Challenges for Reliable Measurements across the Boundaries Physics-Chemistry-Biology

Hendrik Emons
European Commission, Joint Research Centre (JRC)
Institute for Reference Materials and Measurements (IRMM)

Setting the scene

Health & Quality of life

Global trade

Compliance with Legislation

Reliable Measurement Data

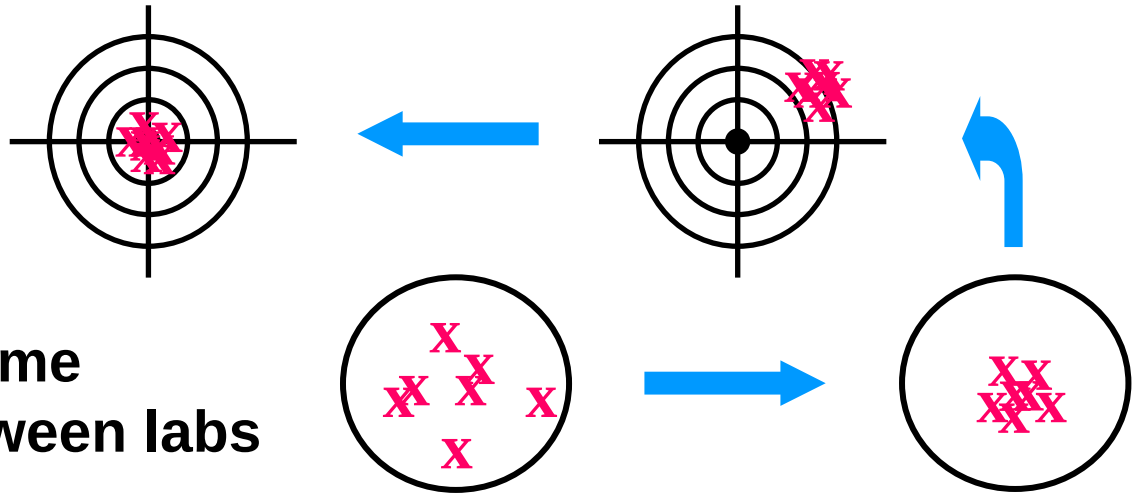
Targeted Information

Sound Knowledge

Qualified Decision

Reliability

(accuracy)

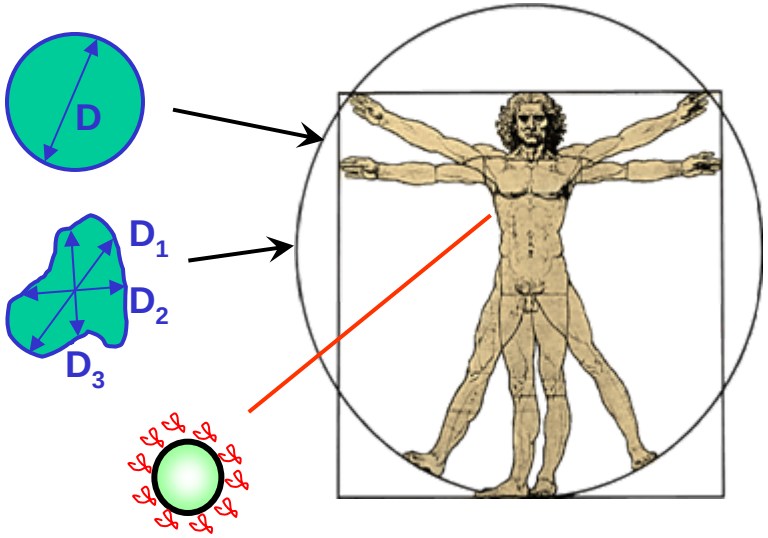


Comparability:

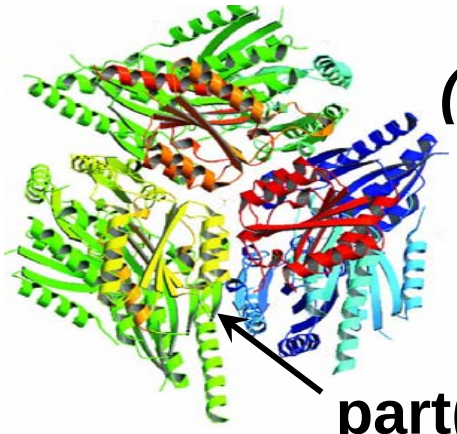
- **in time**
- **between labs**

What to measure ?

Engineered nanoparticles



Complex molecules (functions)

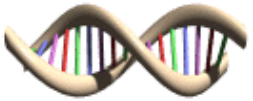


whole molecule ?
(identity, number…)

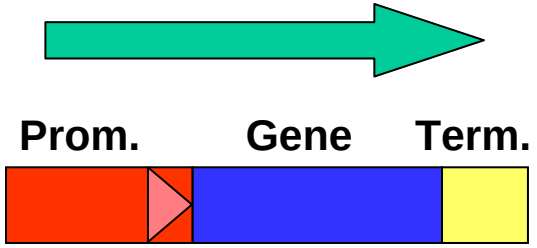
activity/reactivity

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

non-GMO



\+ foreign DNA



GMO

Which 'parameter' ?

Diameter ? **Mass ?** **Activity/reactivity ?**

3D morphology ? **Number ?** **Ratio ?**

Definition of decision-relevant measurand -

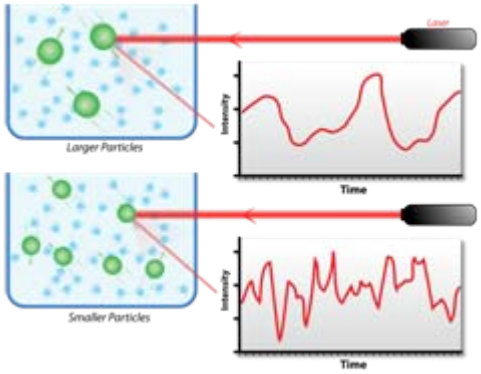
targeted property 'structural', 'functional', other?

'Temporary' approach in Physics – Chemistry - Biology:

Measurands defined by the measurement procedure

Nanoparticle size

Dynamic Light Scattering



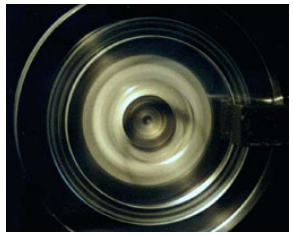
ISO 22412

19.0 ± 0.6 nm

Hydrodynamic diameter

EHS-(decision) relevant parameter?

Centrifugal liquid sedimentation

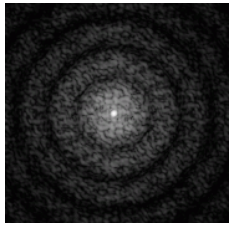


20.1 ± 1.3 nm

Stokes diameter

ISO 13318-1

Small angle X-ray scattering

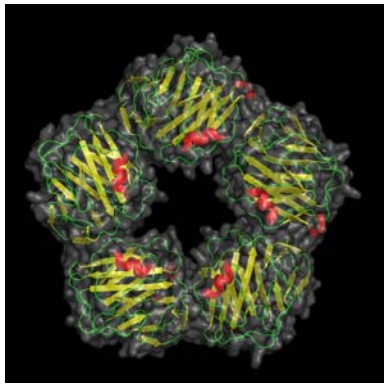


21.8 ± 0.7 nm

from Guinier radius of gyration

and: particles unstable & reactive ↷ transformations & dynamics

C-reactive protein



- **Clinical marker of inflammation**
- **Marker of cardiac risk**

CRP	Normalized relative CRP mass concentration by with different immunoassays						
	IA-1	IA-2	IA-3	IA-4	IA-5	IA-6	IA-7
Pentamer in serum	100 %	89 %	107 %	100 %	89 %	98 %	100 %
Pentamer in buffer	103 %	49 %	59 %	79 %	96 %	117 %	100 %

Standardisation required !

GMO quantification

How to determine & report the 'genetically modified' content of feed / food ?

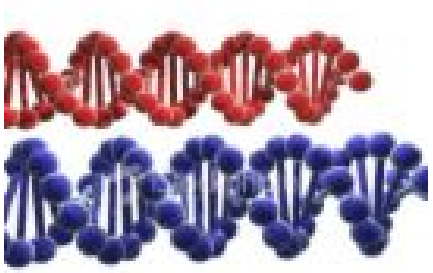
Mass fraction

$$\frac{\text{GMO species mass}}{\text{total species mass}}$$

?

DNA copy number ratio

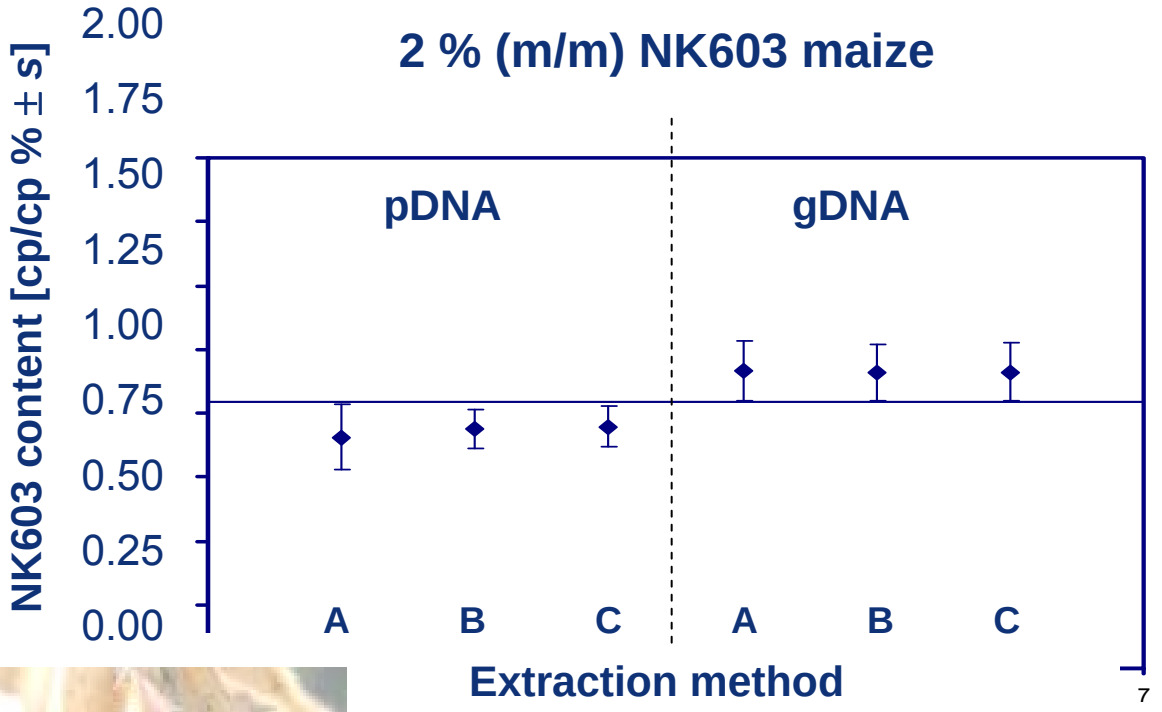
= number fraction



$$\frac{\text{copies of transgenic DNA}}{\text{copies of species-specific DNA}}$$

How to calibrate the (PCR) measurements ?

DNA copy number ratio



1.17 % ± 0.21 %

using gDNA for calibration

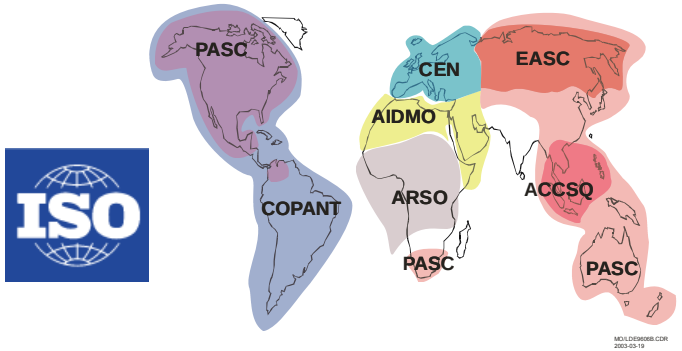
0.90 % ± 0.19 %

using pDNA for calibration

Towards Comparability

Approach: **Standardisation** → ***Legislation***

"harmonized methods"

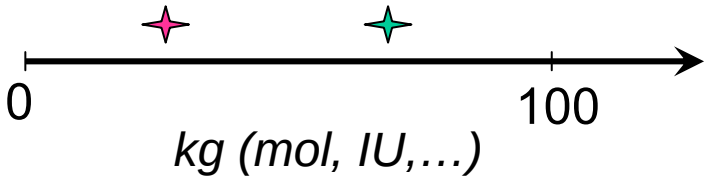


Prescribed methods/procedures

Improving knowledge on structure-property relations

establish/realize measuring scales

Prescribed method-performance characteristics



→ **'material' standards required**

Metrological Traceability

SI standard

International standard

Reference Material

= *anchor point*

National mass standard

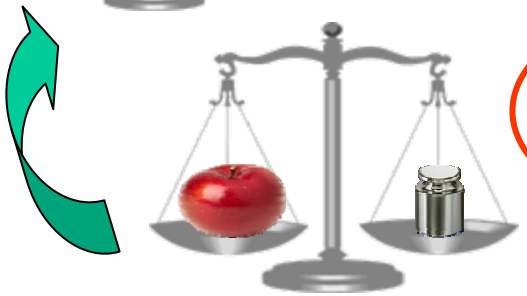
Laboratory calibration standard

Local Mass standard

(Bio)chemical analysis

involving 'method-defined' steps

calibrating a balance



Measurement result

GMO content ?

Traceability anchor

Non-destructive measurements

Artefacts

Destructive measurements

Certified Reference Material

Reference substance

Standard material

Reference standard

Calibrant / Calibrator

Analytical standard

Challenge:

sustainable primary standard

- homogeneous subsamples
- appropriate stability
- metrologically valid property value with small uncertainty

'Across borders' solution for operationally defined measurands

Reference Methods

Reference Laboratories

e.g., particle size as measured by DLS ISO method 22412

GM content as measured by PCR method…

C-reactive protein in human serum via method…

Parameter ('quantity') definition

Traceability anchor

Reference Material

VAMAS

ISO

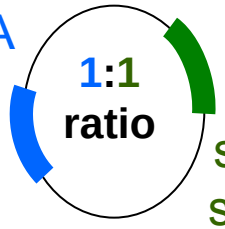
IFCC International Federation of Clinical Chemistry and Laboratory Medicine

Reference Measurement System

for measurements of GM DNA copy number ratio by quantitative PCR

Plasmid

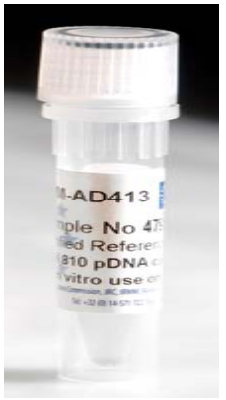
Transgenic DNA sequence (1)



Species-specific DNA sequence (1)

pDNA CRM

Independent calibration



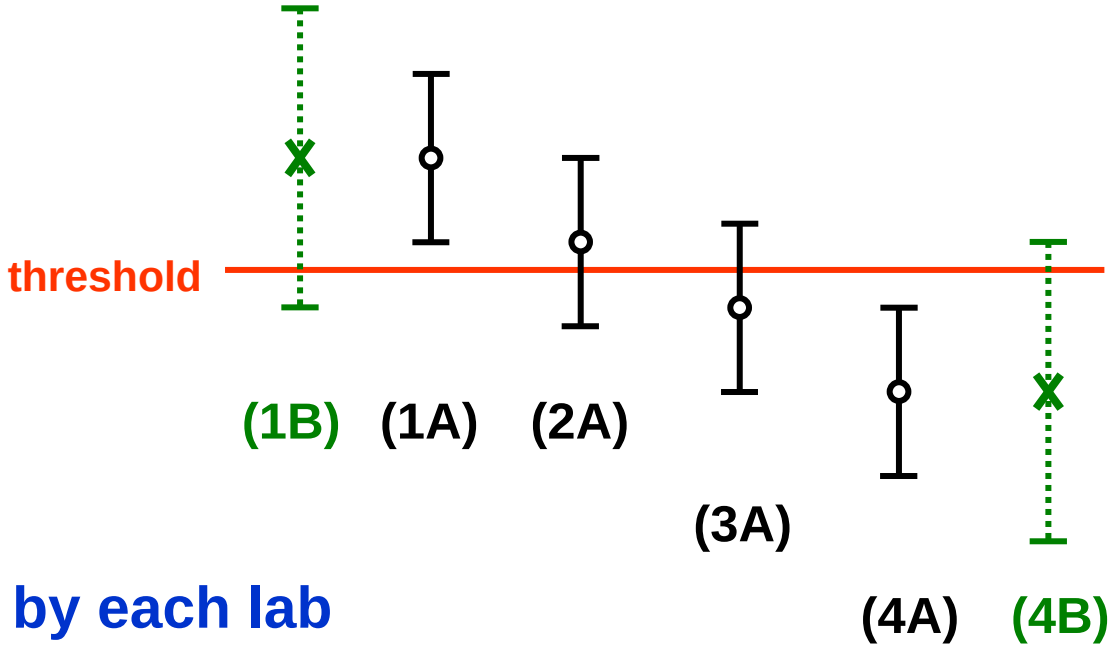
Food/feed sample → **Sample preparation** → **DNA extraction / purification** → **Real-time PCR** → **Data evaluation** → **Measurement result**

Also: 'highest order' CRMs for human proteins *(chemistry)*, impact toughness of steel *(physics)*, etc.

Uncertainty of decisions

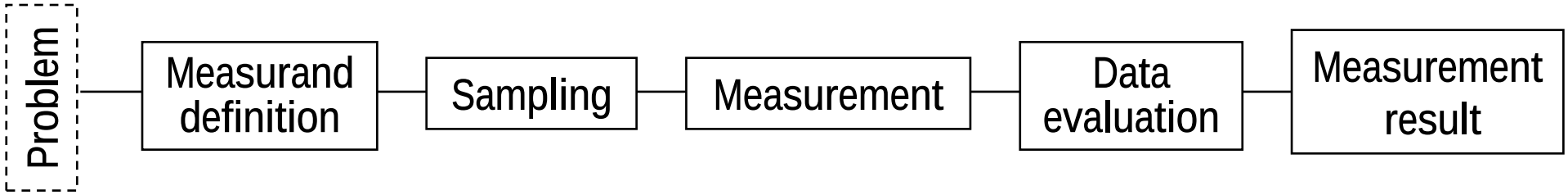
Measurement result:

$$\bar{x} \pm U$$



Challenges:

- adequate estimation of U by each lab
- harmonized application of U



Take-home messages

Across scientific & regulatory & geographical borders:

- identify & specify the relevant measurands
- develop & agree on adequate reference measurement procedures for functional properties, sum parameters etc.
- combine documentary with material standards for ensuring comparable results of emerging measurement tasks
- design & realize globally accepted anchor points for sustainable metrological traceability
- tackle the scientific challenges for establishing & qualifying 'highest order' reference materials
- exploit knowledge & progress of various scientific disciplines for general measurement solutions and uncertainty estimations

Final conclusion

"You may think you know a subject, but until you can measure it and calculate it your knowledge is of a vague and unsatisfactory kind"

Ernest Rutherford

(1871-1937)