

# Developing benchmarks for measurements – The IRMM approach



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**JRC's Mission is to provide customer-driven scientific and technical support for the conception, development, implementation and monitoring of EU policies.**

**As a service of the European Commission, the JRC functions as a reference centre of science and technology for the Union...**



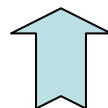
**The mission of the IRMM is to promote a common and reliable European measurement system in support of EU policies.**

## EU Stakeholders:

- *Policy Directorates of the European Commission*
- *European Agencies*
- *EURL/NRL networks*
- *CEN, EA, EURAMET*
- *Member States (authorities & laboratories)*



Development of  
'global' RMs



Compliance with  
Legislation

Health & Quality of life

Global trade

## Global Stakeholders:

- *ISO, ILAC, CIPM*
- *other international organisations (IAEA, Codex, OECD,...)*
- *Sector-specific bodies (IFCC, VAMAS, AOAC,...)*
- *control/monitoring laboratories*

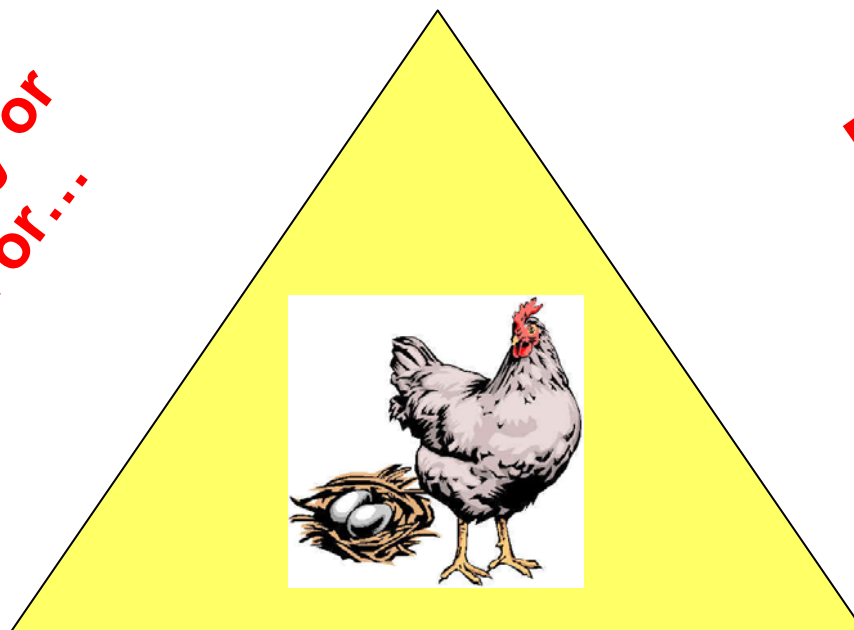
~~Driver:  
Curiosity ?~~

Analytical problem  
with decision relevance

Driver:  
Toxicology or  
Fraud or...

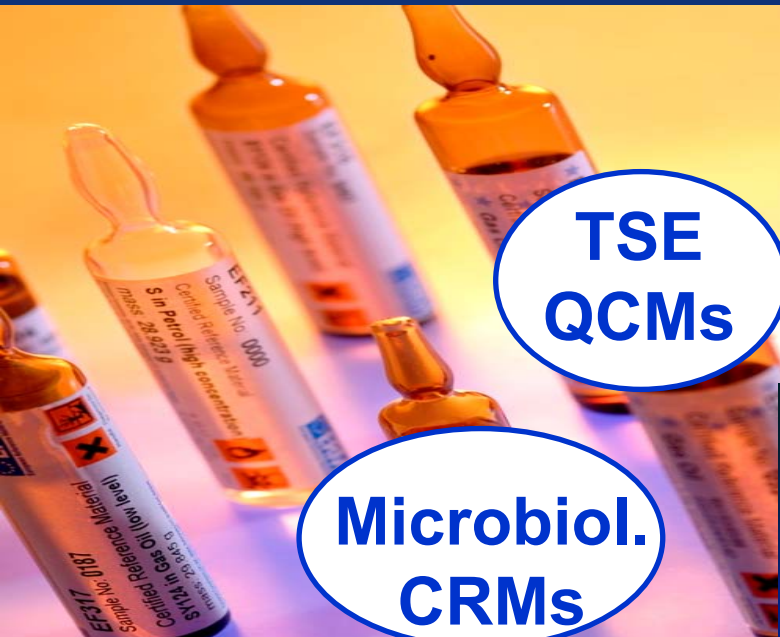
Driver:  
Legislation

Validated  
analytical  
methods



Reference  
Materials

Driver:  
Accreditation



**TSE  
QCMs**

**Microbiol.  
CRMs**



**Food  
CRMs**



**Clinical  
CRMs**

**GMO  
CRMs**



**Soil/  
Sediment  
CRMs**



**Water  
CRMs**

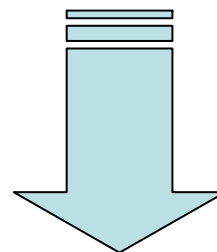


**Nuclear  
CRMs**



**Engin. Mat.  
CRMs**

We are able to measure cadmium in homogeneous water, 'Kjeldahl-nitrogen' in dried foodstuff, solid particle diameters by electron microscopy,...

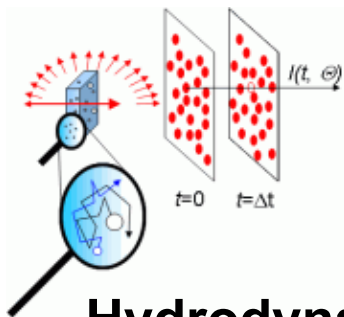


**(currently)  
measurable  
parameters**

**?  
=**

**parameters with  
decision relevance**

## Dynamic Light Scattering

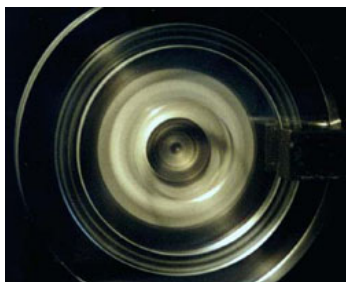


$46 \pm 2 \text{ nm}$

Hydrodynamic diameter

## Disc sedimentation

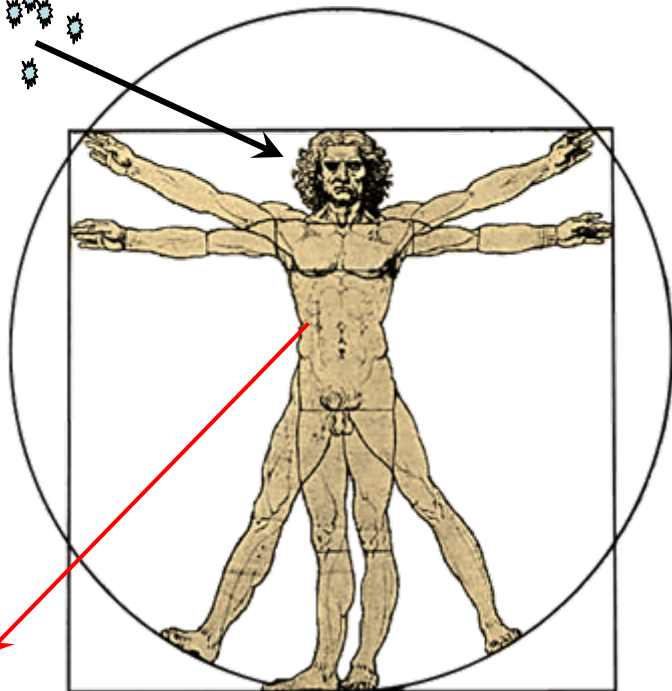
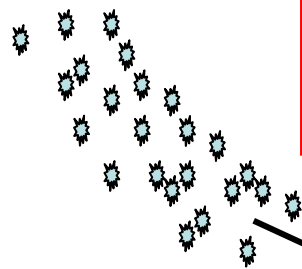
$35 \pm 1 \text{ nm}$




Stokes diameter

Nano-  
particle  
size ?

EHS-(decision)  
relevant parameter?



nanoparticle  
suspension 

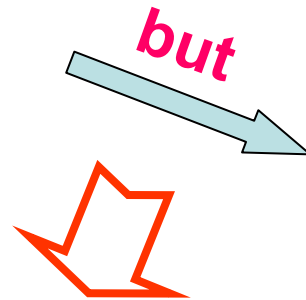
but: particles unstable & reactive  various transformations  
 measure also dynamics

## VIM-3 (ISO Guide 99) definition of 'measurand':

“Quantity intended to be measured”

### Measurand:

*Mass fraction of proteins  
in food*



**Real measurement subject:**

often 'Kjeldahl nitrogen'

**Understanding of the whole  
measurement process &  
transformations required**



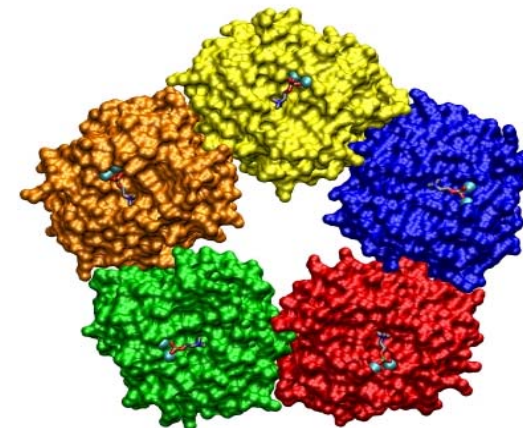
**Potential fraud  
(melamine)**

## Example: C-reactive protein (CRP)

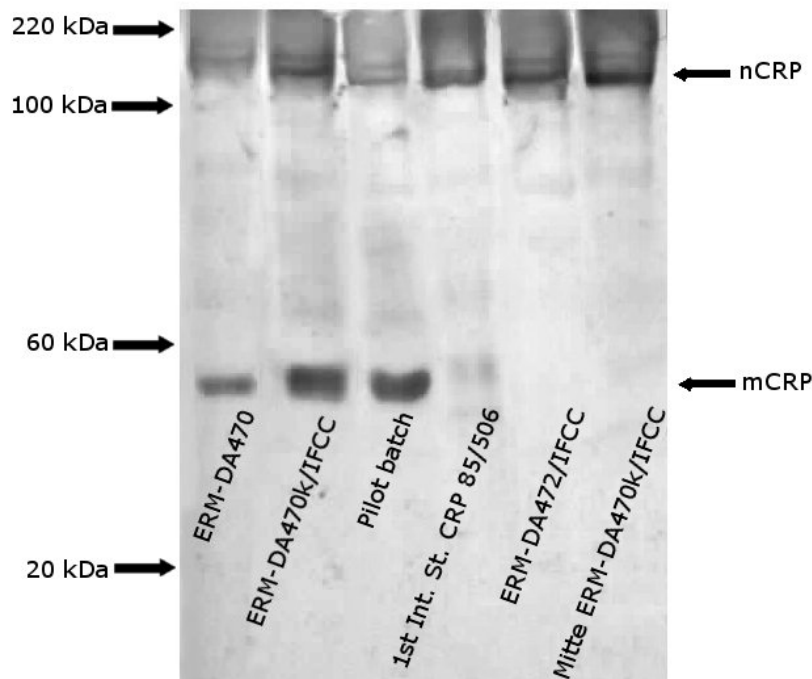
### - Clinical marker of inflammation:

- ~ 1 mg/L ▶ normal
- 10-40 mg/L ▶ mild inflammation, viral infections
- 40-200 mg/L ▶ severe bacterial infections, burns

### - Marker of cardiac risk: >2.4 mg/L ▶ increased risk

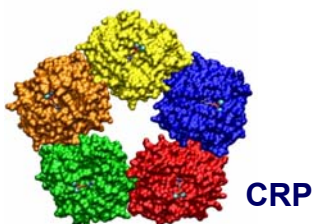


**Sample  
treatment  
(e.g.,  
freeze-  
drying)**

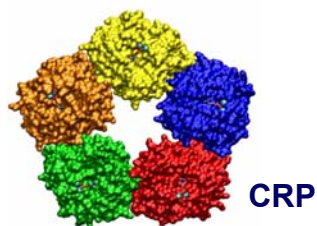


**MS signal**

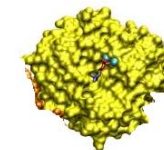
**Immuno-  
assay  
response ?**



**Pentamer in serum matrix**



**Pentamer in buffer**



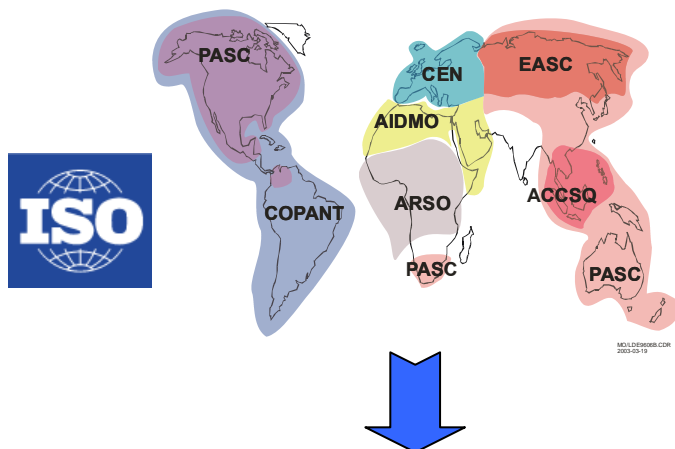
**Monomer in buffer**

Material	Normalized relative CRP mass concentration by with different methods						
	IA-1	IA-2	IA-3	IA-4	IA-5	IA-6	IA-7
ERM-DA472/IFCC	<b>100 %</b>	<b>89 %</b>	<b>107 %</b>	<b>100 %</b>	<b>89 %</b>	<b>98 %</b>	<b>100 %</b>
Pentamer In buffer	<b>103 %</b>	<b>49 %</b>	<b>59 %</b>	<b>79 %</b>	<b>96 %</b>	<b>117 %</b>	<b>100 %</b>
Monomer In buffer	<b>12 %</b>	<b>0.01 %</b>	<b>&lt; 0.01 %</b>	<b>&lt; 0.1 %</b>	<b>&lt; 0.1 %</b>	<b>0.02 %</b>	<b>0.02 %</b>

**Standardisation required !**

## Approach: **Standardisation**

“harmonized methods”



**prescribed  
methods/procedures**

*sampling,  
method-defined parameters*

**‘extractable’ Pb, SCCP**

**Legislation**

## Approach: **Metrology**

“ultimate” analysis

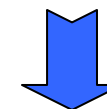


Comité international des poids et mesures

Bureau  
international  
des poids  
et mesures

Organisation  
intergouvernementale  
de la Convention  
du Mètre

- Metrological traceability
- Measurement uncertainty



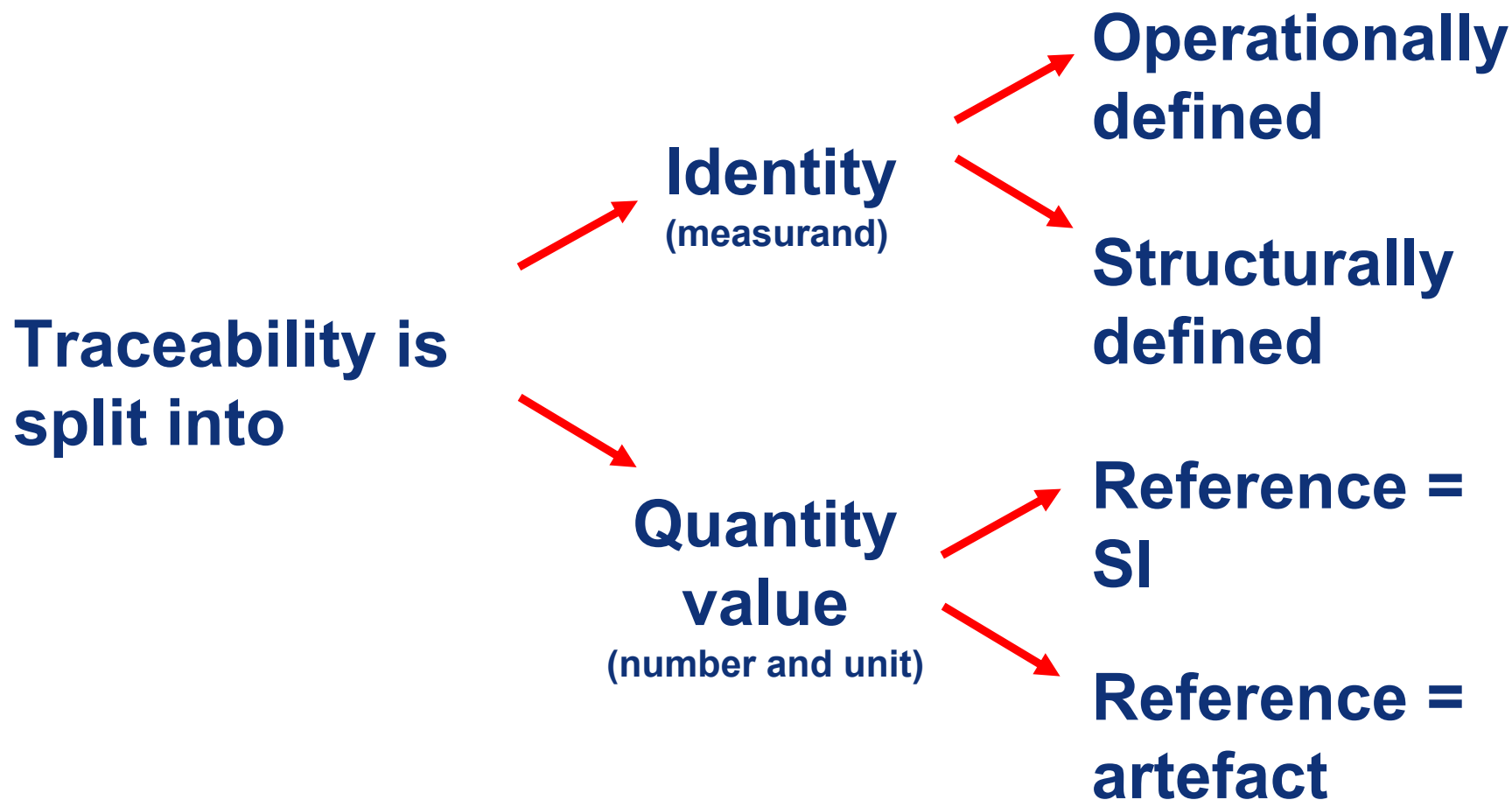
**prescribed  
method-performance  
characteristics**

*“SI-traceable” parameters*

**Cd, B[a]P,...**

**Consequences for required measurement standards !**

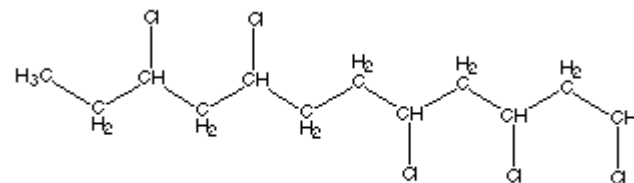
## Traceability statements on ERM<sup>®</sup> Certificates



## Example: SCCPs

= highly complex technical mixtures of *polychlorinated n-alkanes*

- chain length C10-C13, 50-70 % Cl
- up to 6300 isomers



**Environmental and health concern:**

*persistent, toxic, bioaccumulative, possibly carcinogens (2B)*

**Directive 2000/60/EC: Water Framework Directive**

**Decision 2455/2001/EC: Introduction in the list of Priority Hazardous Substances**

### *Environmental Quality Standards:*

C<sub>10</sub>-C<sub>13</sub> Chloroalkanes (µg L<sup>-1</sup>)

AA-EQS

MAC-EQS

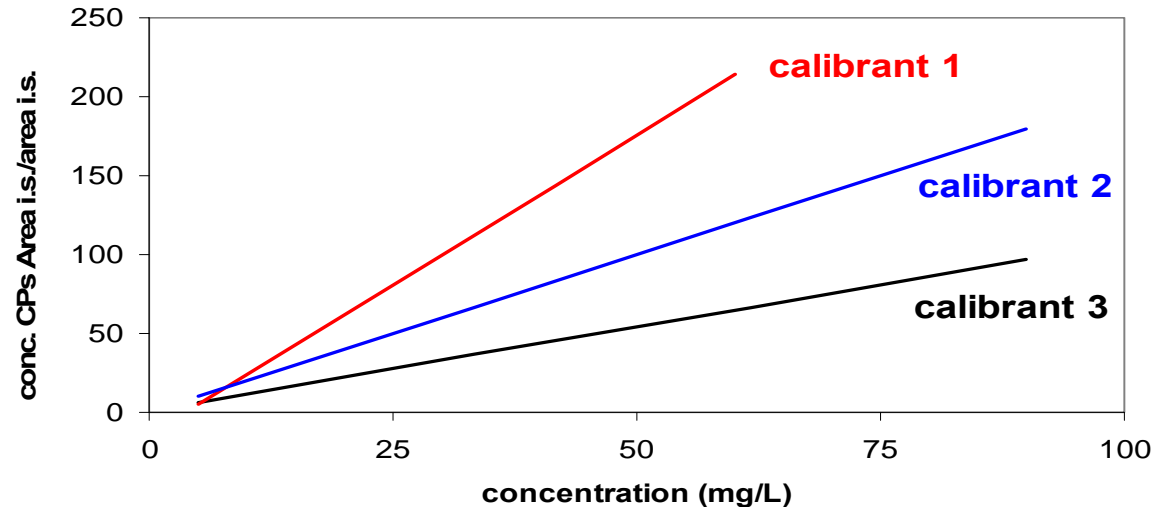
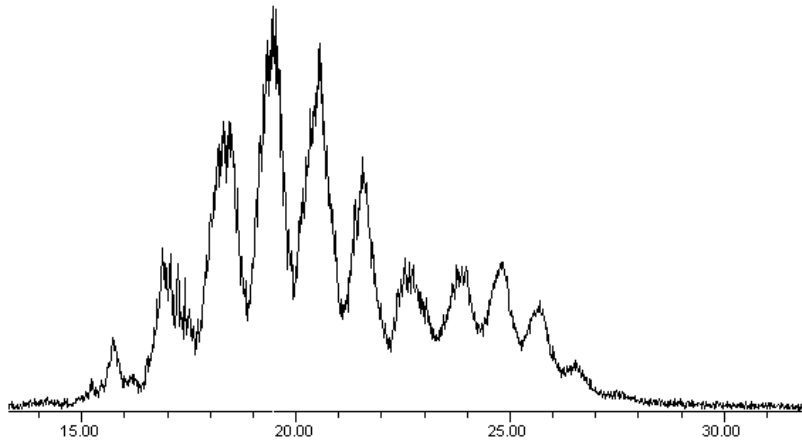
0.4

1.4

AA...annual average

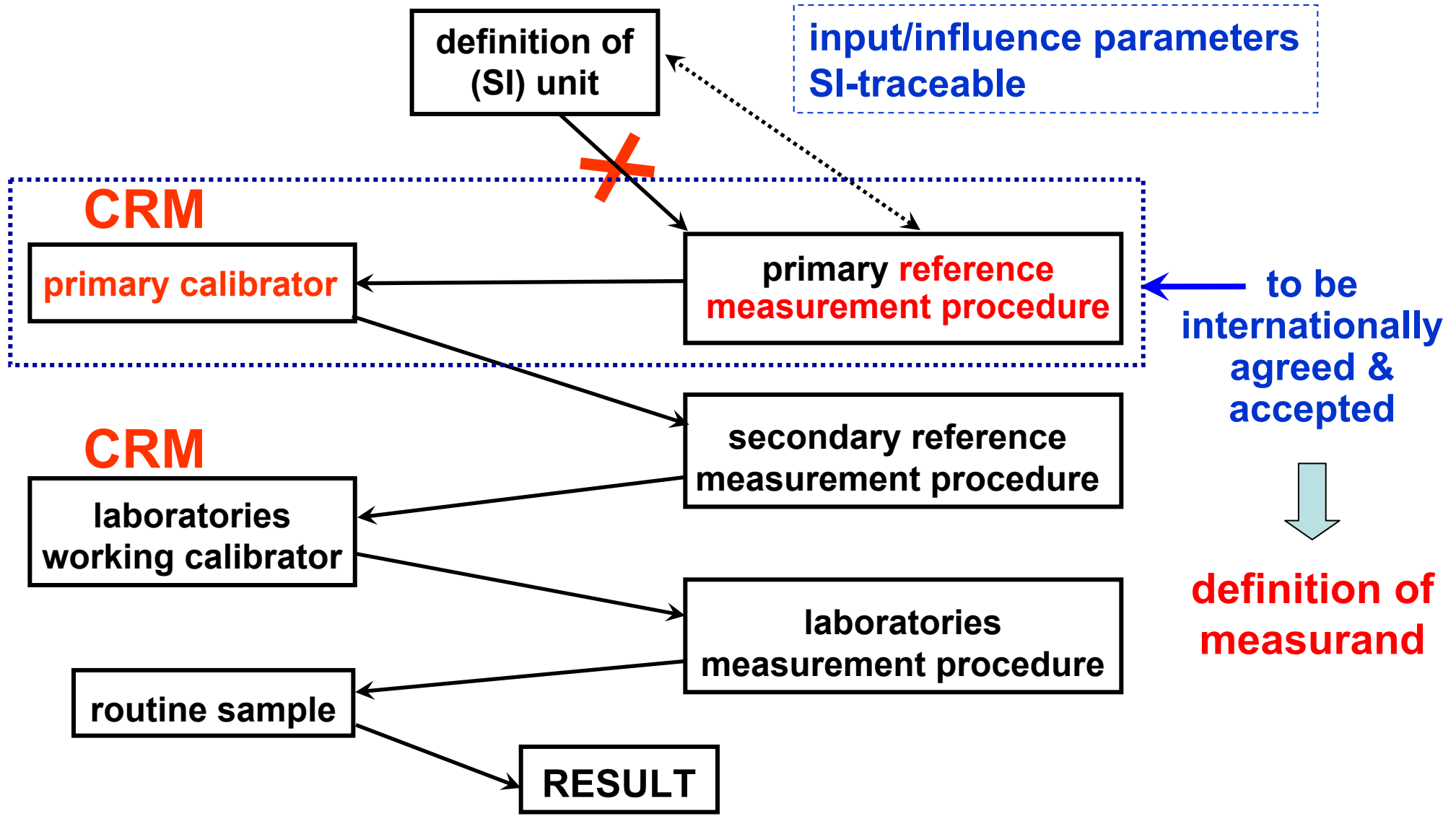
MAC...maximum allowable concentration

## SCCPs measured with GC-ECNI-MS

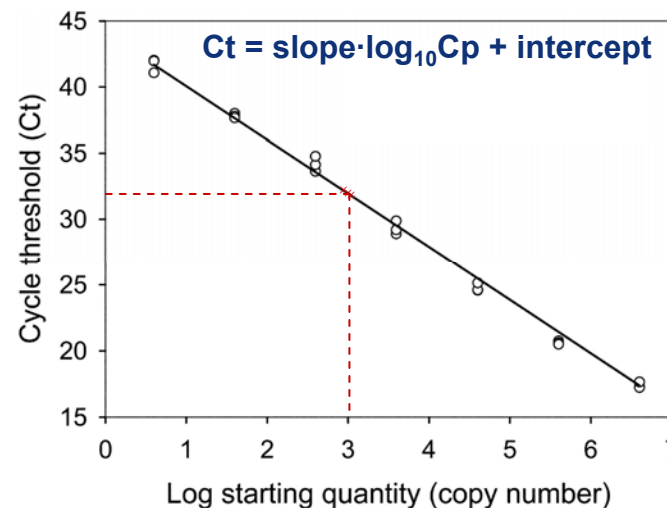
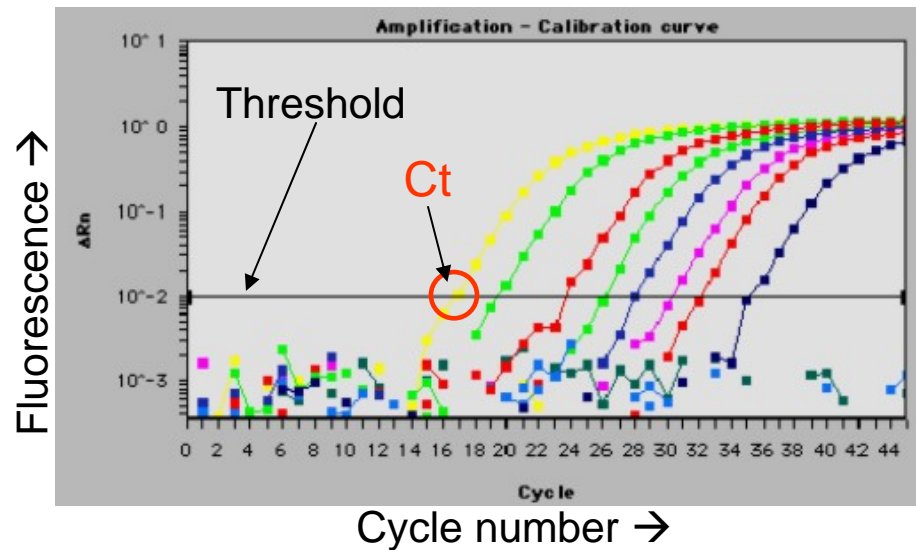
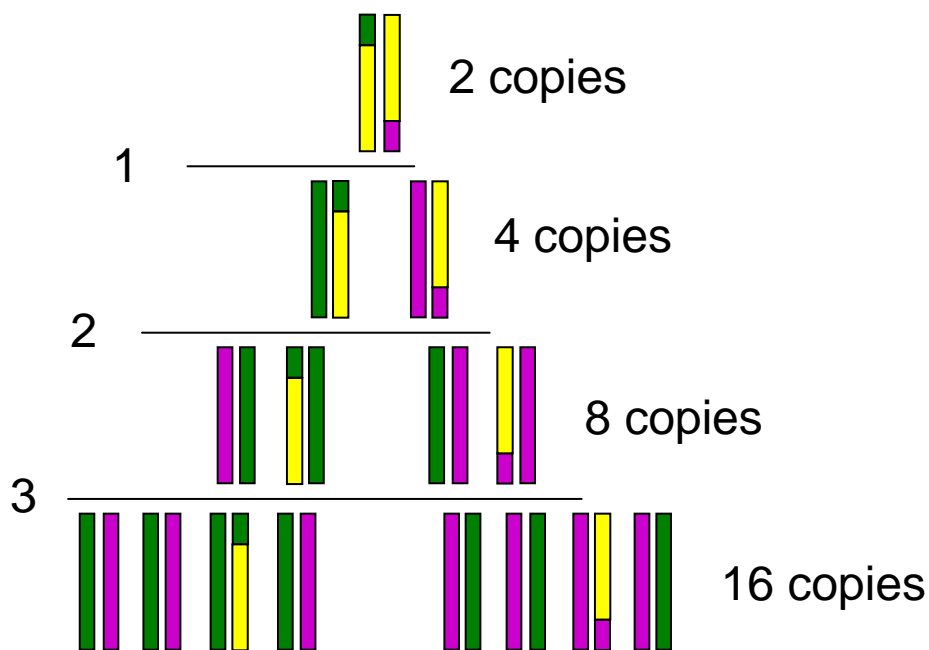


**TRACEABILITY**

- Sufficient definition of the ‘measurement subject(s)’
- Proper selection & description of the calibrants & calibration hierarchy

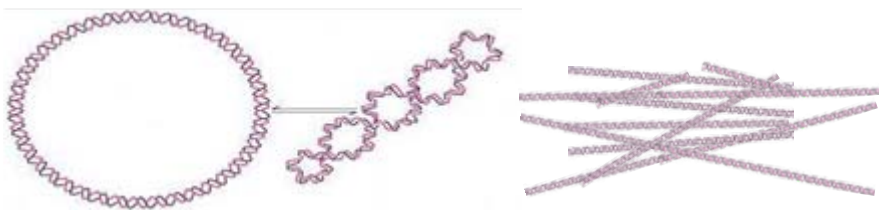


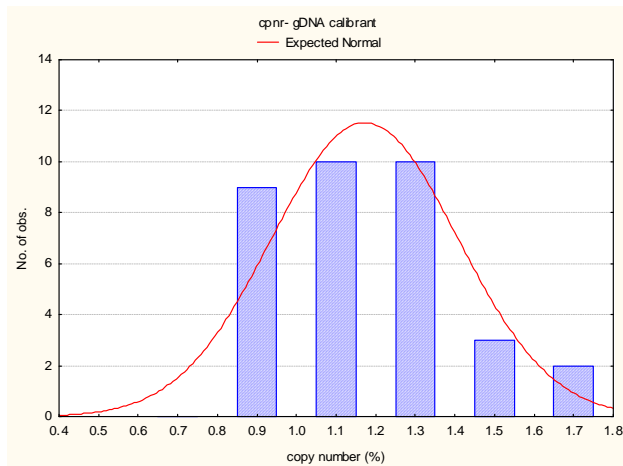
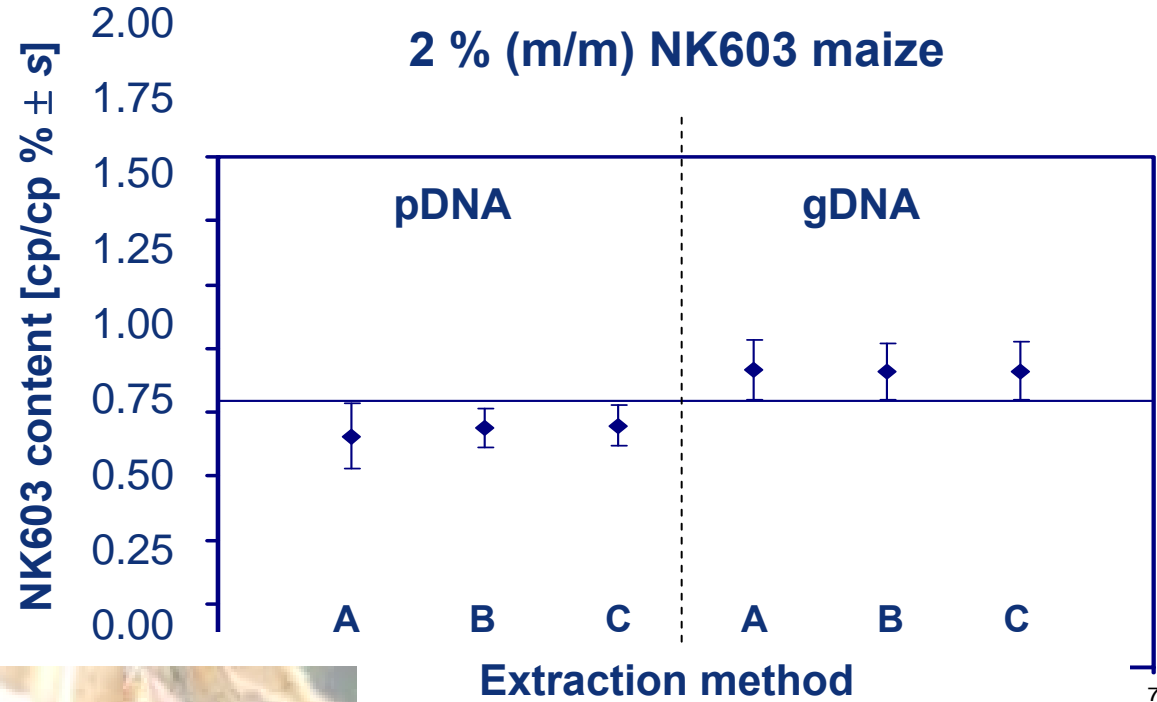
## Polymerase Chain Reaction (PCR)



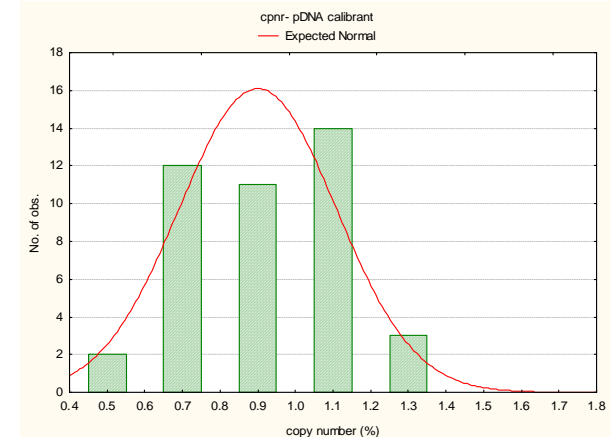
with ?

**Calibration needed !**



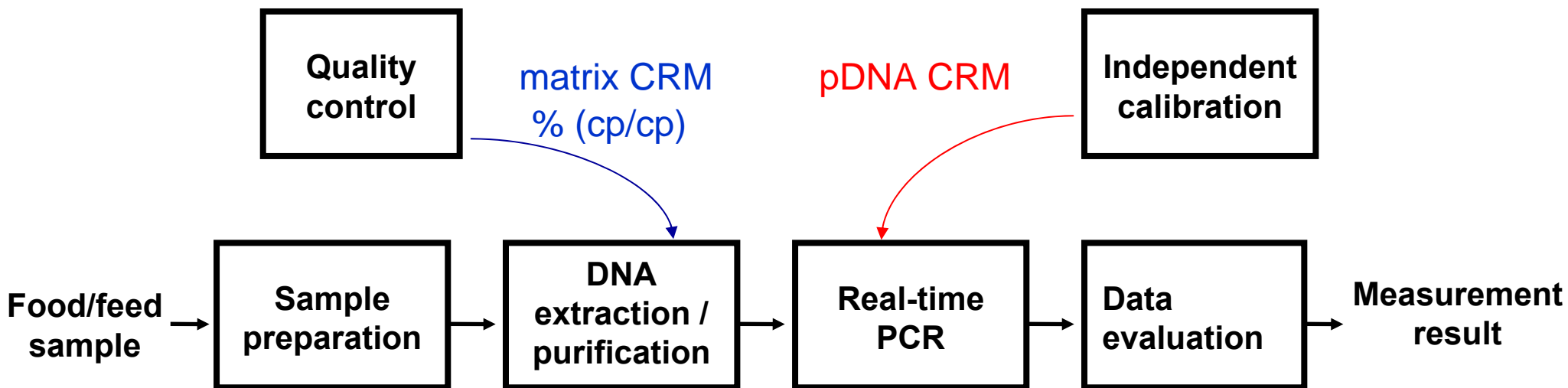


**gDNA for calibration: 1.17 % ± 0.21 %**



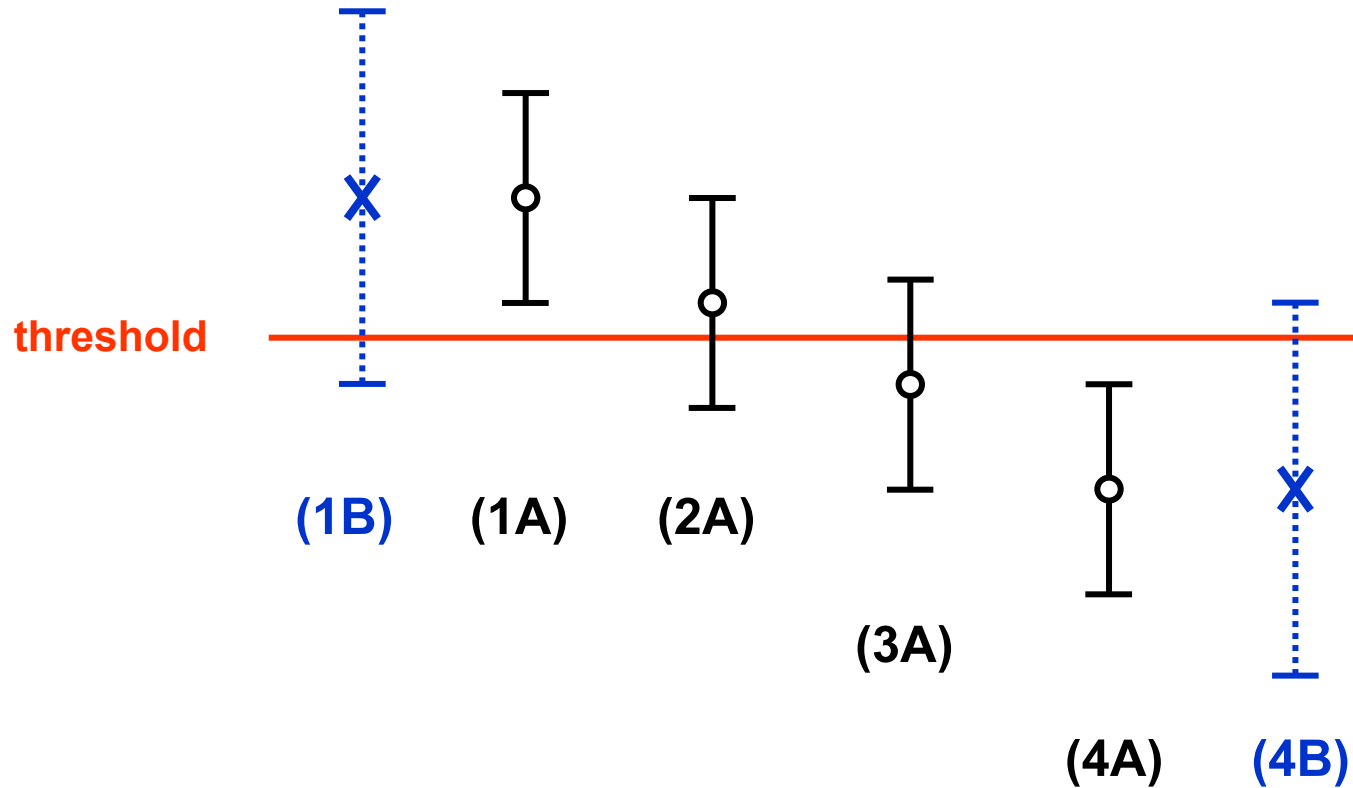
**pDNA for calibration: 0.90 % ± 0.19 %**

## for measurements of GM DNA copy number ratio by quantitative PCR

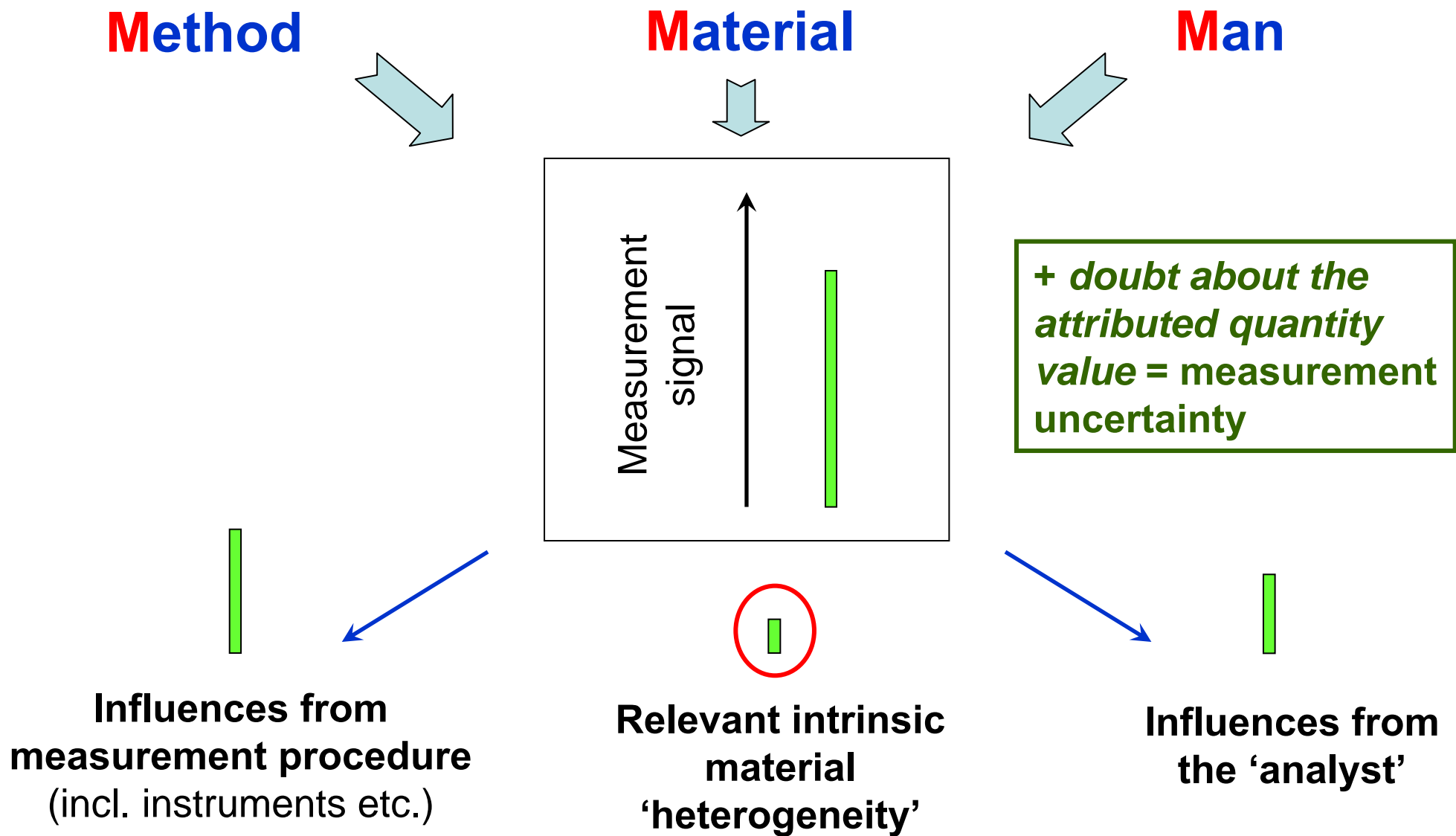


- PCR = limited precision** ➔
- consequences for CRM production & monitoring
  - consequences for GM surveillance

Analytical result:  $\bar{x} \pm u$



**Fit-for-decision:** by adequate uncertainty



Minimum requirements for lab performance set by safeguards authorities:

- ▶ **International Target Values (ITV) for measurement uncertainties**  
*lowered in recent years due to improved measurement capabilities*

 **New demands on CRMs used as IDMS spikes**

CRM	certified value [mol·g <sup>-1</sup> ]		U <sub>rel</sub> (k=2)	
	year 1995	year 2010	year 1995	year 2010
IRMM-046b <sup>233</sup> U	4.112 6·10 <sup>-6</sup>	4.115 38·10 <sup>-6</sup>	0.15 %	0.020 %
IRMM-046b <sup>242</sup> Pu	4.657 1·10 <sup>-7</sup>	4.650 4·10 <sup>-7</sup>	0.15 %	0.039 %
	year 1997	year 2010	year 1997	year 2010
IRMM-049c <sup>242</sup> Pu	3.666 5·10 <sup>-7</sup>		0.13 %	
IRMM-049d <sup>242</sup> Pu		(3.666 8·10 <sup>-7</sup> )		(0.030 %)

## *and related IRMM approaches*

- **R&D across scientific disciplines and application sectors:** Team with multidisciplinary background and interdisciplinary tasks; communication & collaboration networks; involvement in various international committees and scientific bodies
- **Expansion of RM concepts and QA/QC systems into 'new' fields:** Identity CRMs for human genetic testing & microbiology; QCMs for BSE testing...
- **Development & production of a broad range of RMs:** collaborative projects; early-on coordination with other RMPs
- **Providing new CRMs which imitate closer real-world samples:** systematic checks of the equivalent analytical behaviour of RM & test sample in RM characterisation studies
- **Qualification of RM users:** Training courses; ERM Application Notes; guidance documents; customer services...

**All  
Conference  
participants**

**Our  
collaborators  
and cooperation  
partners all  
over the world**

**Current  
and former  
coworkers  
of the RM  
Unit &  
supporting  
IRMM staff**

**THANK YOU !**

# The Future of Reference Materials

## Science and Innovation

23-25 November 2010

Institute for Reference Materials and Measurements (IRMM)  
Geel, Belgium



# THANK YOU !