Handling allowable limits for recovery - a puzzle

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Introduction

- Who sets limits for analytical recovery?
- Limits and measurement uncertainty
  - Handling specification limits in measurement uncertainty evaluation
- Is analytical recovery just another 'input quantity'?
- When should permitted limits contribute to measurement uncertainty?

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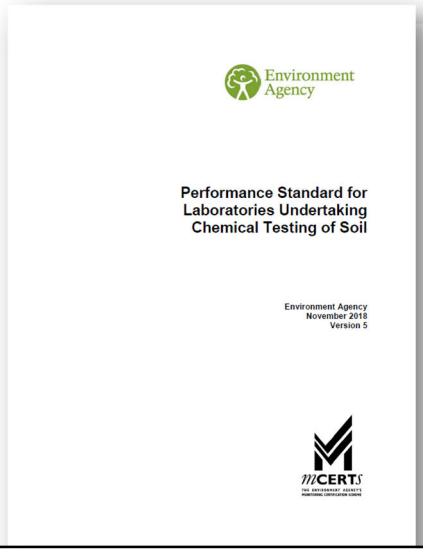
Who sets limits for analytical recovery?



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Who sets limits for analytical recovery?

Table 1 - Metals and organometallics

Parameter[1]	Precision[2]	Bias[3]
antimony	7.5	15
arsenic	7.5	15
barium	7.5	10
beryllium	7.5	10
boron (water soluble)	10	20

Table 3 - Organics

Parameter[1]	Precision[2]	Bias[3]
benzene	15	30
benzo[*a*]pyrene	15	30
chlorobenzene	15	30
chloromethane	15	30
chlorophenol	15	30

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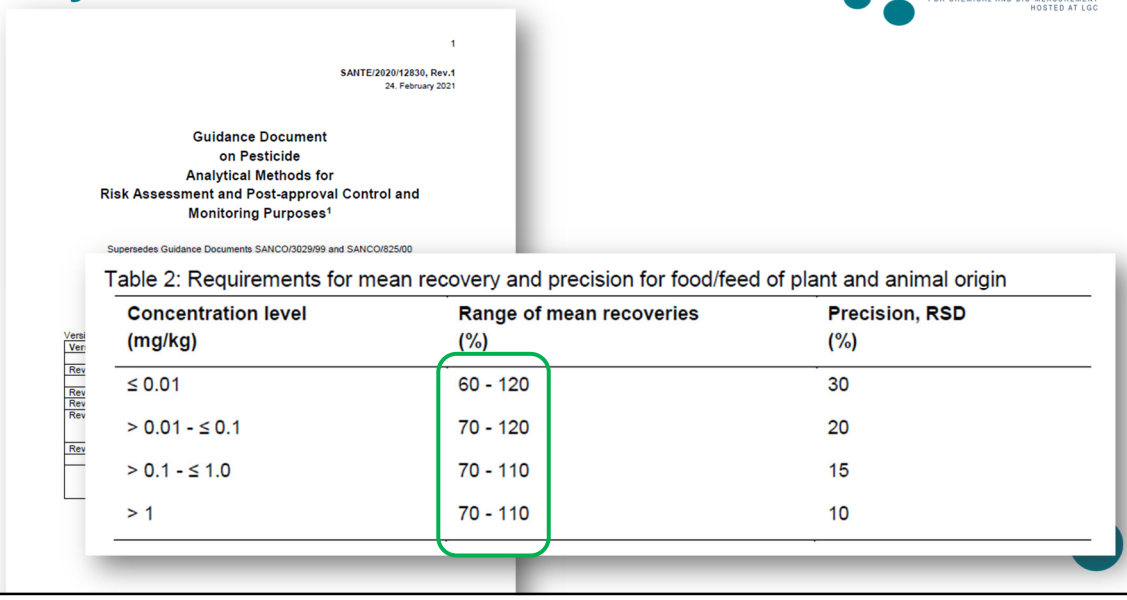
Who sets limits for analytical recovery?



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SANTE/2020/12830, Rev.1
24. February 2021

Guidance Document
on Pesticide
Analytical Methods for
Risk Assessment and Post-approval Control and
Monitoring Purposes[1]

Supersedes Guidance Documents SANCO/3029/99 and SANCO/825/00

Table 2: Requirements for mean recovery and precision for food/feed of plant and animal origin

Concentration level (mg/kg)	Range of mean recoveries (%)	Precision, RSD (%)
≤ 0.01	60 - 120	30
> 0.01 - ≤ 0.1	70 - 120	20
> 0.1 - ≤ 1.0	70 - 110	15
> 1	70 - 110	10

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Who sets limits for analytical recovery?

Regulators

- Limits set for validation to ensure sufficient performance for regulatory use
- May also set QC limits for regular spike recovery

Laboratories

- Voluntary limits set for validation
- QC limits for regular spike recovery

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Limits and measurement uncertainty

Manufacturer specification:

$$\pm 0.02 \text{ ml}$$

Triangular* distribution

$$u = \frac{0.02}{\sqrt{6}} = 0.008 \text{ ml}$$

** Rectangular more conservative*

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Limits and measurement uncertainty

Manufacturer specification:

$$\pm 0.02 \text{ ml}$$

Triangular* distribution

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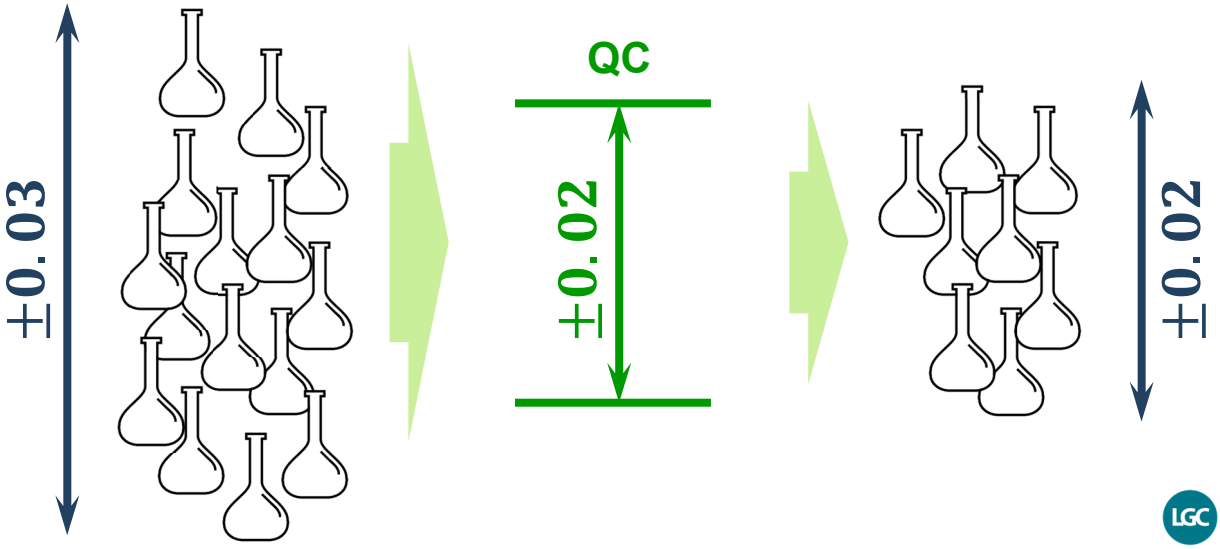
Specifications as a 'filter'



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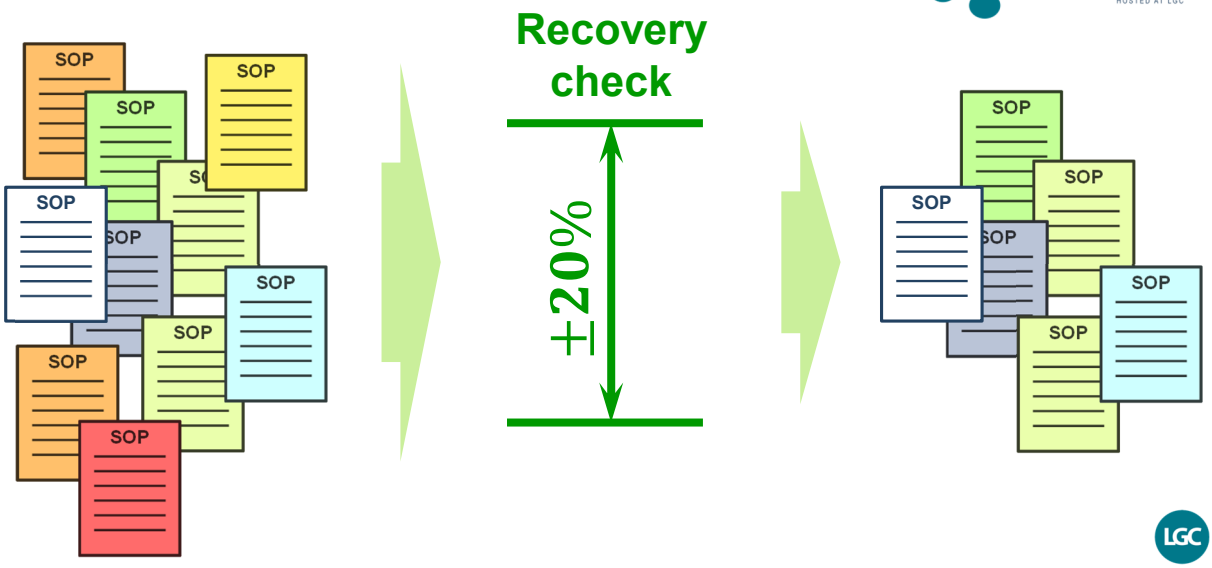
Specifications as a 'filter' – Validation



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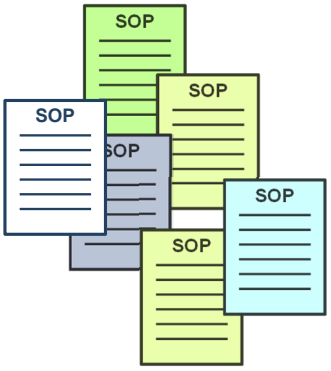
Limits and measurement uncertainty



Recovery
$100 \pm 20\%$

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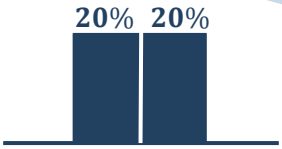
$100 \pm 20 \%$



Rectangular distribution

$$u = \frac{20}{\sqrt{3}} = 11.5\ \%$$

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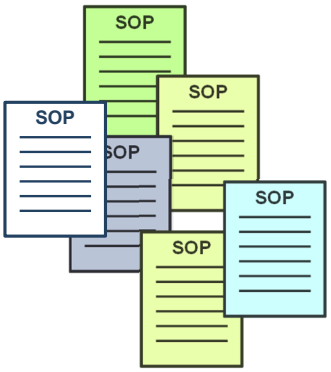
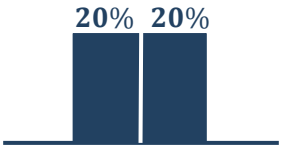
Some considerations



Recovery
$100 \pm 20\%$



What does this distribution describe?

- Uncertainty about the recovery for one particular SOP/lab?
- The spread of recoveries a regulator can expect across many laboratories?

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Considerations

- **Laboratories have estimated their own recovery**
  - During method validation
  - Regularly, for quality control
- **Each laboratory has more information about recovery than is provided by the permitted limits**
- **We already know how to use laboratory estimates of recovery (or bias) in MU evaluation**

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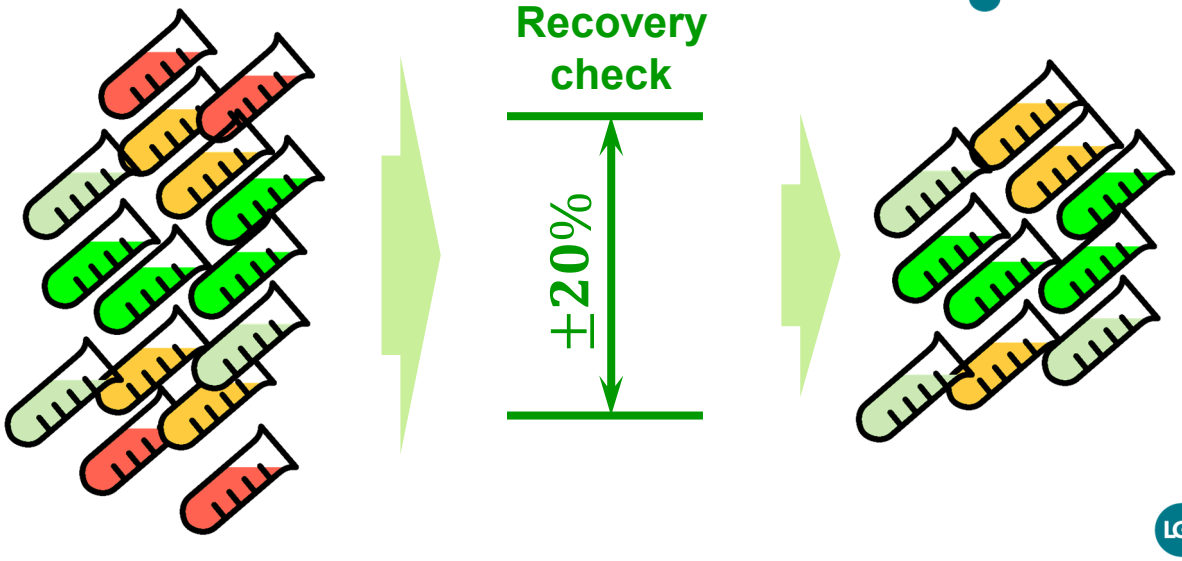
Specifications as a 'filter' – Quality control



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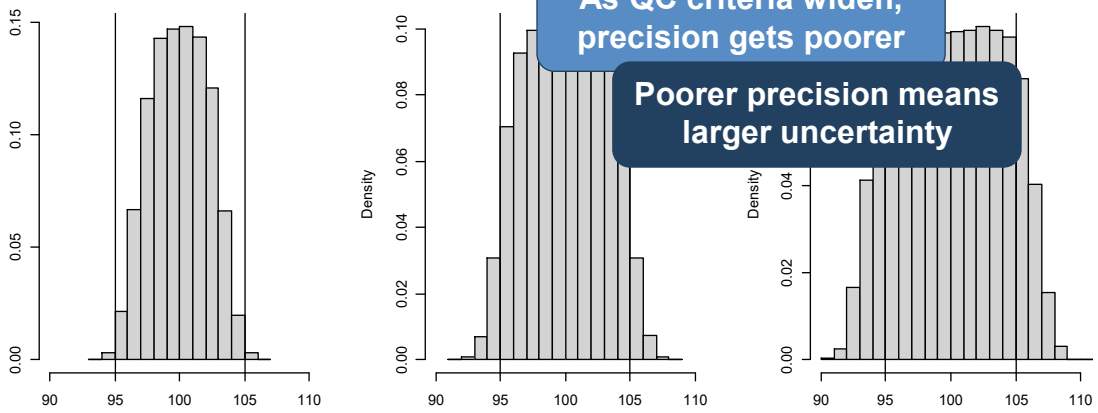
Effect of widening QC limits on analytical results*



* Assuming wide dispersion of possible recoveries

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Further considerations

- **Adjusting QC limits to 'permitted recovery' can reduce precision**
  - Increasing uncertainty
- **Intermediate precision studies should reflect QC limits**
  - If recovery varies from run to run
- **Recovery limits used in QC could be used in MU evaluation if not reflected by observed precision**

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Conclusions

- Permitted limits for Recovery at validation
  - Primarily a quality assurance check
  - Labs should ideally use measured recovery in evaluating measurement uncertainty
- Adjusting QC limits to 'permitted recovery' can reduce precision
  - Increasing uncertainty – may be visible in within-lab reproducibility
- Regulatory limits for Recovery are relevant for uncertainty evaluation **when there is no other available information**

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