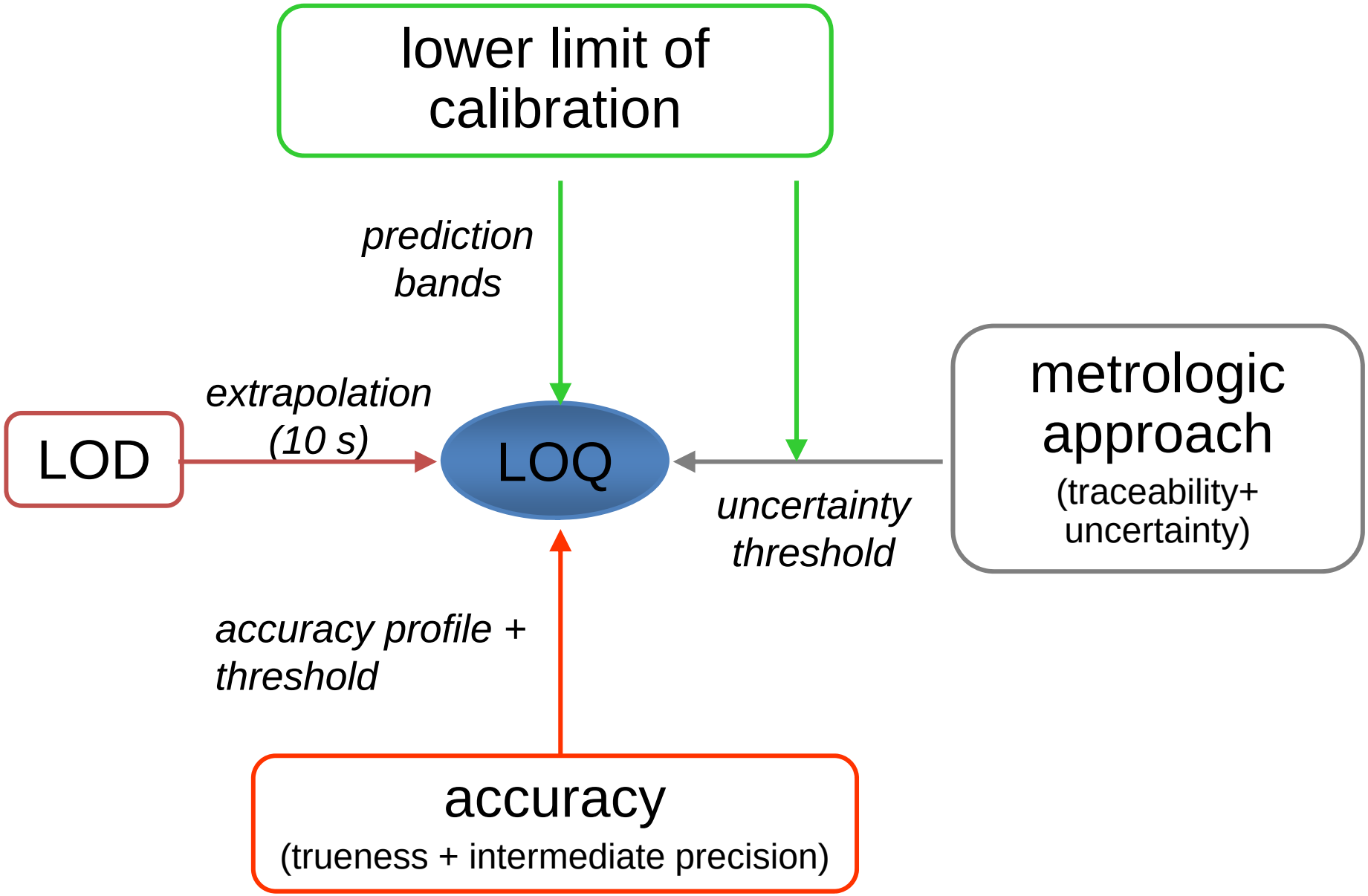
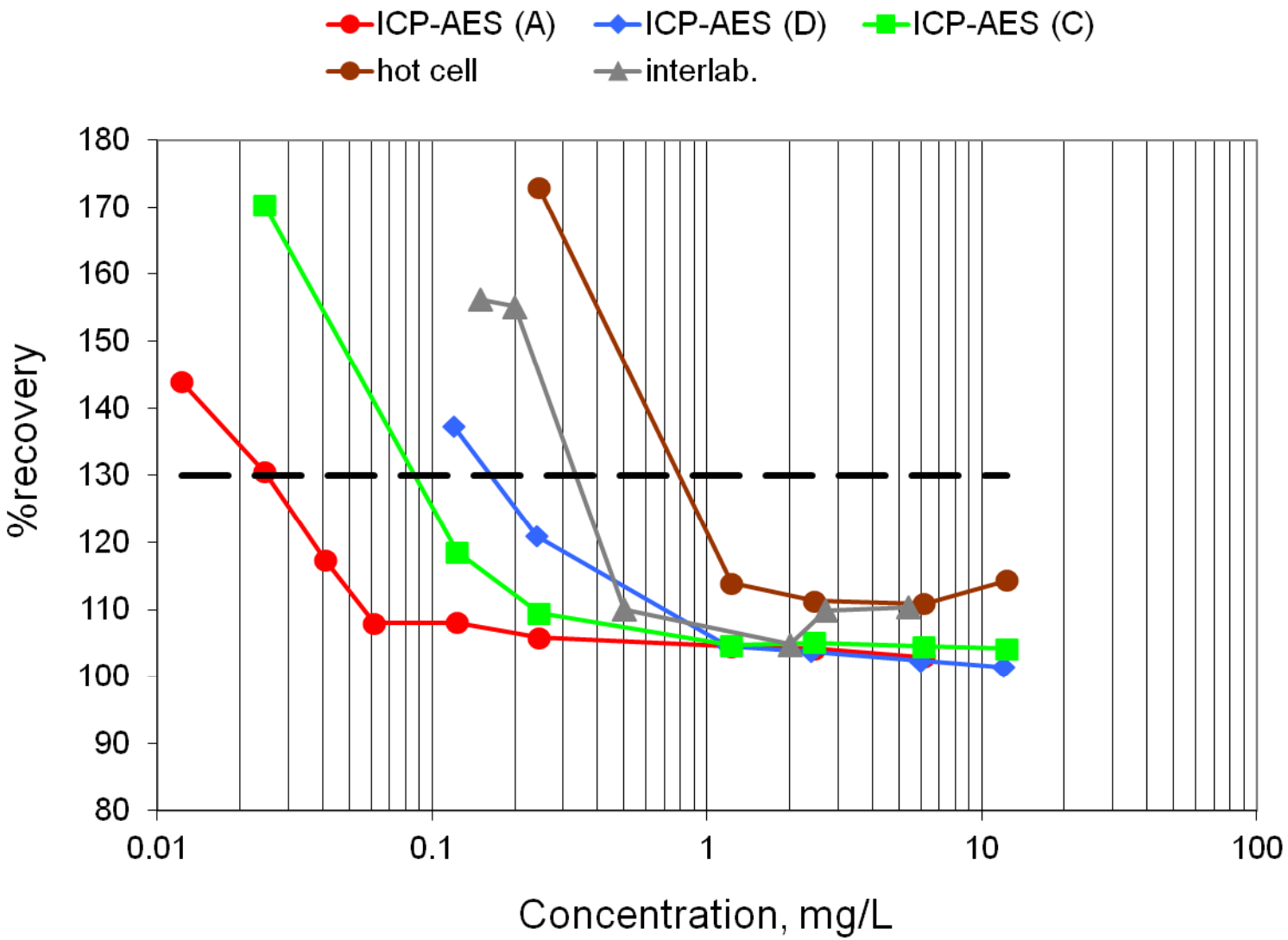
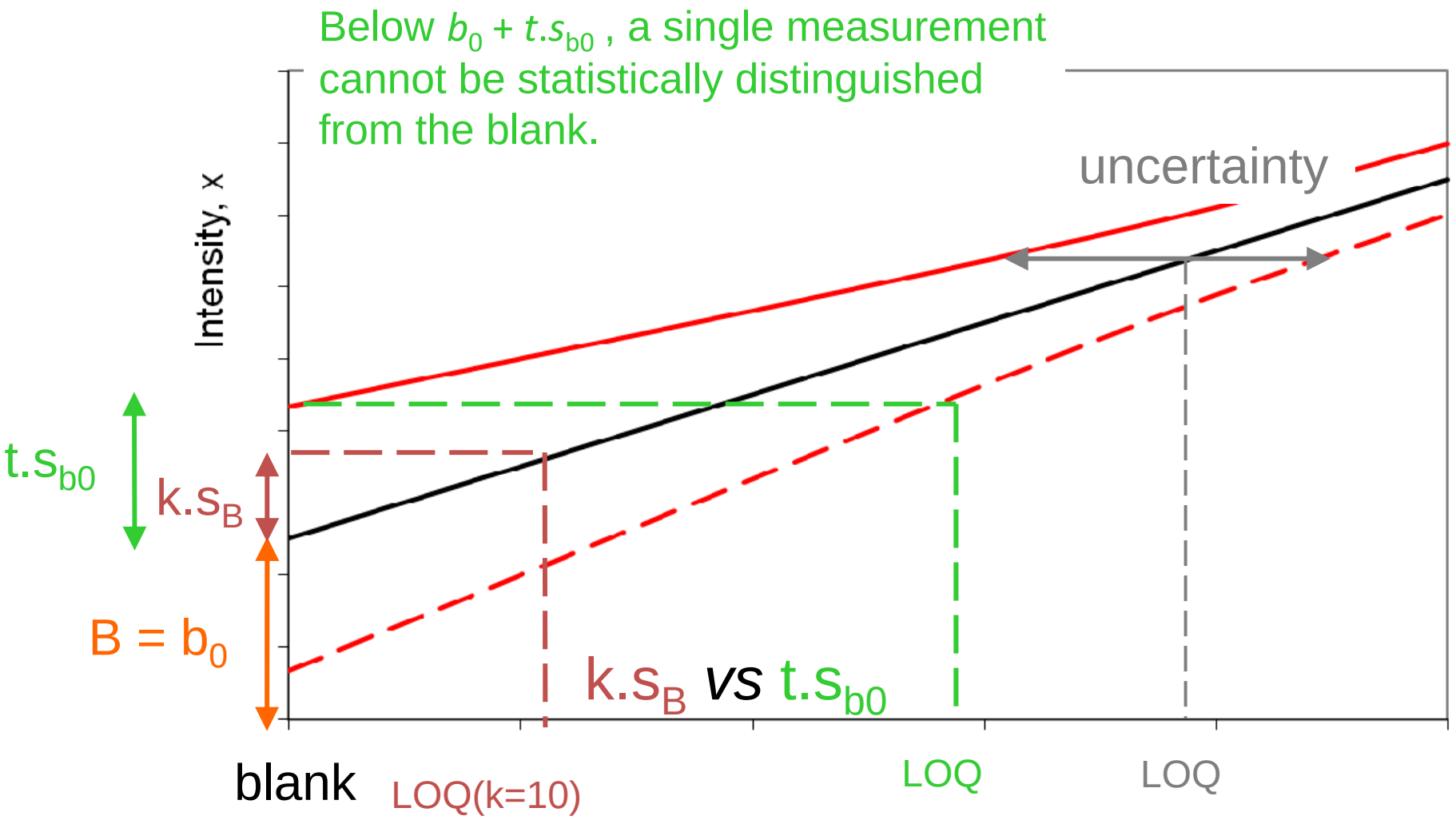

lower limit of calibration
prediction bands
extrapolation (10 s)
LOD
LOQ
uncertainty threshold
metrologic approach
(traceability+ uncertainty)
accuracy profile + threshold
accuracy
(trueness + intermediate precision)

U in ICP-AES: LOQ from the profile



LOQ related to prediction bands

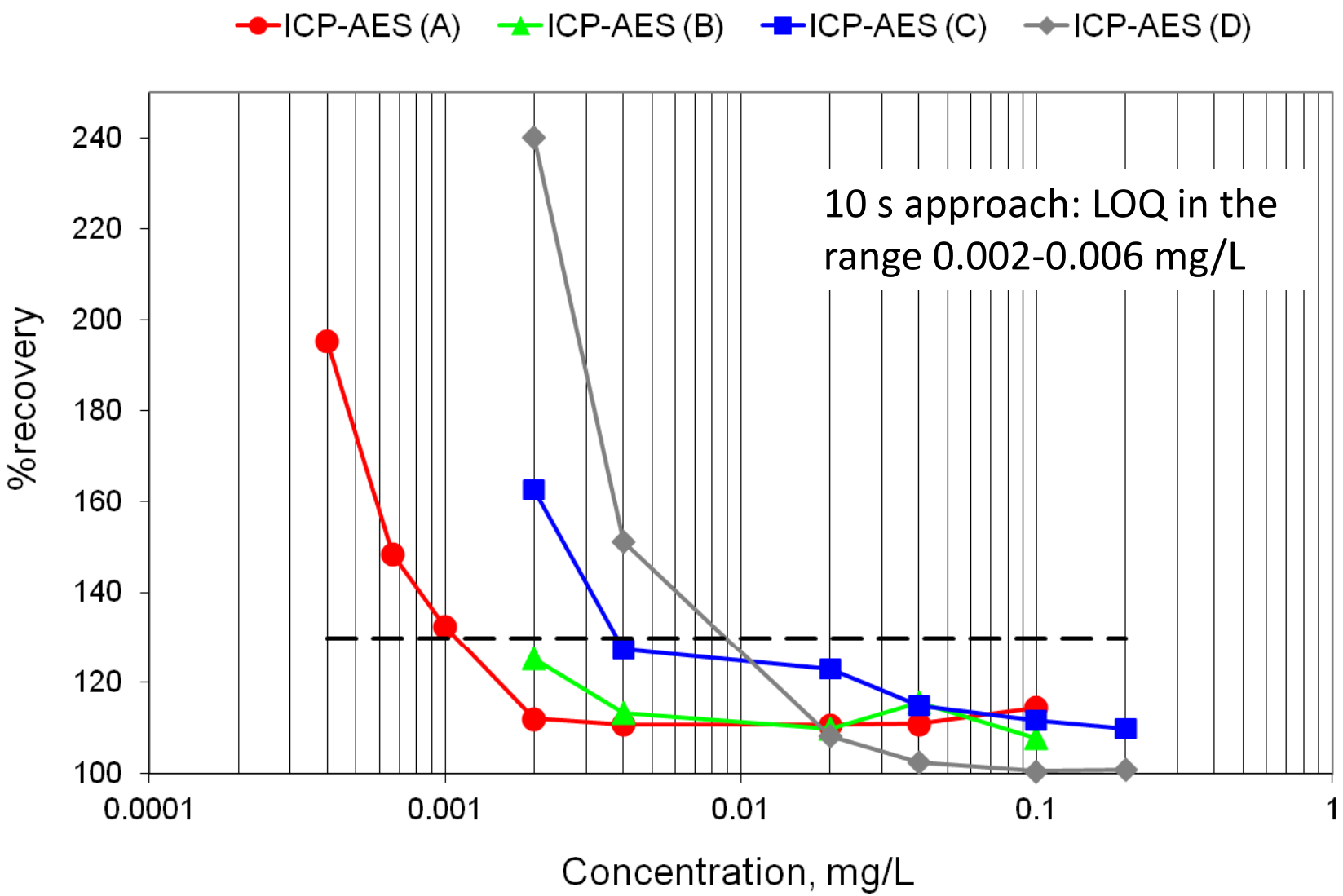


U in ICP-AES: various LOQs (mg/L)

	A	C	D
10 s "classical" approach	0.09	0.04	0.16
accuracy profile, 30%	0.025	0.08	0.15
calibration uncertainty, 30%	**0.1**	**0.15**	**0.4**
prediction bands	0.05	0.09	0.2

☞Results were obtained by using non-weighted calibrations. Using weighted calibration, values become smaller than the « 10 s classical approach ».

B in ICP-AES: LOQ from the profile



Conclusions

- ☺ Real experiments at low concentrations.
- ☺ Real capabilities of an instrument, a method and a laboratory.
- ☺ Realistic LOQs really dealing with accuracy (to be compared with the « classical LOQ»
- ☹ Tedious and time-consuming experiments, but only needed for validation.
- ☹ Which tolerance and acceptability limits?
- ☹ Need for CRMs at various concentrations, including low ones, and if possible, with matrices of concern.

- Many thanks for your attention
- Merci pour votre attention
- Bedankt voor Uw aandacht
- Herzlichen Dank für Ihre Aufmerksamkeit
- Muchas gracias por su atención
- Grazie per la vostra attenzione
- Спасибо за внимание
- Takk for oppmerksomhet
- Tack för er uppmärksamhet
- Hvala za vaso pozornost
- ご清聴ありがとうございました

The end