European Commission

Traceability in Chemical Analysis – Are we ready to deliver?

Hendrik Emons

Joint Research Centre – Institute for Reference Materials and Measurements

Metrological Traceability

European Commission

Property of a measurement result

whereby the result can be related to a reference

through a documented unbroken chain of calibrations,

each contributing to the measurement uncertainty

ISO Guide 99 (2007)

Today's topics:

- **Relevance**
- **Identity**
- **Traceability 'chain'**
- **Reference points**

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Relevance: What to measure?

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'customer' question

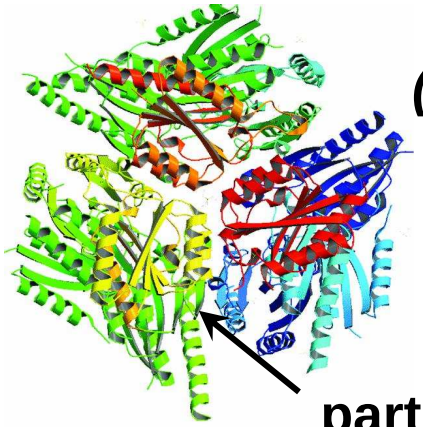
↓

information need

↓

measurement task

Example: Health-status marker



whole molecule ?
(identity, number…)

activity/reactivity

part(s) of the molecule ? *(identity…)*

Definition of decision-relevant measurand –

targeted property 'structural', 'functional', other?

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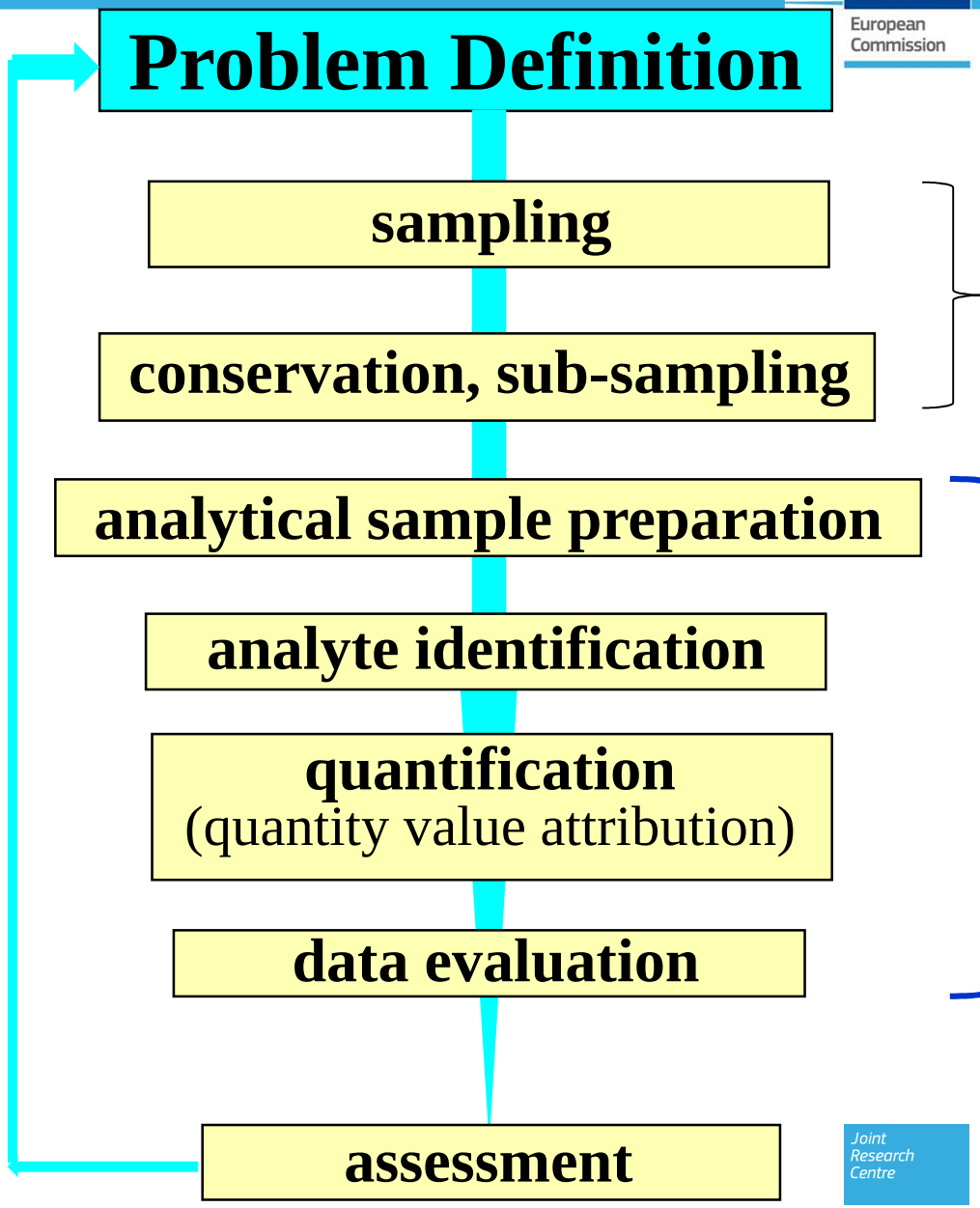
Total Analytical Process



Representativity?

Focus of this talk

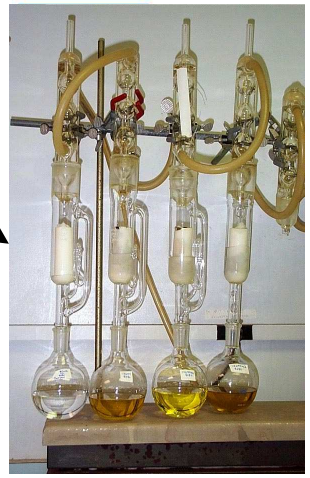
Starting point in this process for the traceability 'chain' ?

Measurement in chemistry

European Commission

sample

weighing, milling

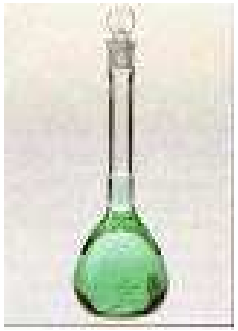


extraction

clean-up

Traceability 'chain' ?

Relevance ?



fill to volume

quantification
e.g., by LC-FLD

Traceability & Identity

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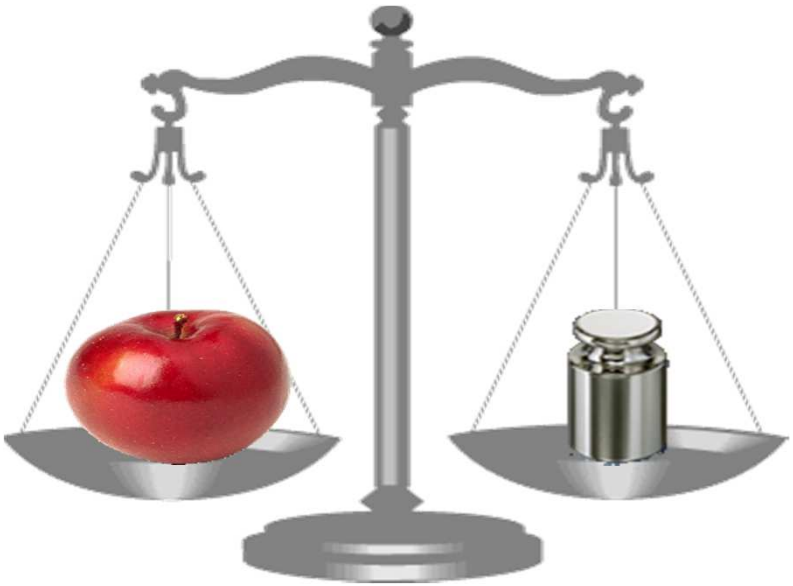
Challenge for measurements in chemistry

(bio/life sciences, material science,…)**:**

What

is on the

'balance' ?



How much

is on the

'balance' ?

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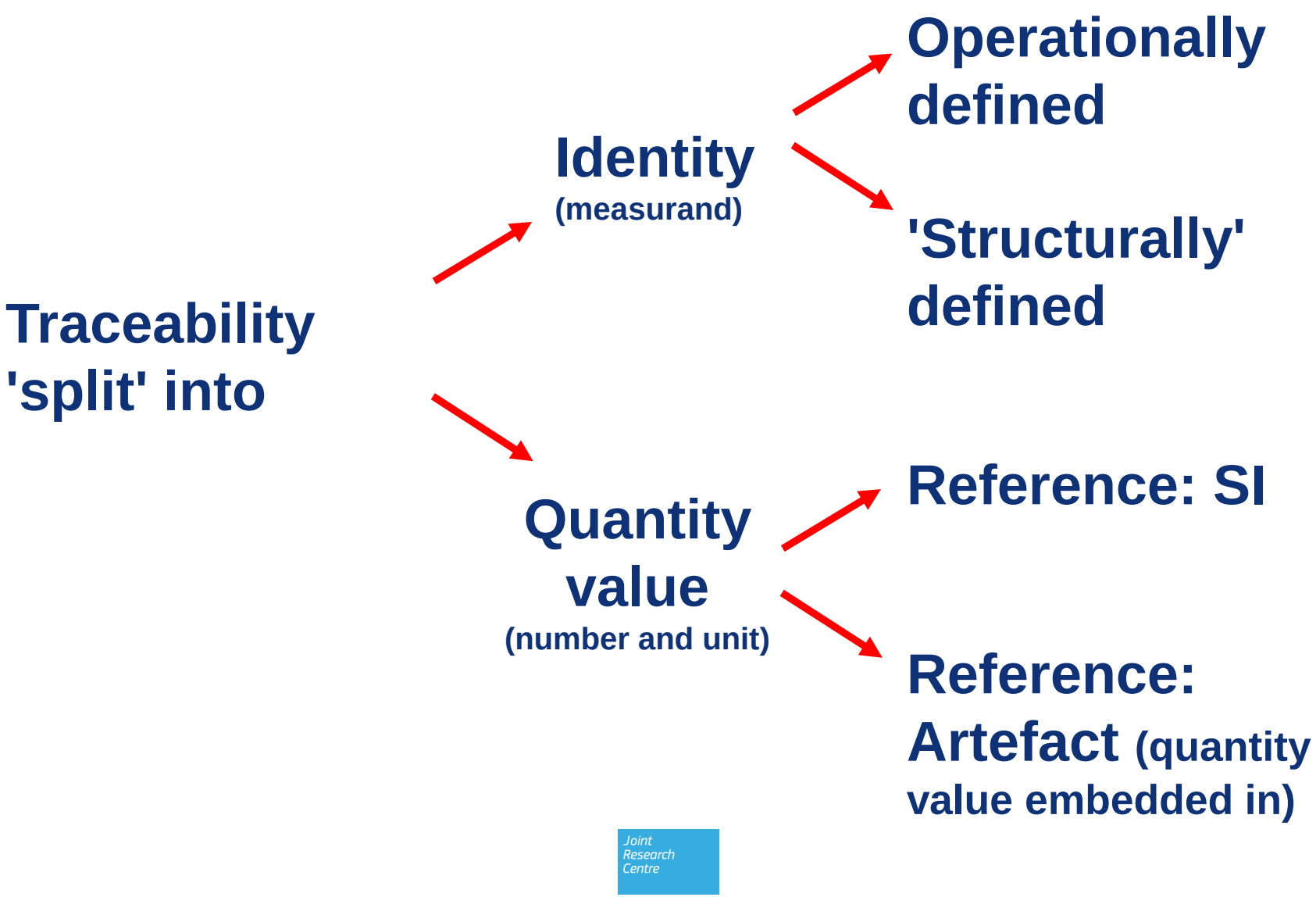
Traceability 'components'



Quality Assurance of identification

Quality assurance

Analytical sample

↓

Sample preparation

↓

Analyte identification

&

Quantification
(attribution of quantity value)

↓

Data evaluation

CRMs for qualitative analysis

- ***chemical identity***

Selectivity?

Classification?

5′-CTTTGGCCA**T**GAGGCTGG-3′

5′-CTTTGGCCA**C**GAGGCTGG-3′

Example: Identity benchmarks

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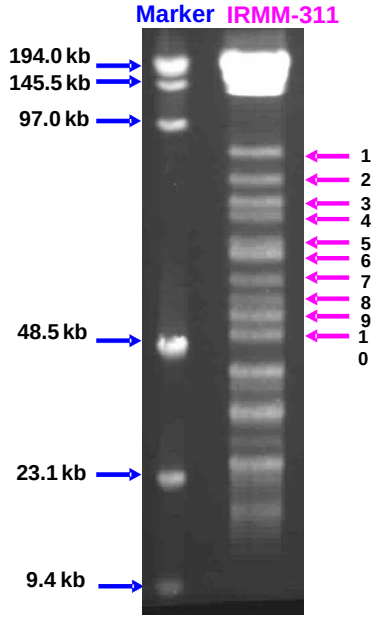
Taxonomic identification of authorised probiotic feed additives or food pathogens



CRM: Genomic DNA agarose inserts for Pulsed Field Gel Electrophoresis (PFGE):

Bacillus licheniformis DSM 5749 (IRMM-311)
Bacillus subtilis DSM 5750 (IRMM-312)

CRM: Lyophilised gDNA as **positive control** for diagnostic PCR

Listeria monocytogenes (IRMM-447)
Campylobacter jejuni (IRMM-448)
Escherichia coli O157 (IRMM-449)

gi|7375970|emb|AJ812225.1| Listeria monocytogenes prfA gene for positive regulatory factor A, strain SLCC2755
Length=714
Score = 464 bits (234), Expect = 6e-128
Identities = 234/234 (100%), Gaps = 0/234 (0%)
Strand=Plus/Minus

```
Query 14   TTTACCATACACATAGGTCAGGATTAAAAGTTGACCGCAAATAGAGCCGAGCTTCCCGTT 73
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct 468  TTTACCATACACATAGGTCAGGATTAAAAGTTGACCGCAAATAGAGCCGAGCTTCCCGTT 409
Query 74   AATCGAAAAATCATTAAATTTGGCTAGGCTGTATGAAACTTGTTTTTGTAGGGTTTGGAA 133
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct 408  AATCGAAAAATCATTAAATTTGGCTAGGCTGTATGAAACTTGTTTTTGTAGGGTTTGGAA 349
Query 134  AACATAGAAAAAGTGCGTAAGATTCTTGCTCAGTAGTTCTTTTAGTTCGTTTATTTTGAT 193
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct 348  AACATAGAAAAAGTGCGTAAGATTCTTGCTCAGTAGTTCTTTTAGTTCGTTTATTTTGAT 289
Query 194  AACGTATGCGGTAGCCTGTTCGCTAATGACTTCTAAATTATAATAGCCAACCGA 247
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct 288  AACGTATGCGGTAGCCTGTTCGCTAATGACTTCTAAATTATAATAGCCAACCGA 235
```

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Analytical process & identity

$\bar{x} \pm U$

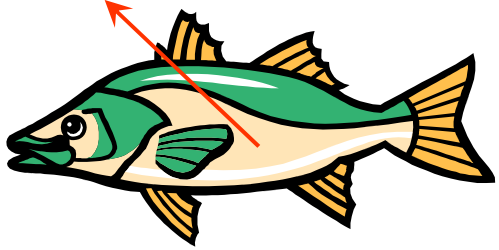
↑

absorption measurement

Hg^0

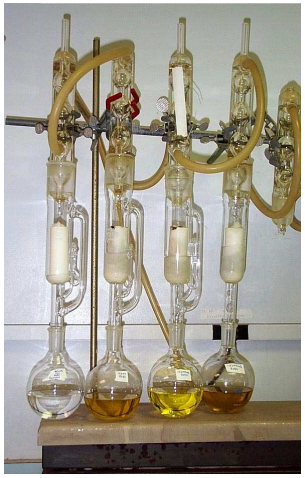
vaporisation

Me-Hg



extraction

$Me\text{-}Hg^+$



demethylation

↓

Hg^+

reduction

↓

transformations known?

transformation yield?

transformation reproducibility?

losses / interferences?

Hg^0(sol) ← Hg^0(air) ← Hg(Au) ← Hg^0

vaporisation ***amalgamation*** ***vaporisation***

Establishing traceability

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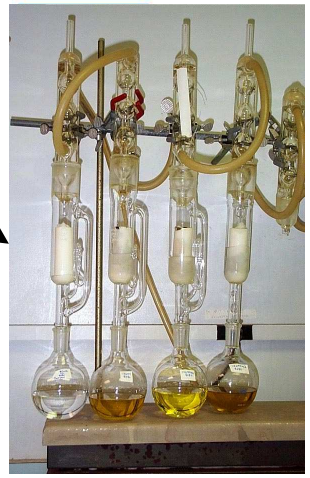
sample

weighing, milling



extraction

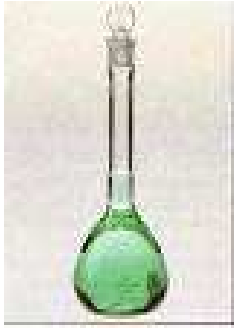
clean-up

?

Traceability ‘chain’ ?

?

‘calibration’



fill to volume

quantification
e.g., by LC-FLD

Establishing traceability

Further challenges:

- ❖ availability of appropriate calibrants
- ❖ known purity of calibrants
- ❖ often measurand ≠ measured quantity

  ⇨ knowing the correlations for 'surrogates'
- ❖ operationally defined identity of measurand

Reference Measurement Systems

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Establishing harmonised operationally defined measurands

Reference Methods

Reference Laboratories

e.g., enzyme activity according to method …

GM content as measured by PCR method…

C-reactive protein in human serum via method…

Reference Material

Parameter ('quantity') definition

Traceability anchor

often relevant for parts of procedures

essential for functional properties !

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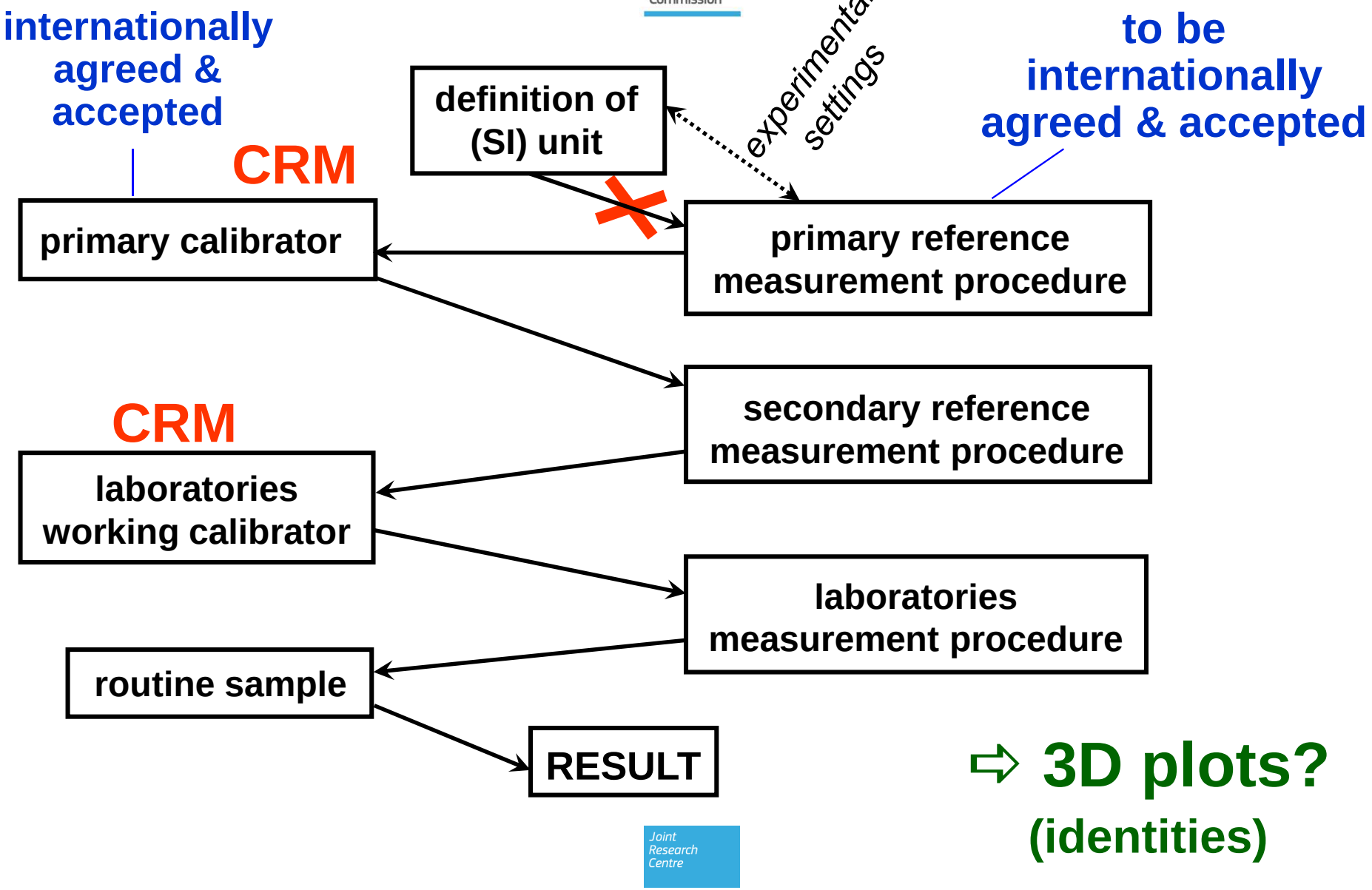
Which reference?

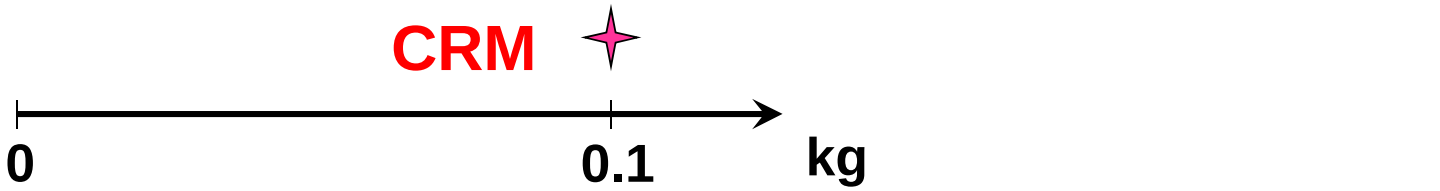
for operationally defined measurands



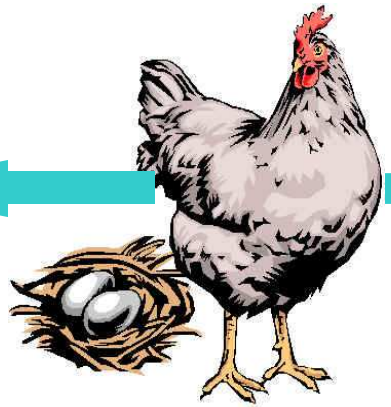
⇨ 3D plots?

(identities)

Establishing measurement scales



Reference measurement procedure



Certified Reference Material

How to realise the reference points?

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Reporting traceability

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Dienestrol in bovine urine as obtained by enzymatic deconjugation, clean-up and subsequent chromatography in combination with mass spectrometry

Traceability

Mass fraction:
(5.5 ± 1.4) µg/kg

Identity

- **Operationally defined**
- **'Structurally' defined**

Quantity value

- **Reference: SI**
- **Reference: Artefact**

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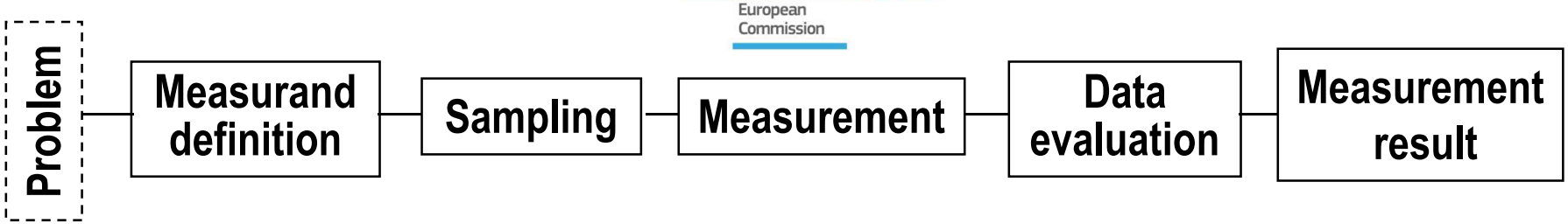
Are we ready to deliver?

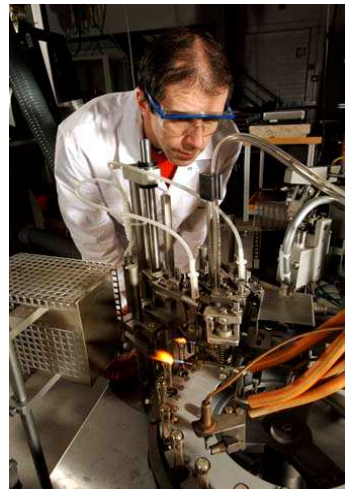


- **Chemical 'measurements' require calibration of procedures** (not only of instruments)
- **Most procedures for chemical measurements contain operationally defined steps** (relevant for stated 'identity')
- **A 'primary realisation of the unit' requires for chemical measurements more than a 'value realisation'**
- **However, pragmatic approaches exist for anchor points** (references) **in the traceability chains → multitude of CRMs**
- **Adequate uncertainty estimations, needed for traceability claims, are still very challenging for many labs**

Are we ready to deliver?

- **Concepts & guidance documents for relevant measurement tasks**
- **Tracability tools such as CRMs**
- **Competent assessors** ('calibrated')
- **Teaching & training**

Acknowledgements



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Eurachem / CITAC

Traceability in Chemical Measurement

Co-workers at IRMM

Colleagues all over the world

Various international organisations

Joint Research Centre