Better Standards, Better Life !

Calibration and Purity Assessment in Chemical Analysis

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Philosophical question

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Q: What makes metrology in chemistry so unique?

A: Definition of mole

1. The mole is **the amount of substance** of a system which contains as many elementary entities as there are atoms in 0.012 kilogram of carbon 12; its symbol is "mol".

2. When the mole is used, **the elementary entities must be specified** and may be atoms, molecules, ions, electrons, other particles, or specified groups of such particles.

Fundamental questions

- How pure is pure?
- Purity of element
  - Chemical purity of an element
  - Isotopic composition
  - Oxidation number, valency
- Purity of compound
  - Optical isomers

Question continues

$_{78}$Pt Platinum A_r(Pt) = 195.078(2)

Isotope	Atomic mass/u	Mole fraction
^{190}Pt	189.959 930(7)	0.000 14(1)
^{192}Pt	191.961 035(4)	0.007 82(7)
^{194}Pt	193.962 663(3)	0.329 67(99)
^{195}Pt	194.964 774(3)	0.338 32(10)
^{196}Pt	195.964 934(3)	0.252 42(41)
^{198}Pt	197.967 875(5)	0.071 63(55)

$_{79}$Au Gold (Aurum) A_r(Au) = 196.966 55(2)

Isotope	Atomic mass/u	Mole fraction
^{197}Au	196.966 551(3)	1.0000

Calibration & purity for traceability

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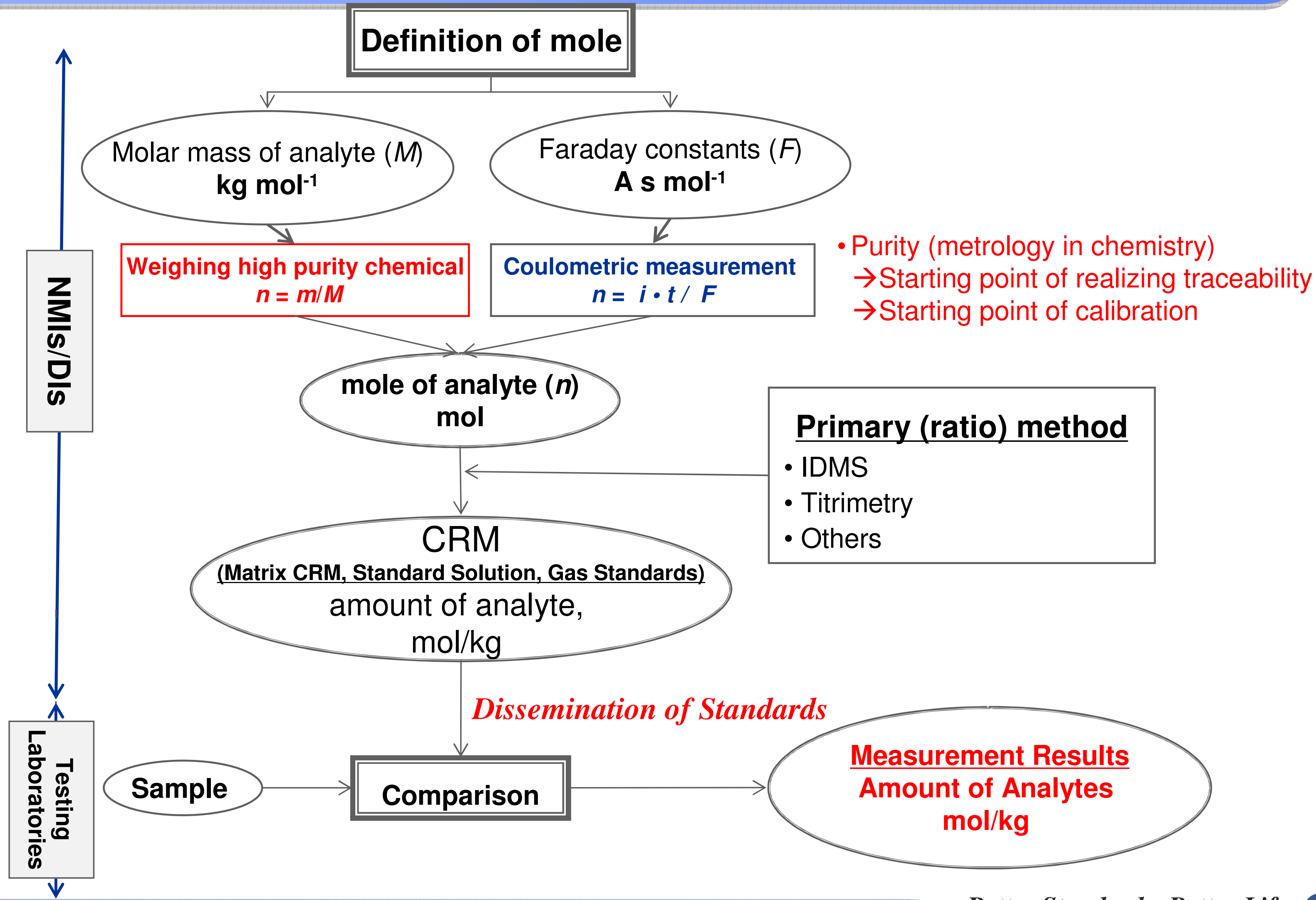

CCQM-K55.a (estradiol)

Introduction

………. The ability to undertake suitable purity assessment on materials that are to be provided as pure substance or calibration solution reference materials or are used as the internal primary calibrators of measurement services is considered a core competency in organic analysis. The purity property value (generally reported as the mass fraction content for organic analysis) assigned to the primary calibrator in a measurement hierarchy underpins the traceability chain. ……

………….. The application of the pure material could be for dissemination to external users either directly as a pure substance CRM or indirectly as a calibration solution or it could be characterized solely for internal use by the NMI/DI as the primary calibrator of a reference measurement procedure.

VIM 2.39 Calibration

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operation that, under specified conditions, in a first step, establishes a relation between the **quantity values with measurement uncertainties provided** by **measurement standards and corresponding indications with associated measurement uncertainties** and, in a second step, uses this information to establish a relation for obtaining a **measurement result from an indication**

NOTE 1 A calibration may be expressed by a statement, calibration function, calibration diagram, calibration curve, or calibration table. In some cases, it may consist of an additive or multiplicative correction of the indication with associated measurement uncertainty.

NOTE 2 Calibration should not be confused with adjustment of a measuring system, often mistakenly called “self-calibration”, nor with verification of calibration.

NOTE 3 Often, the first step alone in the above definition is perceived as being calibration.

Philosophical question continues

Q: Do we measure what we believe to measure?

A: Yes and No.

CCQM GAWG CCQM-P23 (Gravimetric values of CO/N2)
28 Jan 2002 at NMi, Delft

Dr de Leer presented some additional analysis in which it appeared that standards from two laboratories (NIST and KRISS) were above the calibration line by approximately 0.6% at all three concentrations. Dr Guenther said that he had predicted that this problem would occur with the NIST standards when analysed by NDIR. He explained that it was caused by a slight enrichment of the ^{13}C isotope in the most recent sample of pure CO used at NIST. Dr Kim explained that he had analysed the $^{12}C/^{13}C$ ratio of CO used at KRISS and had found it to be 370 rather than 86 (for a natural abundance sample). He explained that a suitable band limiting filter could reduce the sensitivity of the NDIR to isotopic effects.

Purity Assessment for Gases

- Industry needs highly pure gases (6N means better than 0.999999 mol/mol).
- It is easy to obtain high purity gases.
- Most of pure gases are really pure (at least 0.9995 mol/mol).
- When calibration gas mixtures are prepared by gravimetric method, impurity contribution is very minor, excepts very low mol fraction mixtures.

- Purity Analysis of Gas

  Mass-balance method: purity = $1 - \Sigma x_{impurity}$
  - GC (FID, TCD, ECD, AED, DID, MSD), FTIR, Gas MS
  - Dedicated Analyzer: O_2, CO, SO_2, NOx, H_2O, CO_2, Total HC
  - Isotopic ratio: Gas MS, IRMS

Impurity Analysis in CH_4 (CCQM-K66)

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KC Scheme: N_2, Ar, CO_2, ethane were added to pure methane

Analytical Methods

Participants	Nitrogen	Argon	Carbon dioxide	Ethane	Others
NIM	GC-PDHID	GC-PDHID	GC-MS	GC-FID	
VNIIM	GC-TCD	GC-TCD	µGC-TCD	GC-FID	
NPL	GC-DID	GC-DID	GC-DID	GC-DID	
VSL	GC-TCD	GC-TCD	GC-FID	GC-FID	H_2O:CRDS O_2:GC-HID
NMIJ	GC-PID	GC-PID	GC-FID	GC-MS	
NIST	GC-TCD	GC-TCD	GC-FID	GC-FID	
KRISS	GC-DID	GC-DID	GC-FID	GC-FID	HCS : GC-FID

Impurity Analysis in CH_4 (CCQM-K66)

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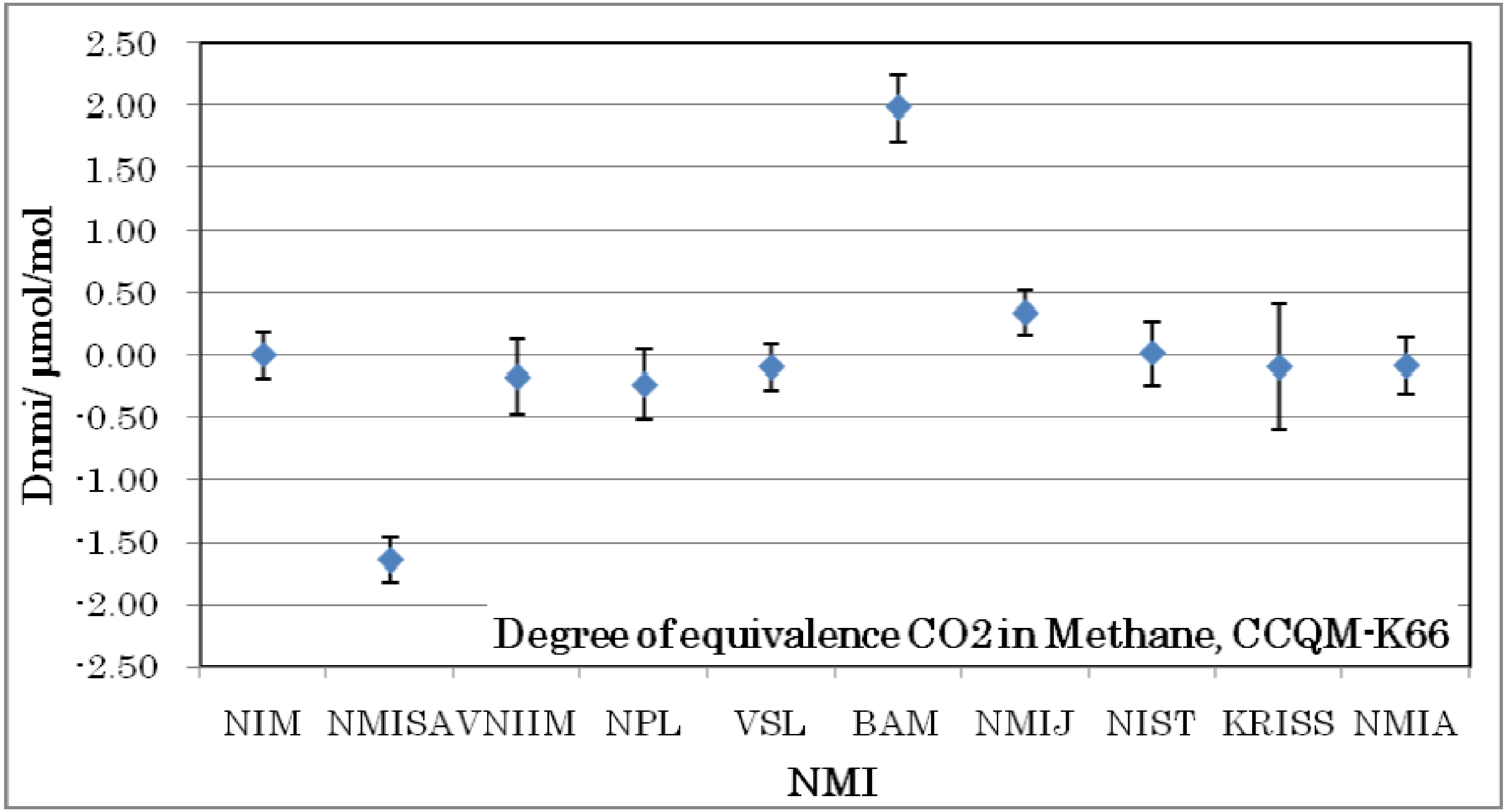

Figure 18. Degree of Equivalence for carbon dioxide impurity in methane.

Purity Study by CCQM/GAWG

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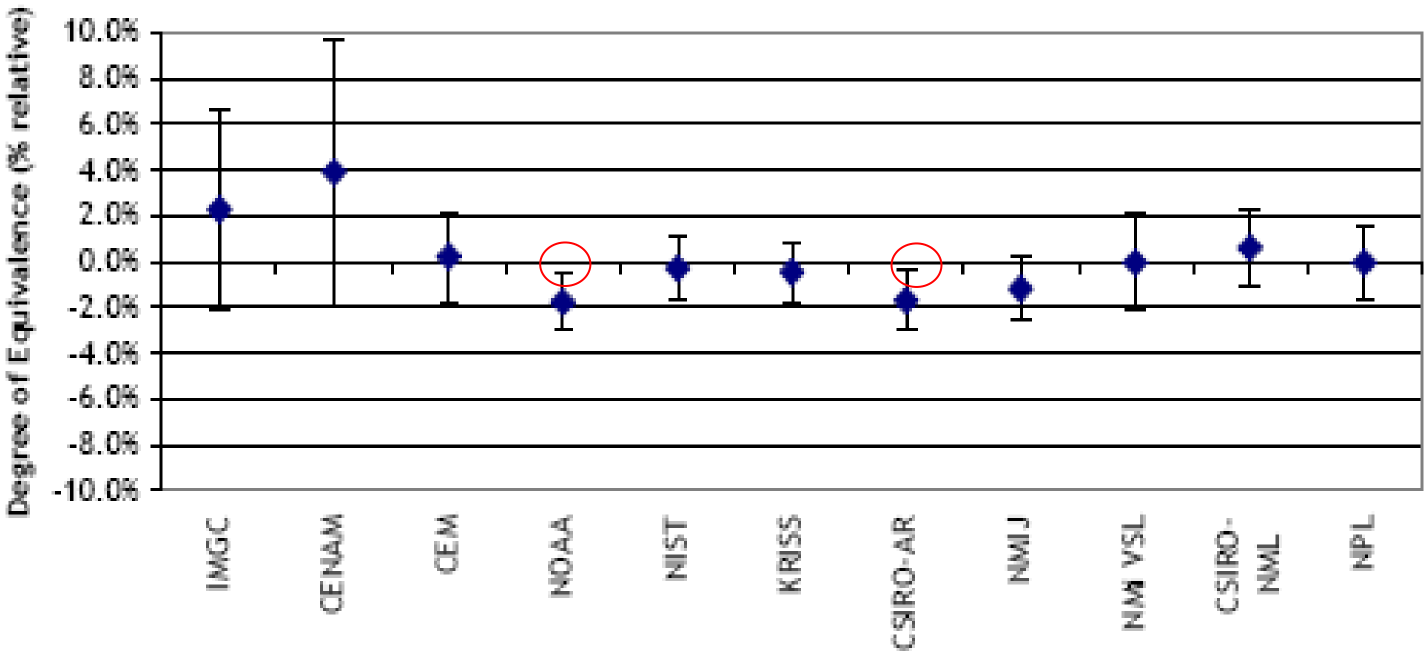
CCQM-P41 CH_4 at 1.8 µmol/mol)



Collaborative efforts found a discrepancy in CH_4 scale between NMIs and the global reference laboratories.

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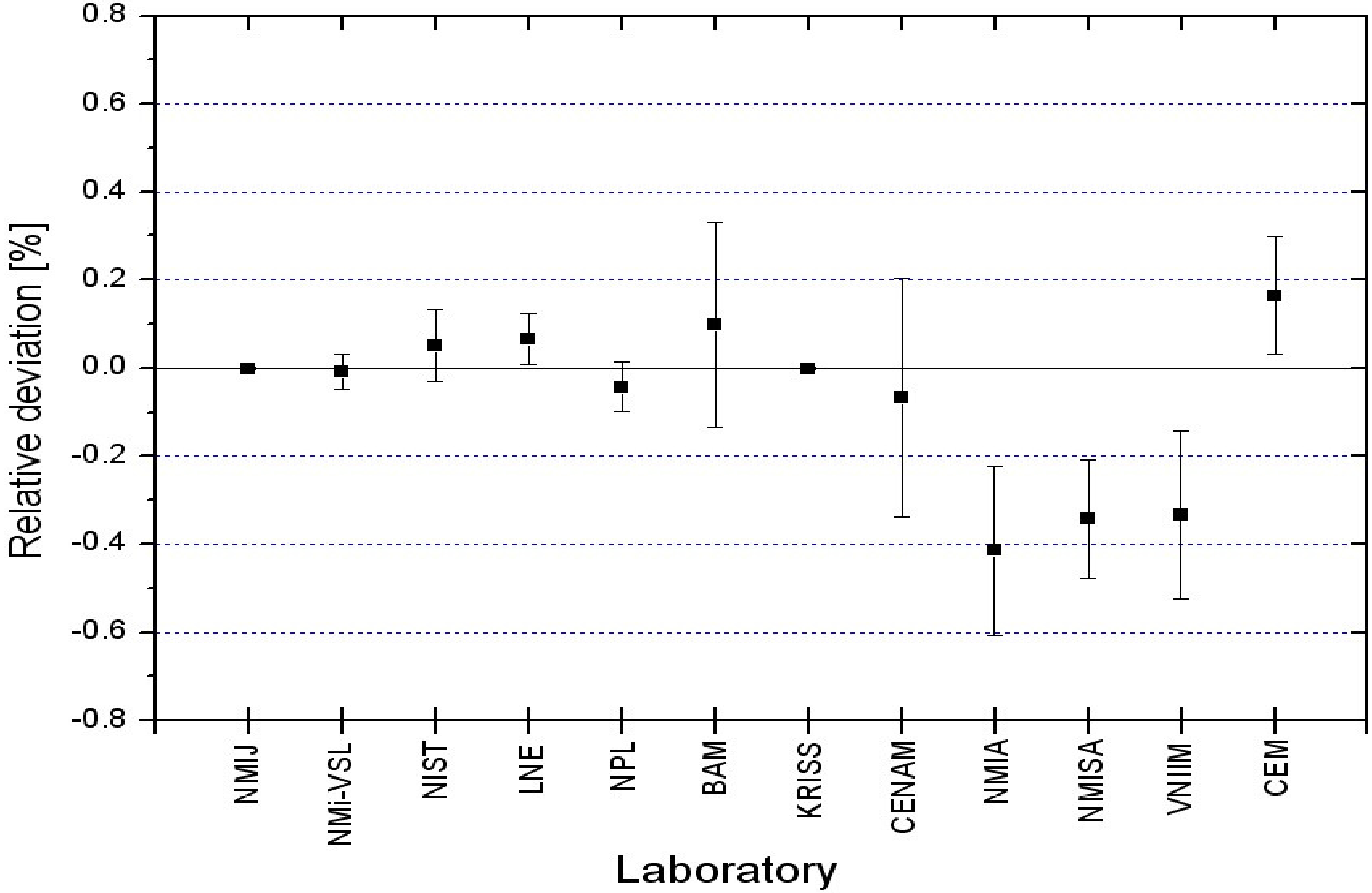
CCQM-K53: 100 µmol/mol of O_2 in N_2



Purity Assessment for Inorganic Substances

◆ Mass-Balance (1-*x*) Method

All possible impurities are quantified and subtracted from 100 %

High purity materials are mainly used for calibration solutions of elements or anions.

For high purity metals and compounds

- ICP/MS and GDMS for impurity elements
- Gas analysis in high purity metals after melting
- Ion chromatography for anion impurities

For organo-metallic compounds

- LC-ICP/MS for impurity species

◆ Coulometry for standard reagents in analytical chemistry

Standard reagents for

- Acid-base titration: potassium hydrogen phthalate (KHP), $NaHCO_3$, …
- Redox titration: potassium dichromate ($K_2Cr_2O_7$), oxalic acid, …
- Argentometry: NaCl, KCl
- Complexometry: EDTA

Purity Assessment Studies done by IAWG/EAWG

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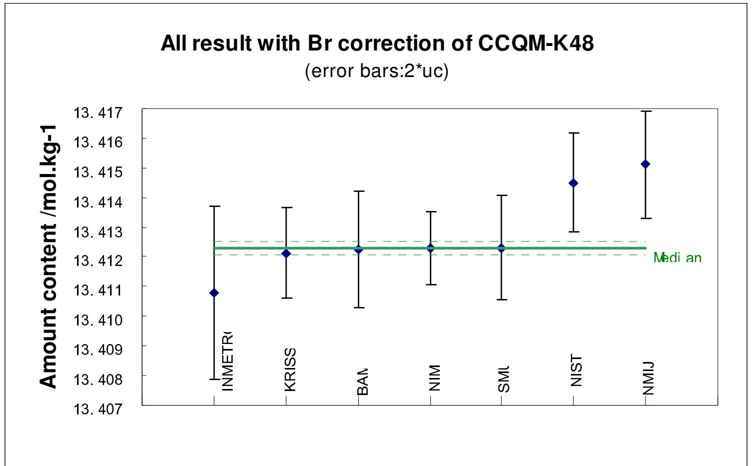
Purity assessment

Comparison No.	Description	Coord. Lab.	Year
CCQM-K34	Assay of KHP	SMU	2004
CCQM-K48	Assay of KCl	NIM	2007
CCQM-K72	Purity of zinc	BAM	2011
CCQM-P8	Purity of KCl, NaCl, $K_2Cr_2O_7$	NIST	1998
CCQM-P36	Assay of KHP	SMU	2002
CCQM-P107	Purity analysis of zinc	BAM	2007
CCQM-P112	Assay of EDTA	BAM SMU	2008



Calibration solutions

Comparison No.	Description	Coord. Lab.	Year
CCQM-K8	Monoelemental calibration solutions	EMPA	1999-2000
CCQM-K29	Anion calibration solutions	EMPA	2003-2004
CCQM-K59	Determination of nitrite and nitrate in calibration solutions	SMU NRCC	2006-2007
CCQM-K87	Monoelemental calibration solutions	PTB	2010-2011
CCQM-P30	Monoelemental calibration solutions (Parallel to K8)	EMPA	1999-2000
CCQM-P32	Anion calibration solutions	EMPA	2002
CCQM-P96.1	AsB standard solution and AsB content in marine fish	NMIJ	2010-2011
CCQM-P124	Monoelemental calibration solutions (Parallel to K87)	PTB	2010-2011

Purity assessment by exhaustive accounting for elemental contents

Concept

Total Analyte-Specific Elemental Content by reductive elemental analysis

e.g., ICP-OES, ID-ICP/MS

+

Element Specific Purity Analysis

e.g., LC-ICP/MS, GC-ICP/MS, CE-ICP/MS, etc.

Advantages

- Simple and comprehensive
- Successfully applied for organometallics and nucleic acids (dNMPs)
- Applicable to any analytes with heteroatomic elements (organometallics, P, S, Cl, Br, As, Se, etc)
- Advantageous especially for **hygroscopic samples** and samples with **mixed salt forms** of which gravimetric preparation is not reliable.

Purity assessment by exhaustive accounting for elemental contents

Solid DBT

Gravimetric preparation

Moisture?
Mixed salt form?

DBT standard

MBT
DBT
TBT

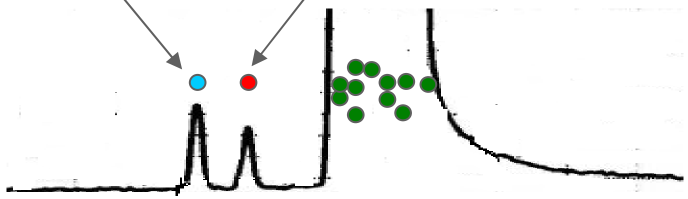
Determination of total Sn

A in mg/kg (as Sn)

MW digestion + ICP-OES
MW digestion + ID ICP/MS

Sn specific purity analysis

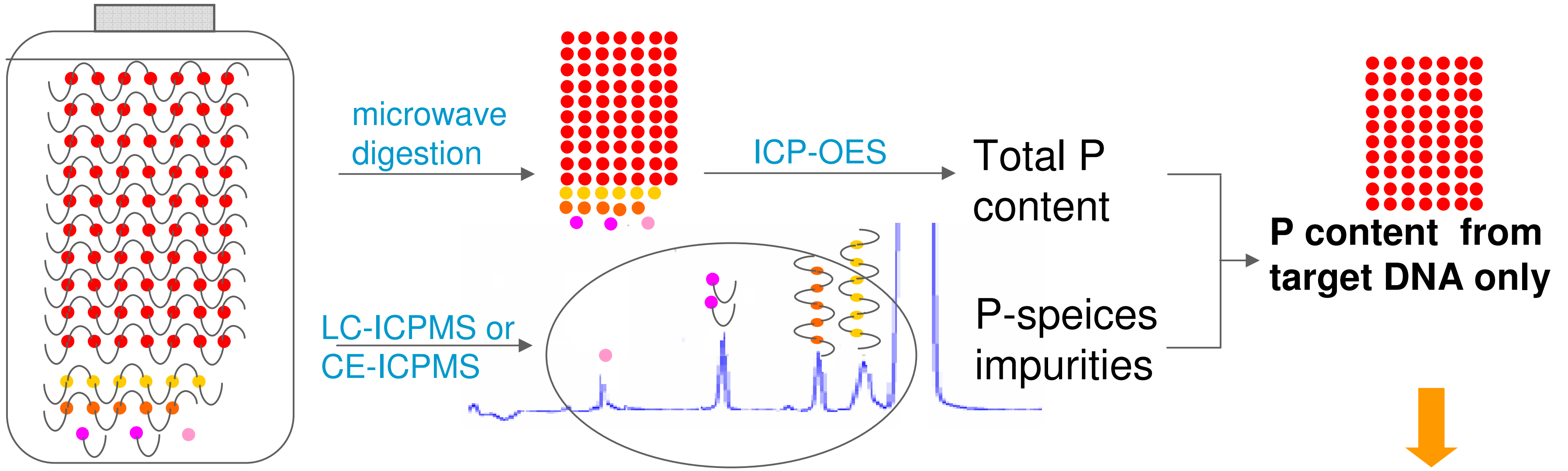
B in mg/kg (as Sn)   C in mg/kg (as Sn)



LC-ICP/MS

DBT in standard = A-B-C (as Sn)

Purity assessment by exhaustive accounting for elemental contents



DNA CRM

phosphorous from different species

- target oligo DNA
- shorter oligo DNA
- shorter oligo DNA
- monomer
- free phosphate

SI traceable
DNA quantification

Purity Assessment by CCQM/OAWG

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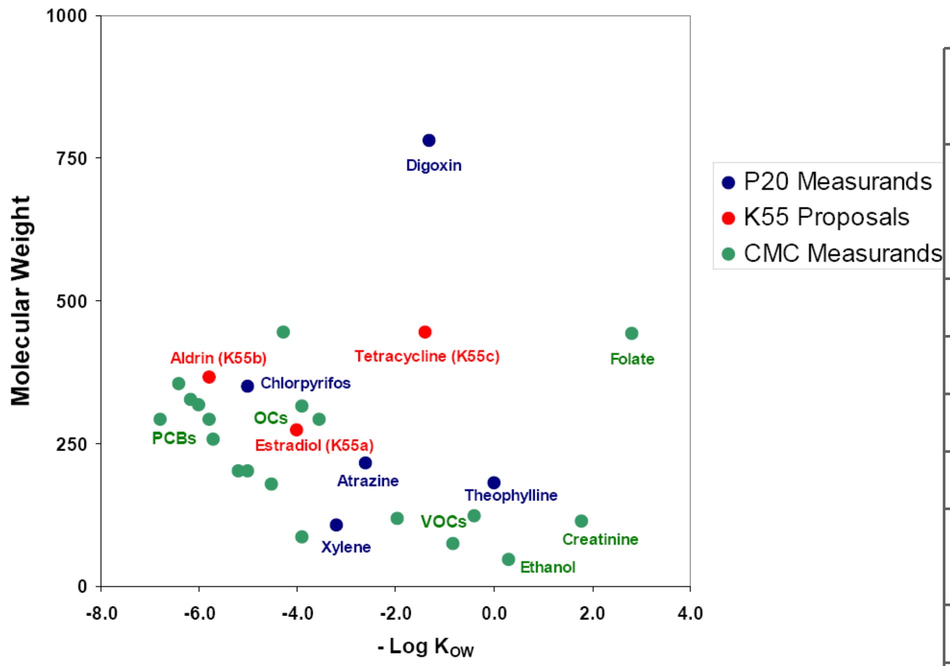

Comparison No.	Purity Assessment	Coordinating Lab.	Year
CCQM-P5	Acetanilide, benzoic acid, naphthalene		
CCQM-P20.a	TBT Chloride	NARL	2001
CCQM-P20.b	*o*-Xylene	NIST	2002
CCQM-P20.c	Atrazine	NARL	2004
CCQM-P20.d	Chlorpyrifos	NARL	2004
CCQM-P20.e.1, e.2	Theophylline	BIPM/LGC	2006
CCQM-P20.f	Digoxin	BIPM/LGC	2007
CCQM-K55a	17β-Estradiol	BIPM	2008
CCQM-K55b	Aldrin	BIPM	2010

CCQM OAWG studies on purity assessment
– Evaluating core-competencies of NMIs
– Harmonization of approach for purity assay
– Improving existing methodologies
– Feasibility study of new methods (q NMR *etc*)
→ Finding sound/scientific solutions for purity assessment

Purity Assessment for Organic Compounds

- Mass-Balance Method

  All possible impurities are quantified and subtracted from 100 %

  Usually purity assay is done by applying several analytical method to identify and quantify all possible impurities

  1) For structurally related organic impurities
     - Quantitation: GC-FID, LC/UV
     - Identification of impurity: GC-FID, LC/UV, GC/MS, LC/MS, NMR

  2) For water content: Karl-Fischer coulometry, TGA, NMR

  3) For residual solvent: TGA, HS-GC(FID,MS), NMR

  4) Non-volatile residue contents
     - TGA: for non-volatile organic & inorganics
     - ICP-MS, XRF, etc: for inorganic contents

- Other Methods
  - QNMR - Could be an universal method

    - Need primary calibrants

      (well-defined high-pure substances for external/internal calibration)
  - DSC – mol/mol ratio. Not applicable to all compounds
  - Adiabatic calorimetry

- **Mass-Balance Method** (KRISS Approach)

  1. Total structurally related organic substances ($P_{aldrin\_chromatogr}$)
     GC/FID : Universal detector for organic compounds
     Linear response to C-H ➔ Linear response to molar mass
     Peak Area ratio ➔ Weight ratio
     GC/MS: Identification of impurity
     LC/UV: complementary quantitation (Response depending on λ)
  2. Water Contents (P_{water})
     K.F. coulometer
  3. Total residual organic solvent / volatile organic substances ($P_{solvent}$)
     TGA (at low temperature)
  4. Total non-volatiles/inorganics ($P_{non\text{-}volatile}$)
     TGA (up to high temperature)

$$P_{\text{aldrin}} = \left(1 - P_{\text{water}} - P_{\text{solvent}} - P_{\text{non-volatile}}\right) \bullet P_{\text{aldrin\_chromatogr}}$$

CONCLUSIONS

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- God has 100% pure substances.
- Knowledge on impurities limits the purity.
- Before entering into the gate of the ultimate traceability, statement of the purity of substances in hands need to be looked into.

"Hey! What are you trying to pull?! You're not dead! Get back down there and keep living until we tell you it's time to come up here!"

Thanks for your attention.

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