Capacity Building & Knowledge Transfer

Specific guidelines for comparisons and CMCs in Chemistry and Biology

Angelique Botha, NMISA

16 November 2017

Bureau International des Poids et Mesures

Outline

- ✓ Impact of chemical and biological measurements
- ✓ Overview of the CCQM
- ✓ Types of comparisons
- ✓ Organisation of comparisons
- ✓ CMC review process
- ✓ Specific requirements for CMCs

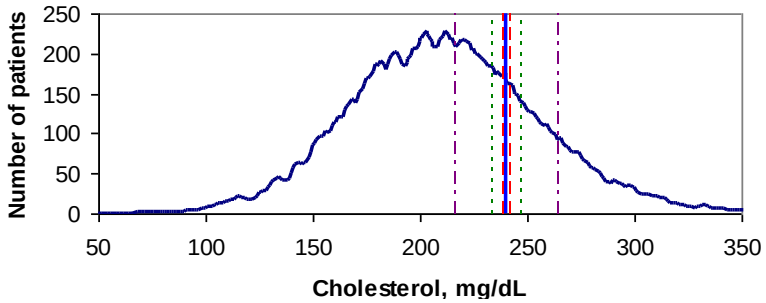
Bureau International des Poids et Mesures

Impact

Healthcare reform is a major issue throughout the world

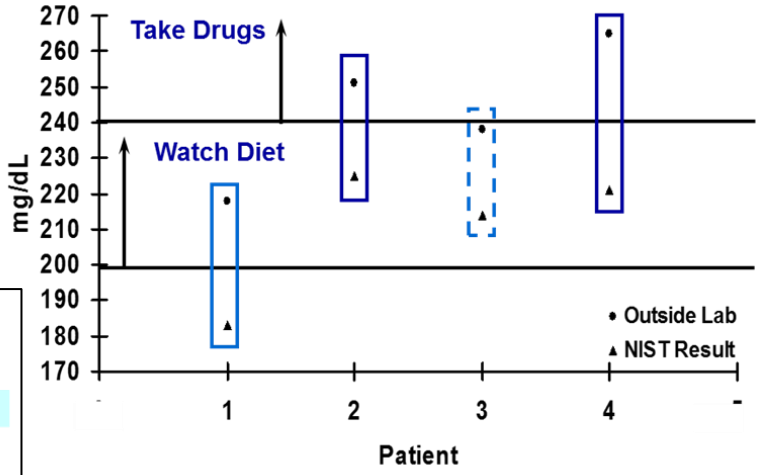
- ✓ **70% of healthcare decisions are based on results from clinical laboratory measurements**
- ✓ **Bias in measurements affects medical decision-making**

Cholesterol Frequency Distribution of >20,000
Mayo Clinic Patients
(with +1%, +3% and +10% limits around 240 mg/dL criteria point)



If measurement bias were:	Positives (>240 mg/dL) per 1000	Predicted Change in "Positives/1000"
-10% bias	120	-129
-3% bias	203	-46
-1% bias	234	-15
0% bias	249	
+1% bias	263	+14
+3% bias	300	+51
+10% bias	446	+197

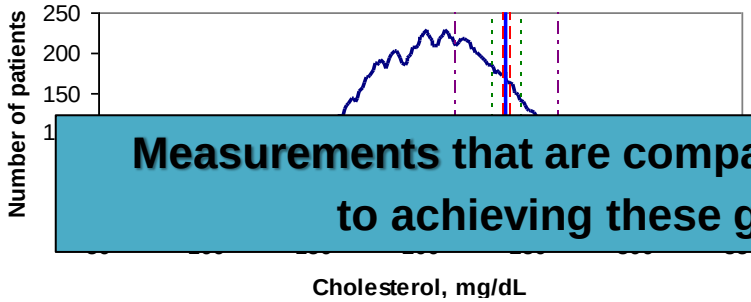
NIST Cholesterol-in-Blood Experiment - Impact of Inaccurate Measurements



Healthcare reform is a major issue throughout the world

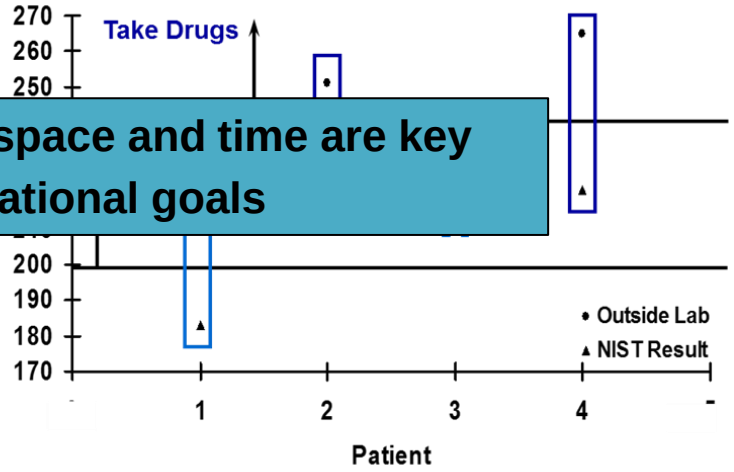
- ✓ **70% of healthcare decisions are based on results from clinical laboratory measurements**
- ✓ **Bias in measurements affects medical decision-making**

Cholesterol Frequency Distribution of >20,000
Mayo Clinic Patients
(with +1%, +3% and +10% limits around 240 mg/dL criteria point)



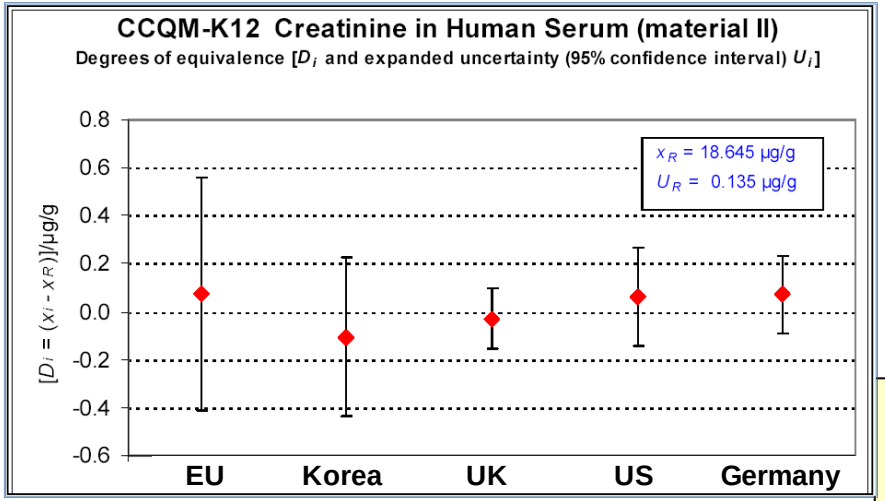
If measurement bias were:	Positives (>240 mg/dL) per 1000	Predicted Change in "Positives/1000"
-10% bias	120	-129
-3% bias	203	-46
-1% bias	234	-15
0% bias	249	
+1% bias	263	+14
+3% bias	300	+51
+10% bias	446	+197

NIST Cholesterol-in-Blood Experiment - Impact of Inaccurate Measurements



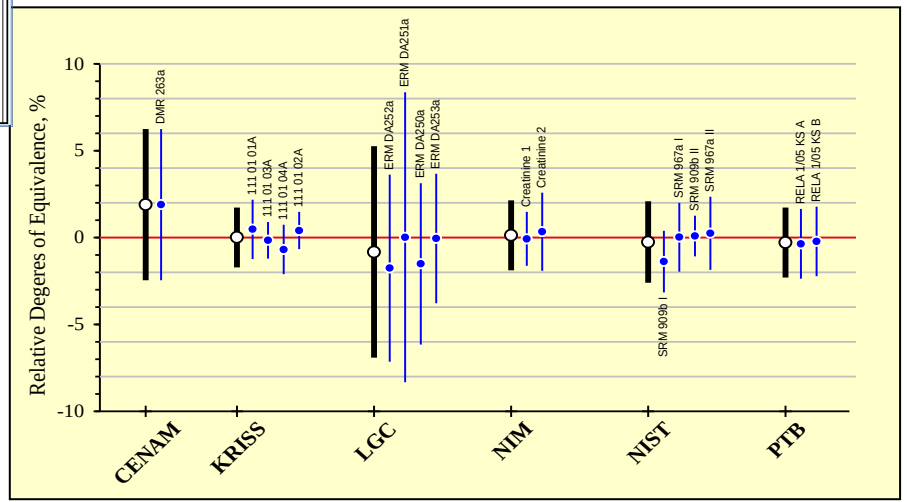
Measurements that are comparable over space and time are key to achieving these global and national goals

Impact of CCQM Key Comparisons



Documented degree of equivalence of measurement capabilities

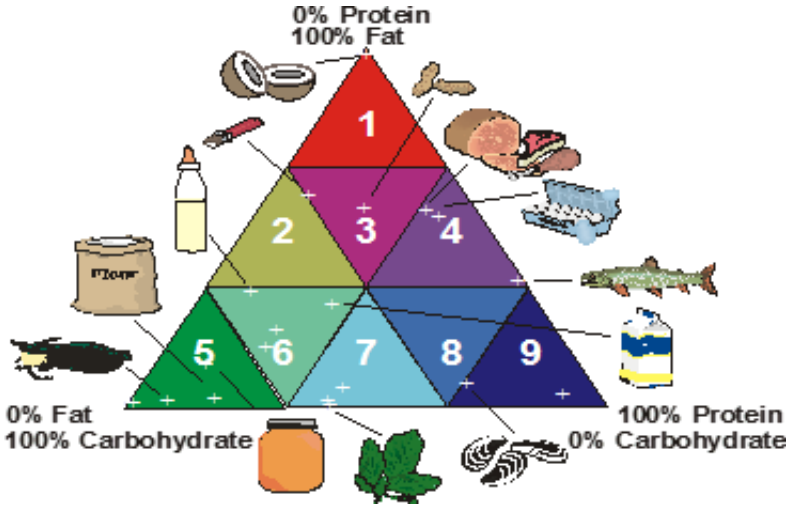
Documented degree of equivalence of measurement services "as delivered"
(Comparison of value-assignments of NMI/DI CRMs for Creatinine in Serum)



Bureau International des Poids et Mesures

Food pyramid

Examples of Food-matrix Certified Reference Materials by Sector



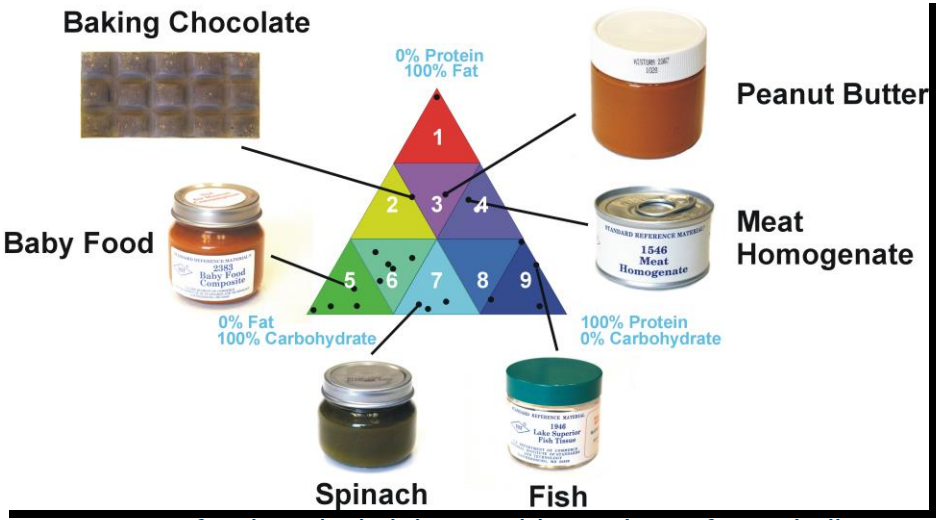
Every food can be placed in one of these 9 sub-triangles according to its ***% protein, % fat, and % carbohydrate*** *coordinates*

- Most food analysis labs provide analyses for a similar set of analytes but in a wide range of food types
- Matrix differences and concentration differences are the primary measurement challenges
- By providing CRMs certified for these common food analytes in each of the major sections of the “food triangle”, NMIs can provide a full suite of CRMs needed for the validation of nutrients and contaminants in the measurement of foods

Bureau International des Poids et Mesures

Food pyramid

Examples of Food-matrix Certified Reference Materials by Sector



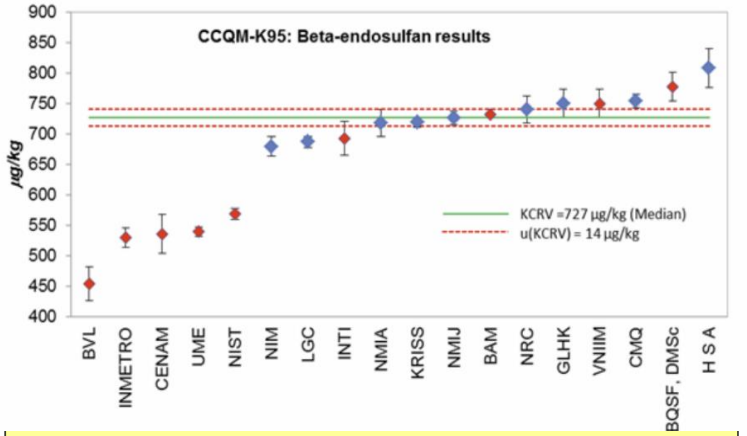
Every food can be placed in one of these 9 sub-triangles according to its ***% protein, % fat, and % carbohydrate*** *coordinates*

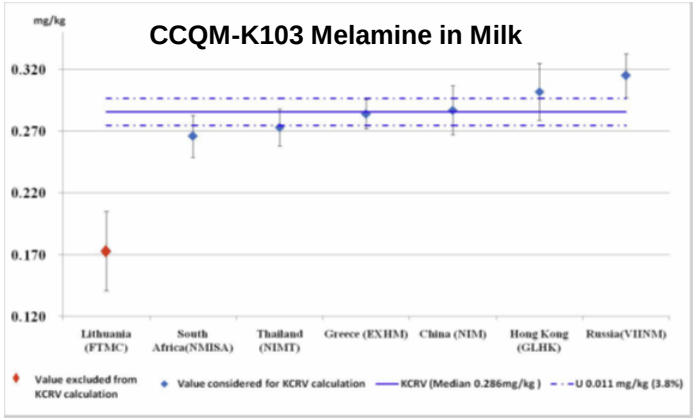
- Most food analysis labs provide analyses for a similar set of analytes but in a wide range of food type
- Matrix differences and concentration differences are the primary measurement challenges
- By providing CRMs certified for these common food analytes in each of the major sections of the “food triangle”, NMIs can provide a full suite of CRMs needed for the validation of nutrients and contaminants in the measurement of foods

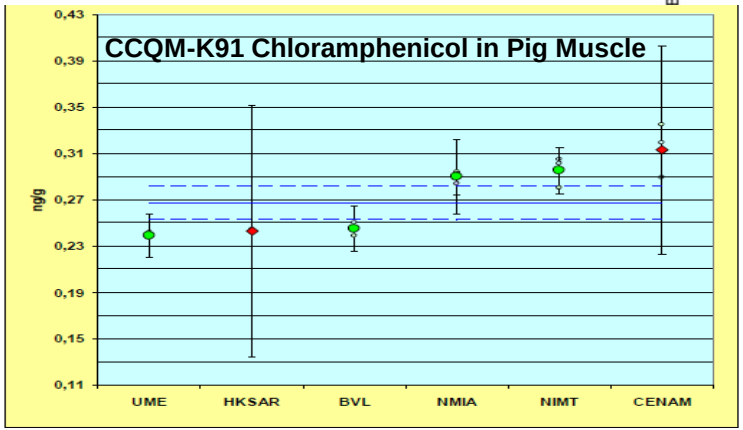
Bureau International des Poids et Mesures

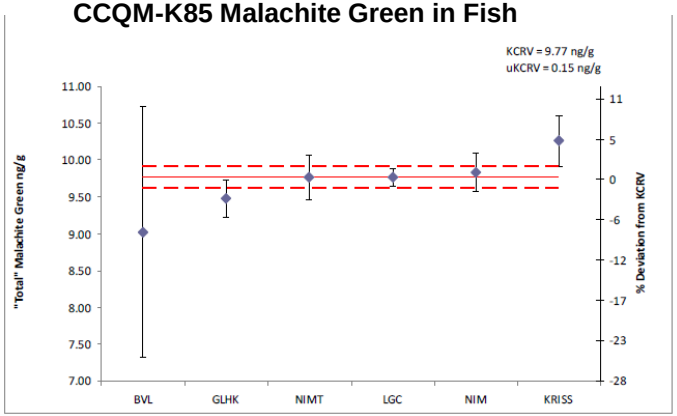
CCQM Key Comparisons for Food Safety (Organic)

International Comparison Studies provide support (under auspices of CIPM) for assessment of global comparability of National Metrology Institutes measurement capabilities

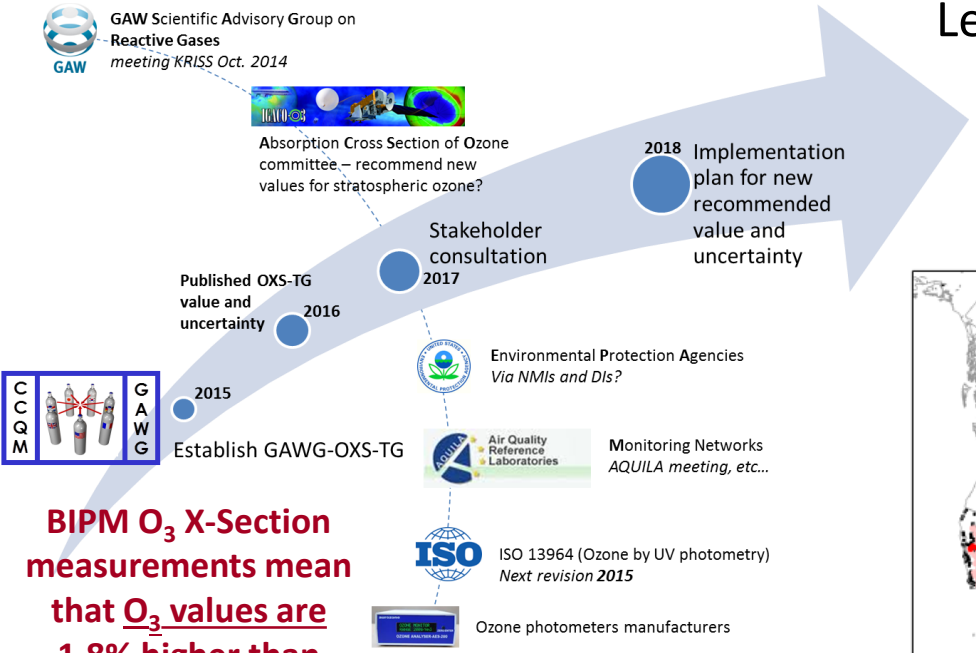








Impact of CCQM Ozone Standards and Comparison Activities

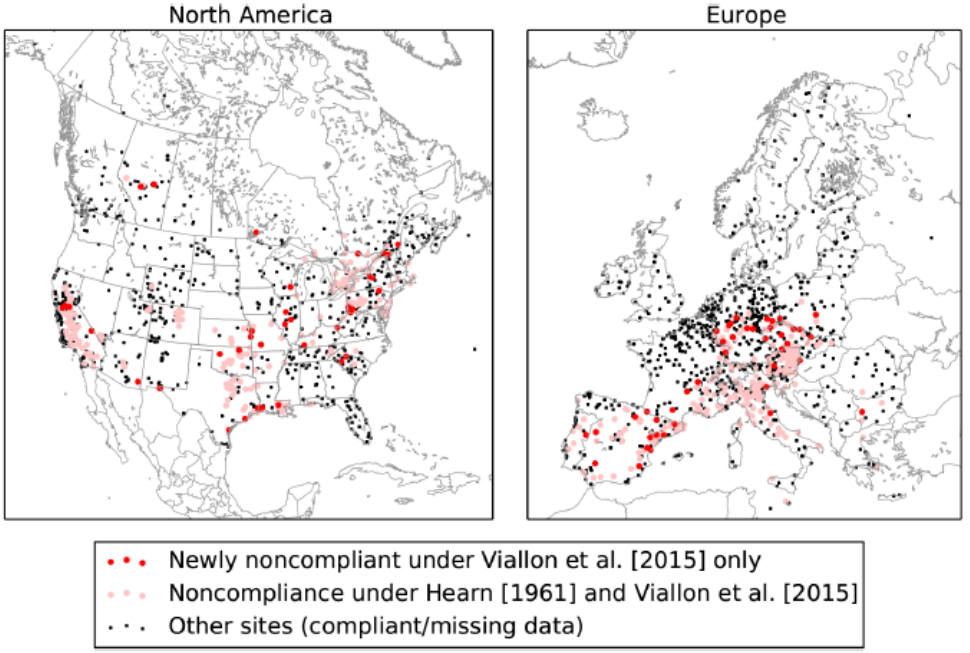


BIPM O_3 X-Section measurements mean that O_3 values are 1.8% higher than historically reported

www.bipm.org

Lead to actions for improved air quality* for the World's Population

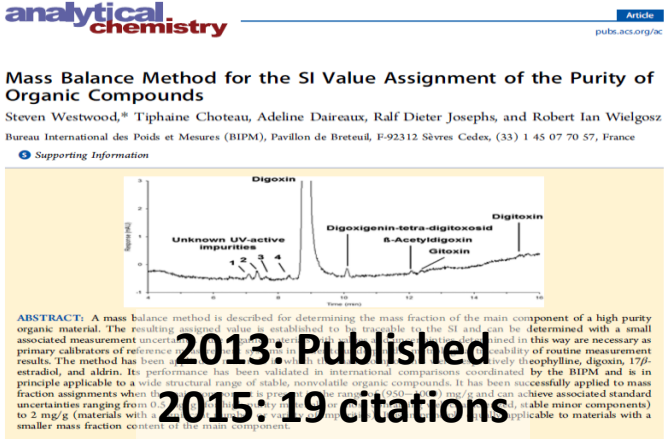
Sofen, E. D., Evans, M. J., and Lewis, A. C.: Updated ozone absorption cross section will reduce air quality compliance, Atmos. Chem. Phys. Discuss., 15, 19537-19551, doi:10.5194/acpd-15-19537-2015, 2015.



*20 % increase in the number of sites that are out of compliance with current US, Canadian, and European ozone air quality health standards for the year 2012

Impact of CCQM Organic Primary Calibrator Comparison Program

Higher profile for Metrology and Traceability in Organic Analysis



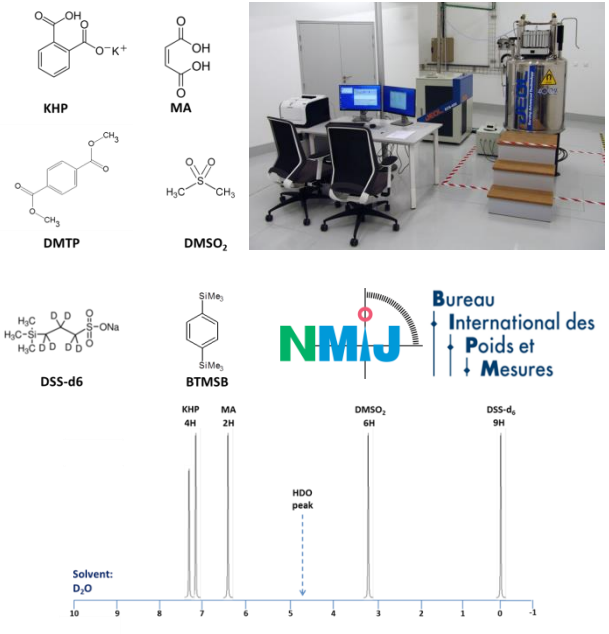
2013: Published
2015: 19 citations

IUPAC

FUNDED

IUPAC Technical Report on *SI Value Assignment of the Purity of Organic Compounds for use as Reference Materials and Calibrators*

Universal Calibrators for qNMR



NMIJ Bureau International des Poids et Mesures

Wider adoption of new technologies for purity assignment and increased availability of primary and secondary calibrator CRMs

Increase in availability of pure material CRMs for IVDs

JCTLM

	2012	2015
Number of CRMs	68	93
NMIs with CRMs	7	7

Improved QA for Pharmaceutical Reference Materials

USP U.S. Pharmacopeial Convention

BRITISH PHARMACOPOEIA

edqm European Directorate for the Quality of Medicines & HealthCare

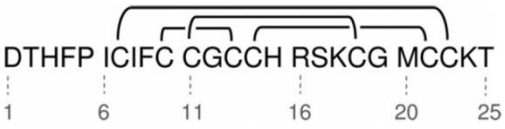
FEUM FARMACOPEA de los Estados Unidos Mexicanos

Impact of CCQM Peptide Primary Calibrator Comparison Program

Enabling the adoption of SI traceable reference measurement systems

Body fluid		Method	‡Mean ALL sample
Urine	**	I	#2.9
		II	44.4
		III	13.4
		IV	35.1
		V	427.1
		VI	7.9
Plasma	*	I	#11.4
		II	13.0
		0	27.4
		IV	16.4
		V	124.6
		VI	17.3
		VII	12.4
		VIII	41.5

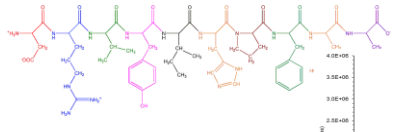
*nmol/L **nmol/mmol Creatinine



LNE Le progrès, une passion à partager

Bureau International des Poids et Mesures

Development of methods for cross-linked peptides and future comparison (Hepcidin)(2015)



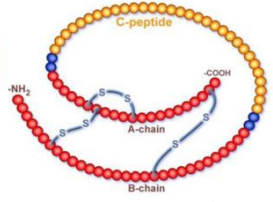
Angiotensin (2010)

NIST Bureau International des Poids et Mesures

Higher profile for Metrology and SI Traceability for Diagnostics and Therapeutics

CCQM-K115: 1st key comparison on peptide purity (2015): C-peptide (Diabetes diagnosis)

NIM Bureau International des Poids et Mesures



Liquid chromatography mass spectrometry method for C-peptide in blood serum

JCTLM

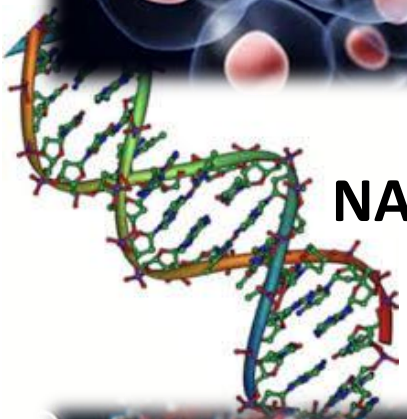
- UMC DDL reference method for serum C-peptide

Applicable matrice(s)	lyophilized, fresh, or frozen human serum or urine
Full description of technique(s)	Liquid chromatography mass spectrometry (LC/MS)
Quantity	Amount-of-substance concentration
Applicable range	0.01 nmol/L to unlimited after appropriate dilution
Expected uncertainty (level of confidence 95%)	0.036 nmol/L to 0.09 nmol/L
Reference(s)	Use of cation exchange chromatography for human C-peptide isotope dilution - Mass spectrometric assay, Stoyanov AV et al., *J. Chromatogr. A*, 2011, **1218**, 9244-9249;
Comparability assessment study(ies)	Human C-peptide Quantitation by LC-MS Isotope-Dilution Assay in Serum or Urine Samples, Stoyanov AV et al., *J. Chromat. Separation Techniq.*, 2013, **4**, 172
Comment(s)	University of Missouri-Columbia Diabetes Diagnostic Laboratory (UMC DDL)
JCTLM DB identification number	C10RMP12_C-Peptide

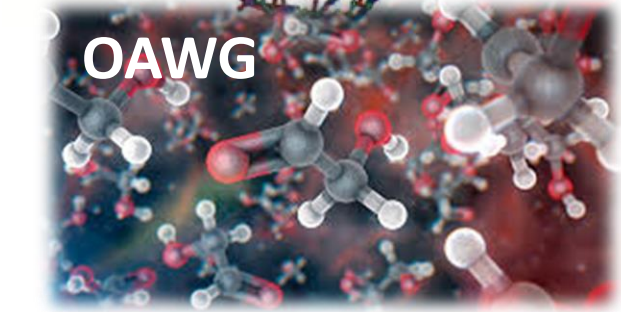
Realizing SI traceability for Therapeutic Peptide Characterization: Meeting Industry and Regulator needs as production methods move to chemical synthesis and away from recombinant technologies (Oxytocin and Calcitonin with NIM: 2016-2019)

Overview of the CCQM

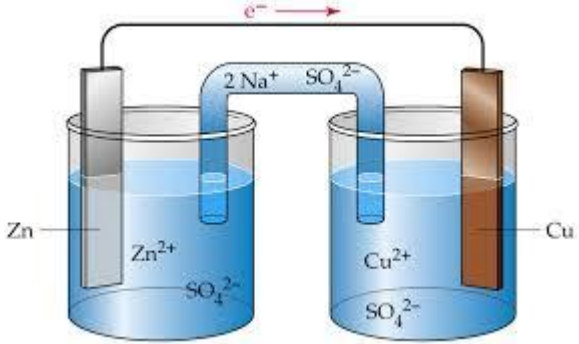
CAWG

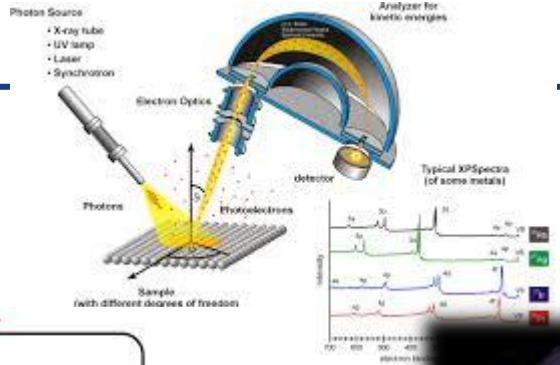


NAWG



EAWG

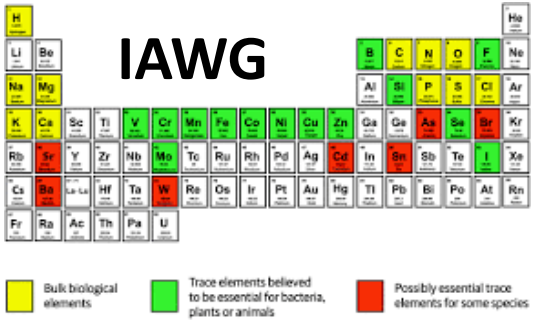




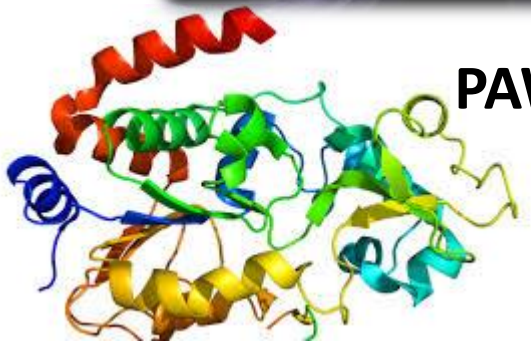
SAWG

GAS

IAWG



PAWG



Overview of the CCQM (cont.)

- ✓ 2 other working groups
  - ✓ Working Group on Key Comparisons and CMC Quality (KCWG)
  - ✓ Strategic Planning Working Group (SPWG)
- ✓ 2 ad-hoc groups
  - ✓ Ad-hoc Steering Group on Microbial Measurements (MBSG)
  - ✓ Ad-hoc Working Group on the Mole

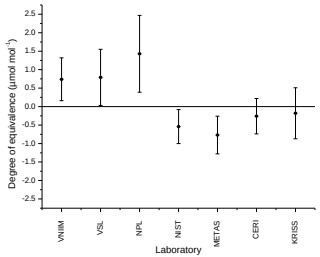
Types of CCQM comparisons

key comparisons

pilot studies

RMO comparisons

CCQM-K46 NH_3 in nitrogen



on-going comparisons

supplementary comparisons

OAWG Four-Track Strategic Approach for Comparison Studies

Track A: Key comparisons that test Core Competencies for the delivery of Measurement Services to Customers

- Providing Primary Calibration Reference Services
- Providing Accuracy Control Reference Services

Limited number in which all NMIs with relevant claims expected to participate

Track B: Key Comparisons that Assess the Equivalence of Measurement Services actually provided to Customers

- Certified Reference Materials
- Value-Assigned PT Samples

Limited number to be assessed over time after reviewing services

Track C: Key Comparison studies in emerging areas of global interest and importance

5 NMIs must agree to participate for study to go forward as Key Comparison

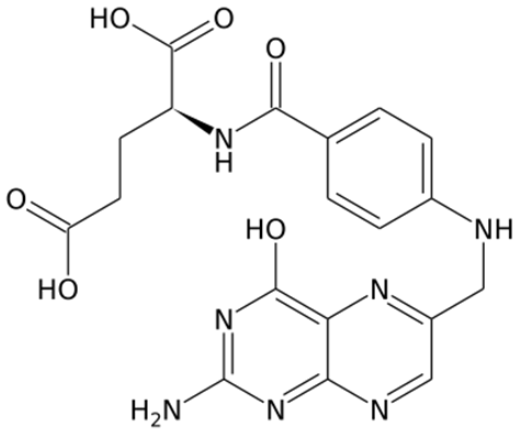
Track D: Capability Assessment studies

Results of these Studies will not be used for assessment of CMCs

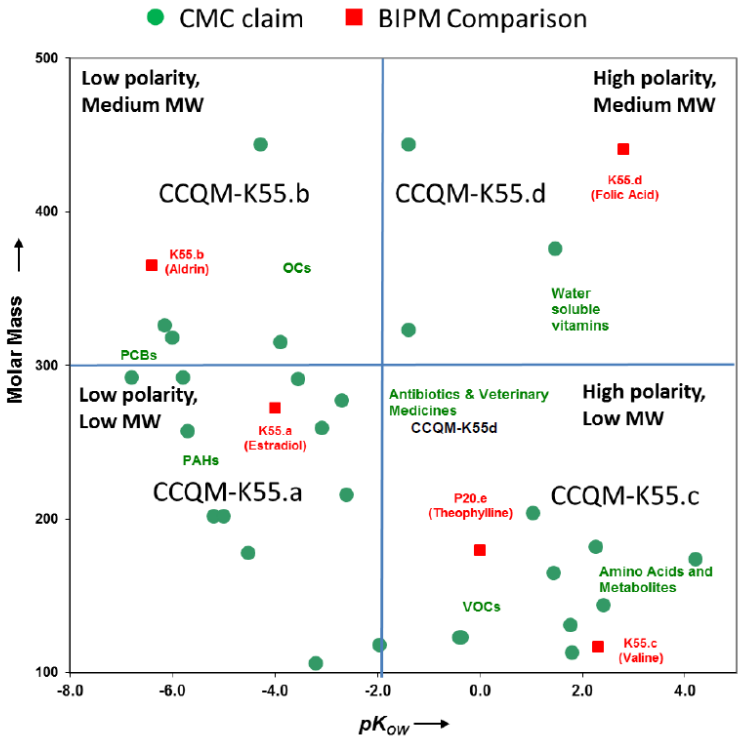
Bureau International des Poids et Mesures

Analysis space for high purity organic calibrators

CCQM-K55.d: High polarity organic - Folic Acid



HFTLS: Purity assignment of organic compounds of medium complexity [300-500 Da] and high polarity [*pKow* > -2]



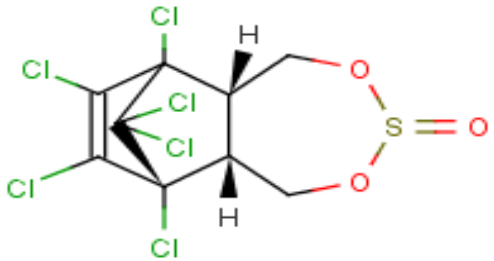
August 2015 – January 2016

First Track A “Matrix” Key Comparison

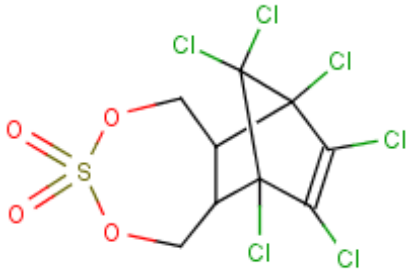
Non-Polar Analytes in Food Matrix: Pesticides in Tea

Co-organised by GLHK and NIM

CCQM-K95 Key Comparison
CCQM-P136 Pilot Study



Endosulfan II
(synonym: *beta*-Endosulfan)
CAS No.: 33213-65-9
MW: 407
Log K_{ow}: 3.83

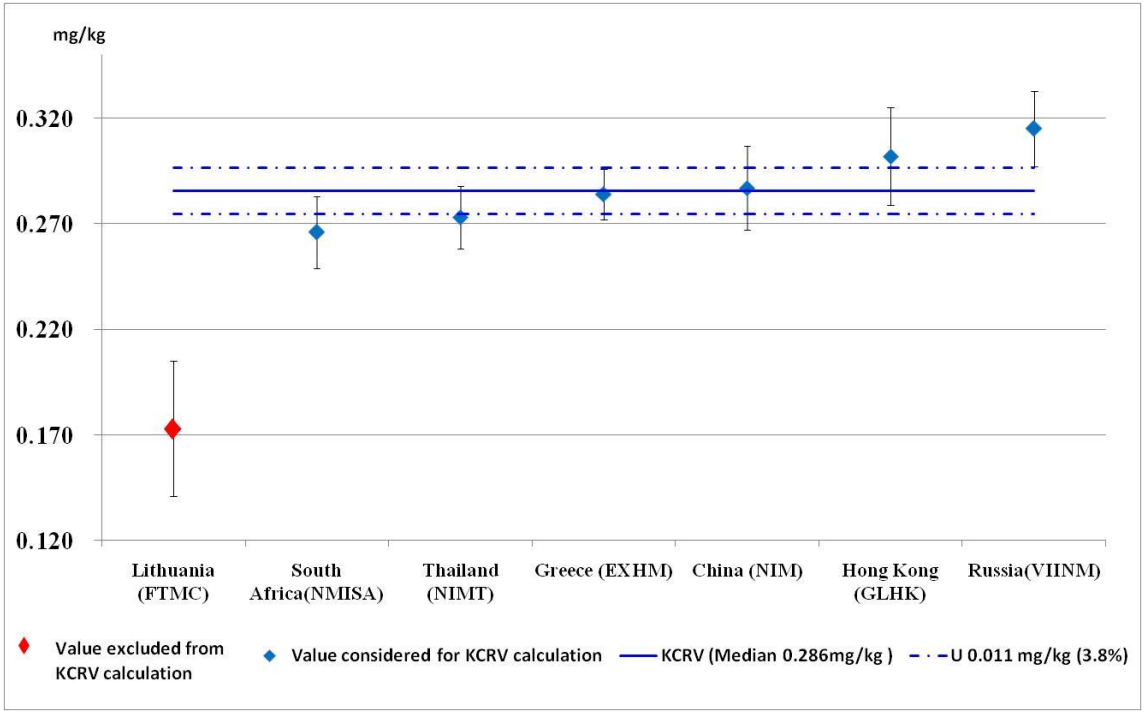


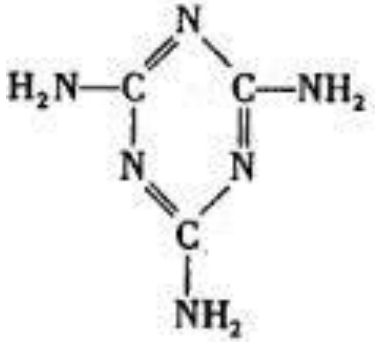
Endosulfan Sulphate
CAS No.: 1031-07-8
MW: 423
Log K_{ow}: 3.66

Bureau International des Poids et Mesures

Track C Key Comparison

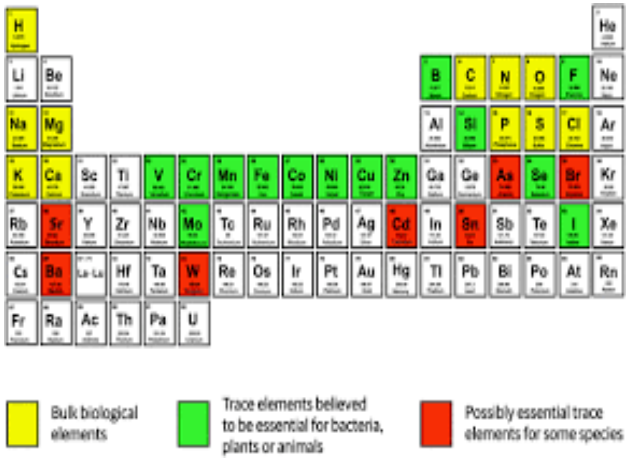
CCQM-K103 Melamine in Milk Powder (NIM/HKGL)





Scope of IAWG activities

- ✓ **CCQM CMC categories** 1, 2, 5, 8, 9, 10, 11, 12, 13 and 14 which include the following **groups of analytes**:
  - ✓ the elements
  - ✓ their isotopes and isotope ratios (absolute or relative)
  - ✓ cations and anions
  - ✓ inorganic compounds
  - ✓ organo-metallic compounds
- ✓ These analytes are determined as the amount of substance fraction or mass fraction in any relevant **sample matrix** including:
  - ✓ pure materials
  - ✓ calibration solutions
  - ✓ complex samples such as those used for chemical reference materials



Bureau International des Poids et Mesures

Key aspects of IAWG strategy

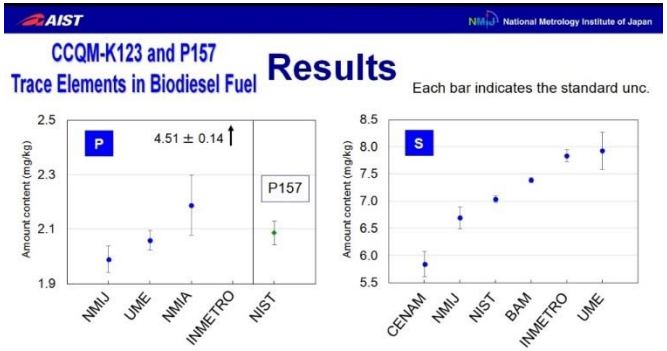
- ✓ Supporting CMCs
  - ✓ '***Core capabilities***' approach for complex matrix samples and development of 'White Paper' guidelines to its use
  - ✓ Conventional KCs for calibration solutions, standards and purity
  - ✓ Laboratories must have some '1:1' KC:CMC checks for uncertainty
  - ✓ Performance of all active participants is regularly checked in ***benchmark studies*** (fourth completed in 2011-12)
  - ✓ '***Report card***' system for laboratories to summarize overall KC performance for use in CMC reviews
- ✓ Implementation of key comparisons
  - ✓ ***Rolling plan*** for key comparisons and special pilot studies
  - ✓ Most KCs and pilot studies ***use candidate CRMs*** to minimise cost to coordinating NMIs and ensure relevance
  - ✓ ***IAWG database*** implemented to collate NMI future plans for CRM production, willingness to coordinate studies, and CMC expansion

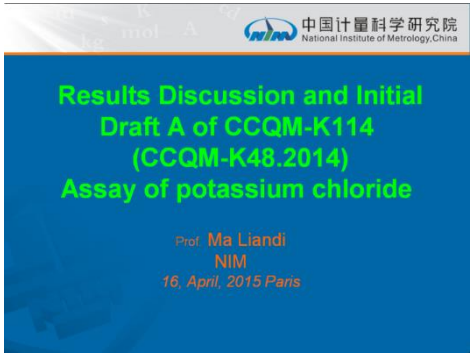
Bureau International des Poids et Mesures

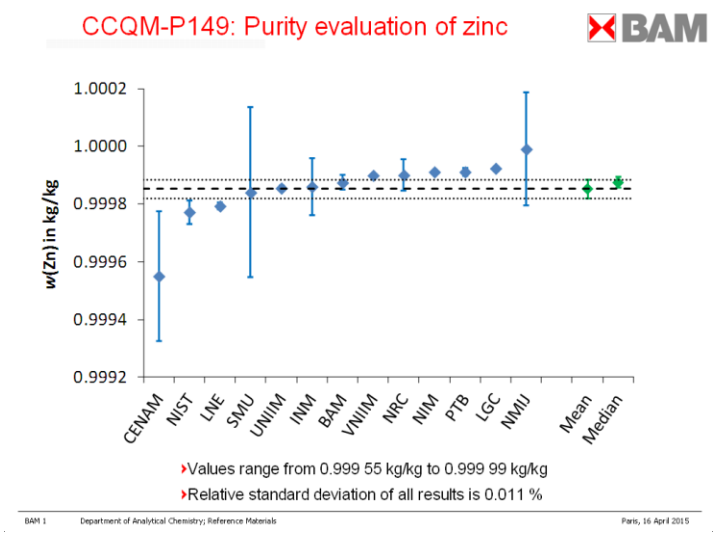
IAWG rolling programme

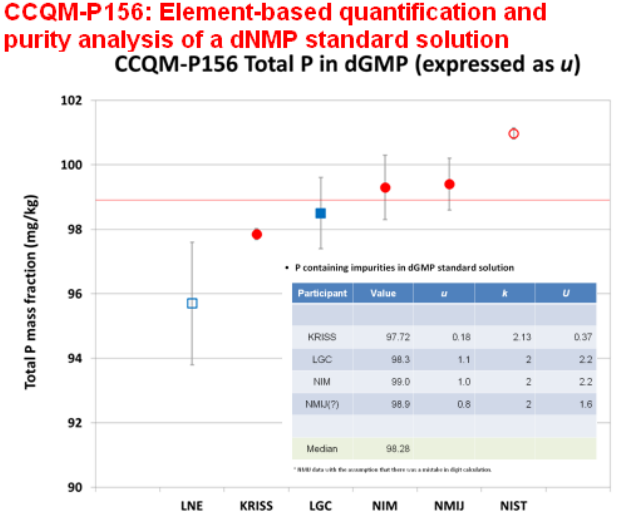
Period	Key comparisons					Special pilot studies
	Sample matrix [CMC category]			Analytes		
2013	[9] Advanced materials K98 (BAM)	[1 & 2] Pure chemicals/solutions K72 (BAM)	[11] Food or plant K108 (NMIJ)	*Elements*	*Isotope ratios*	Determination of P in biological molecules (e.g. DNA)
2014	[5] Water	[14] Other materials K106 (NIM)	[10] Biological K107 (LGC)		*Speciation*	Solid sample analysis by LA-ICP-MS
2015	[13] Sediments/ soils	[11] Food or plant	[12] Fuels		*Anions and inorganic compounds*	Speciation of inorganic Cr (III and VI)
2016	[12] Fuels	[8] Metal and metal alloys	[5] Water		*Isotope ratios*	Speciation of plasma metallo-proteins
2017	[10] Biological	[14] Other materials	[11] Food or plant		*Speciation*	Single particle analysis and composition of nanoparticles

Recent comparisons completed by the IAWG

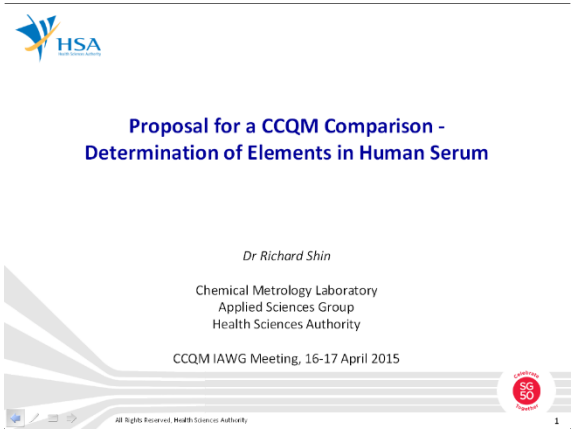


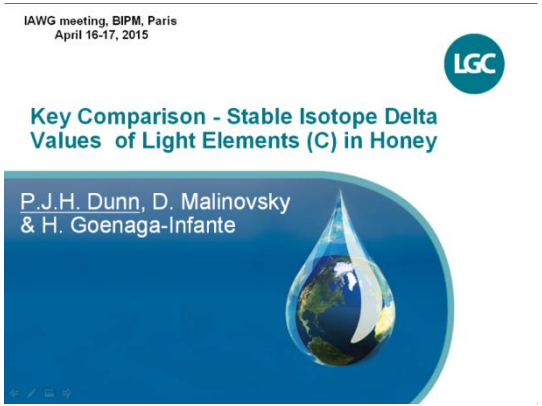


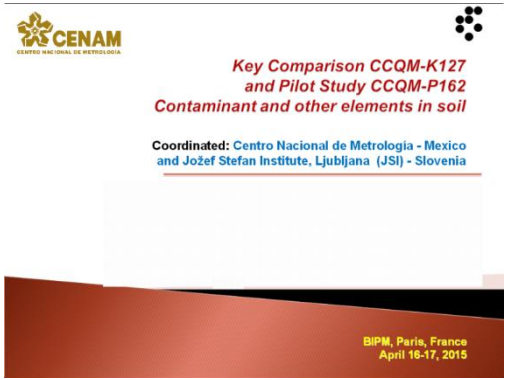




Recent comparisons completed by the IAWG





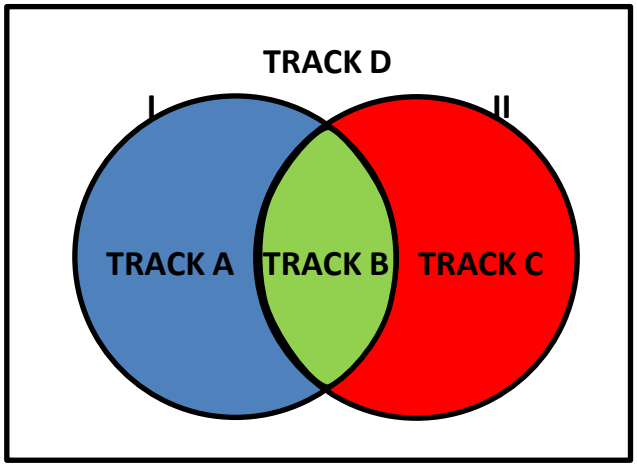


GAWG Strategy

- ✓ Established in 2010
- ✓ Broader application of key comparisons in gas analysis
- ✓ More efficient and cost effective process
- ✓ Focus on analytical challenges and responding to emerging requirements

Track A - **FLEXIBLE**
Comparisons for core competencies - gravimetric preparation, certification and purity analysis

Track B
Analytically challenging components using competencies outside track A (e.g. unstable and reactive gas mixtures)



Track C
Comparisons for emerging areas of global interest and innovation (mixtures not currently in KCDB and provide an analytical challenge)

Track D
All other studies (stand-alone pilot studies and parallel to KC pilot studies)

Track A (core comparisons)

- ✓ Evidence based on track record from previous comparisons
- ✓ Optional - can continue using existing approach

Components and matrix	Amount-of-substance fraction range
CO, CO_2, O_2, CH_4, C_2H_6 or C_3H_8 in N_2 or air	10 µmol/mol – 500 mmol/mol
CO, CO_2, C_3H_8 and O_2 in N_2	10 µmol/mol – 500 mmol/mol
NO in N_2	50 µmol/mol – 500 mmol/mol
SO_2 in N_2 or air	50 µmol/mol – 500 mmol/mol

- ✓ CMCs evidenced by last 3 track A KCs
- ✓ Binary mixture in air or N_2 >10 µmol/mol (NO and SO_2 >50 µmol/mol)
- ✓ Simple mixtures (1 or a few non-interfering components in air or nitrogen)

- ✓ **NMIs can choose to adopt flexible CMC scheme if they have**
- ✓ Participated in at least 3 track A KCs organised by the GAWG
- ✓ Participated in at least 1 track A KC every three years (when available)
- ✓ Established a link between CMCs and performance in track A comparisons
- ✓ Quality system and capability to cover all track A components in KCDB

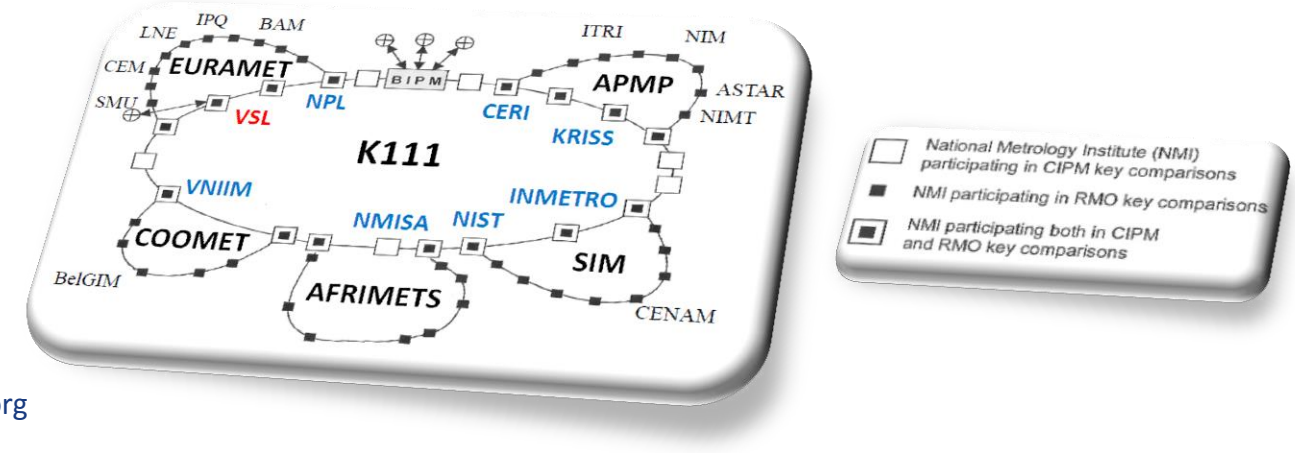
Two statements of HFTLS: a dedicated statement and a broad statement

Linking RMO comparisons

- ✓ Comparisons can be organised by RMO as a satellite to a track A comparison for acceptance in the flexible CMC scheme
- ✓ GAWG shall decide on the coordinating labs for future RMO comparisons during the planning stage of a track A KC (≥1 lab per RMO involved in the track A KC)

Coordinating laboratory of RMO linked comparison shall

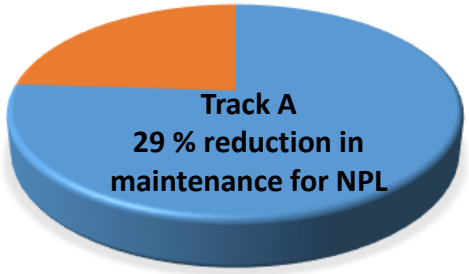
- ✓ Be a participant in the track A KC
- ✓ Submit protocol prior to a track A KC for approval by GAWG
- ✓ Submit a report to the RMO and then to the GAWG for approval

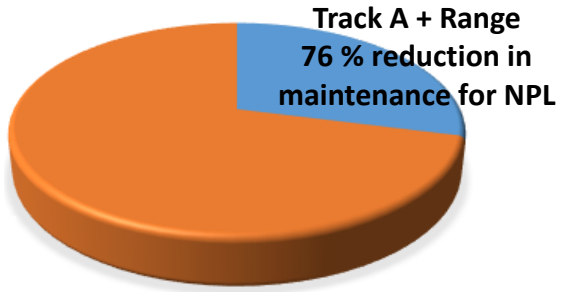


Defining CMCs with a range and equation

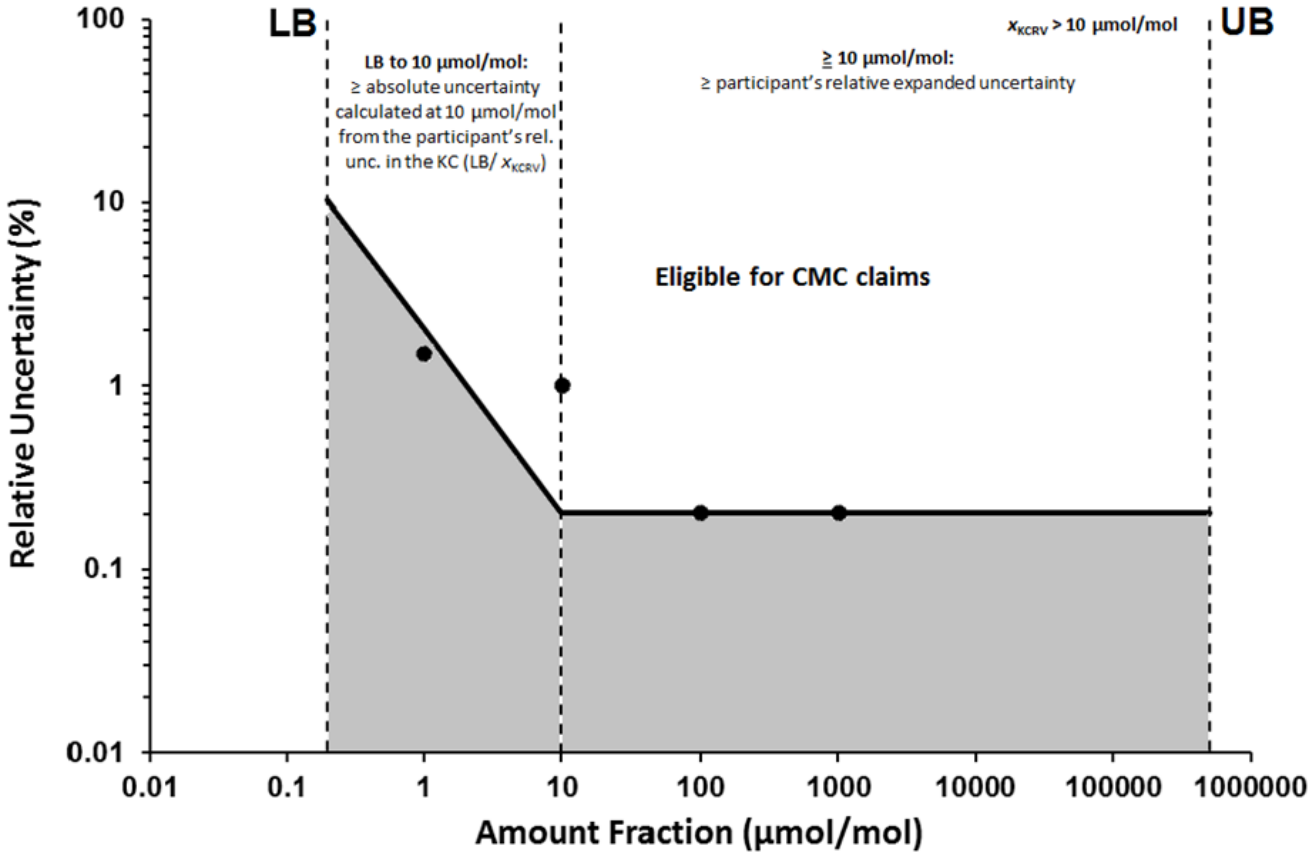
				fraction													calibration	30 July 2009
8 rev 2	Environmental	nitrogen		Amount-of-substance fraction	100	1000	µmol/mol	0.2	0.2	%	Yes	100	1000	µmol/mol	0.2	0.2	%	Yes	PRGM and calibration	Approved on 06 December 2011
9 rev 2	Environmental	nitrogen	carbon dioxide	Amount-of-substance fraction	1	10	mmol/mol	0.2	0.2	%	Yes	1	10	mmol/mol	0.2	0.2	%	Yes	PRGM and calibration	Approved on 06 December 2011
10 rev	Environmental	nitrogen	carbon dioxide	Amount-of-substance fraction	10	100	mmol/mol	0.2	0.1	%	Yes	10	100	mmol/mol	0.2	0.1	%	Yes	PRGM and calibration	Approved on 19 July 2010
10b	Environmental	nitrogen	carbon dioxide	Amount-of-substance fraction	100	200	mmol/mol	0.1	0.1	%	Yes	100	200	mmol/mol	0.1	0.1	%	Yes	PRGM and calibration	Approved on 19 July 2010
8 b 2 rev	Environmental	synthetic air	carbon dioxide	Amount-of-substance fraction	100	1000	µmol/mol	0.2	0.2	%		100	1000	µmol/mol	0.2	0.2	%	Yes	PRGM and calibration	Approved on 06 December 2011
9 b 2 rev	Environmental	synthetic air	carbon dioxide	Amount-of-substance fraction	1	10	mmol/mol	0.2	0.2	%	Yes	1		mmol/mol	0.2	0.2	%	Yes	PRGM and calibration	Approved on 06 December 2011
10b2	Environmental	synthetic air	carbon dioxide	Amount-of-substance fraction	10	100	mmol/mol	0.2	0.1	%	Yes	10	100	mmol/mol		0.1	%	Yes	PRGM and calibration	Approved on 19 July 2010
81	Environmental	synthetic air	carbon dioxide	Amount-of-substance fraction	100	200	mmol/mol	0.1	0.1	%	Yes	100	200	mmol/mol	0.1	0.1	%		PRGM and calibration	Approved on 19 June 2014
				Amount-of-															

One comparison to support the entire amount fraction range
An equation to define the uncertainties



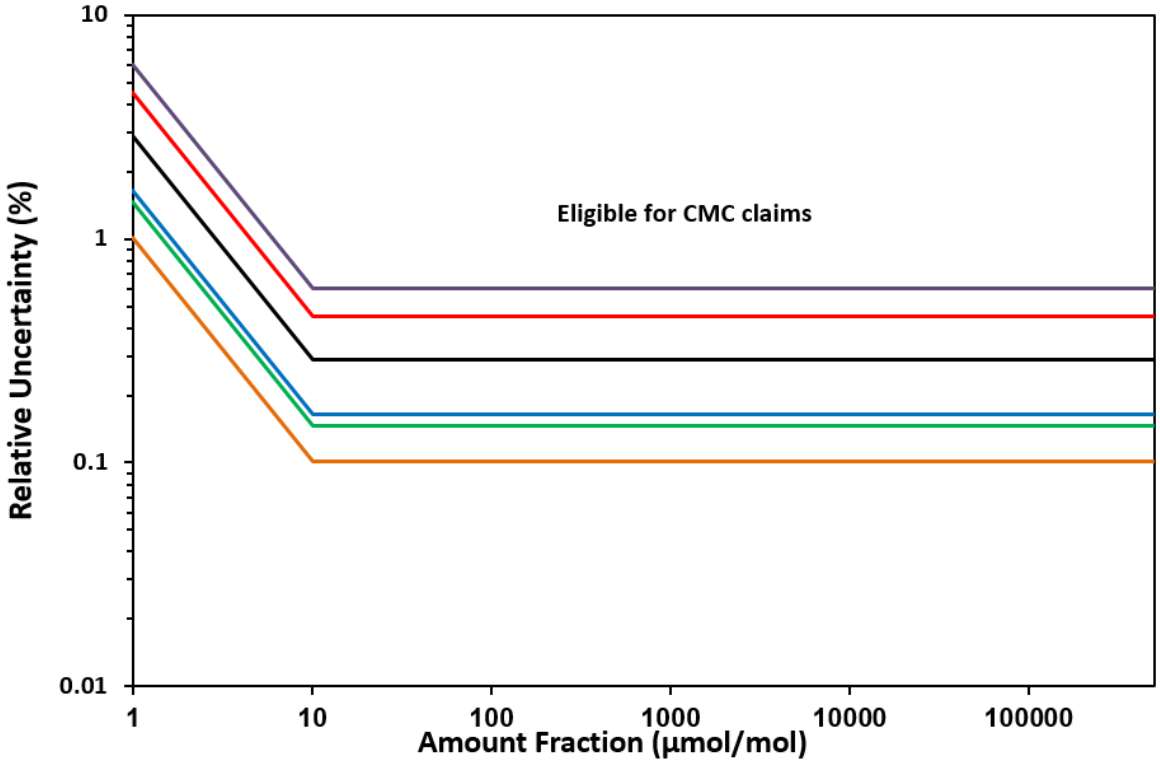


Example track A (K76 - NPL)



Pooling data under the flexible scheme

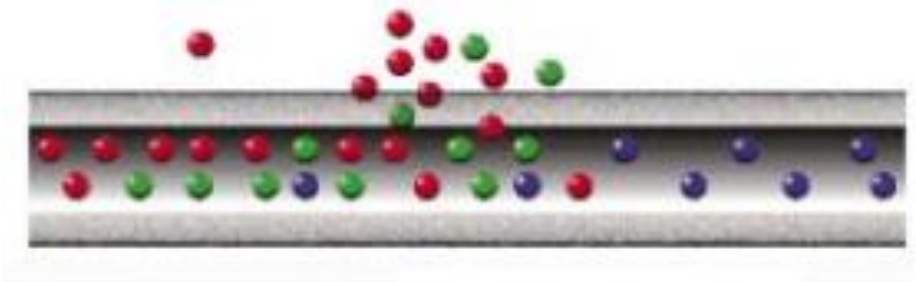
NPL VSL VNIIM NIST LNE KRISS
last 3 track A comparisons (K52, K53, K76)



Purity

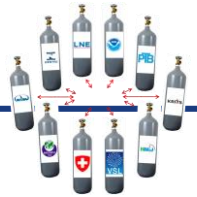
- ✓ Future purity CMCs will be evidenced by the HFTLS statement in all key comparisons, without the requirement for dedicated purity comparisons

- ✓ Participating NMIs in key comparisons are required to report the results of their purity analysis with uncertainties, as far as these are relevant for the CMCs claims to be supported



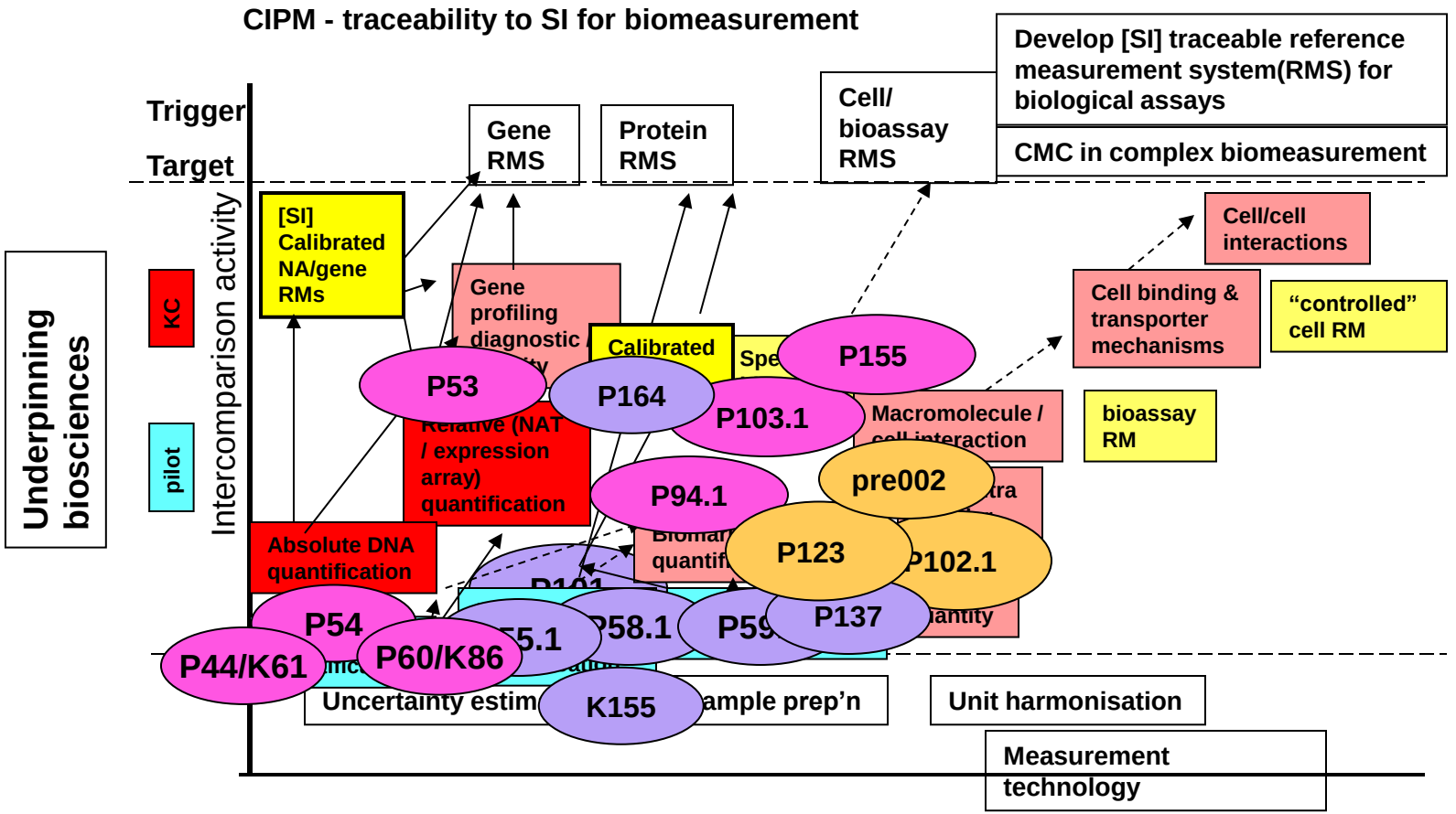
Bureau International des Poids et Mesures

Future comparisons



Reference No.	Description	Coordinating Laboratory	Expected Start date
BIPM.QM-K1	ozone at ambient level	BIPM / 20	2007 -
CCQM-K111	propane in nitrogen (1000 µmol/mol)	VSL	2014
CCQM-K112	biogas	VSL	2014
CCQM-K113	noble gases	KRISS	2014
CCQM-K90	formaldehyde in nitrogen (2 µmol/mol)	BIPM	2015
CCQM-K116	water in nitrogen (10 µmol/mol)	NPL	2015
CCQM-K117	ammonia (10 µmol/mol)	VSL&NIST	2015
CCQM-K118	natural gas	VSL & BAM	2015
CCQM-K119	LPG	NPL	2015
CCQM-K121	monoterpenes in nitrogen (2 nmol/mol)	NIST	2015
CCQM-K120a	CO_2 in air (380 - 480 µmol/mol)	BIPM with NIST	2016
CCQM-K120b	CO_2 in air (380 - 800 µmol/mol)	BIPM with NIST	2016
CCQM-K41.2017	H_2S in nitrogen (10 µmol/mol)	KRISS	2017
CCQM-PXX	micro-scale particles (number/charge concentration)	PTB/NPL	2017
CCQM-PXX	micro-scale particles (mass concentration)	VNIIM	2017
CCQM-K137	NO in nitrogen (30-70 µmol/mol)	BIPM	2018
CCQM-K74.2018	NO_2 in nitrogen (10 µmol/mol)	BIPM	2018
CCQM-K3.2018	automotive gases	VSL	2018
CCQM-K10,2018	BTEX	NIST	2018
CCQM-K26b.2019	SO_2 (300 nmol/mol)	NPL	2019
CCQM-K68.2019	N_2O (320-350 nmol/mol)	BIPM with KRISS	2019
CCQM-PXX	carbon/oxygen isotope ratios in CO_2	BIPM/IAEA	2019

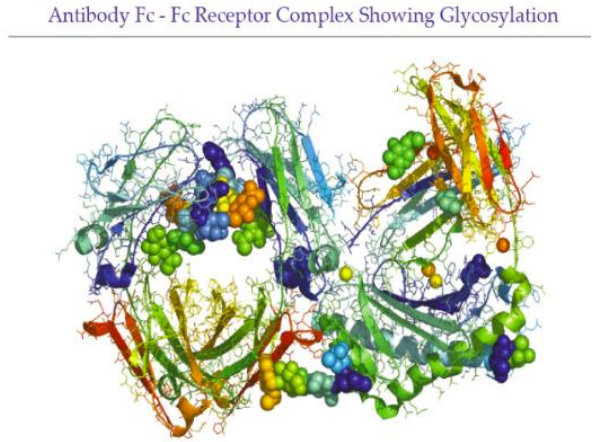
Biomeasurement Routemap



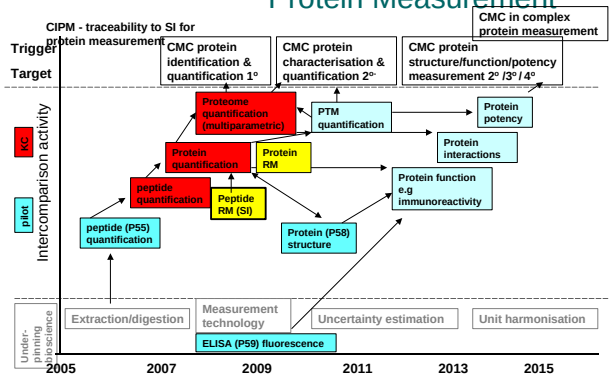
Protein Measurement “Space”: Activities, gaps, etc.

Delivery of Services for Proteins/Peptides:

- ✓ **RMs and CRMs**
  - ✓ Pure substance materials (including a single protein/peptide in solution)
  - ✓ Matrixed materials
- ✓ **Calibration services**
  - ✓ Example: value assignment of materials for clinical PT schemes
- ✓ **Reference data**
  - ✓ Example: peptide MS/MS spectral libraries

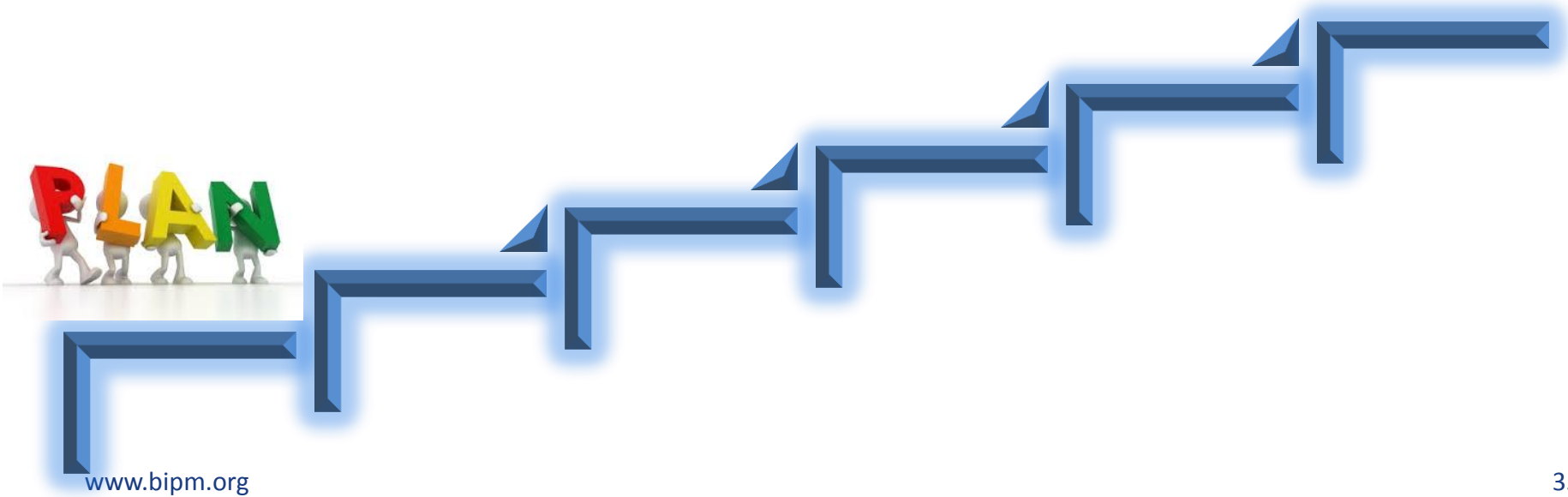


BAWG Routemap (ii)
Protein Measurement

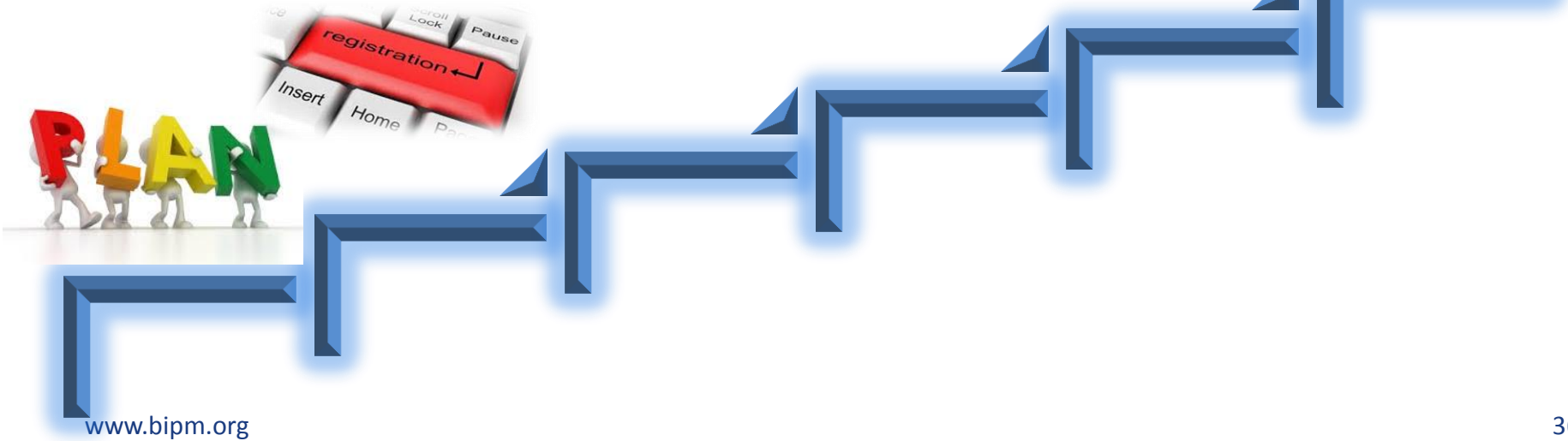


Bureau International des Poids et Mesures

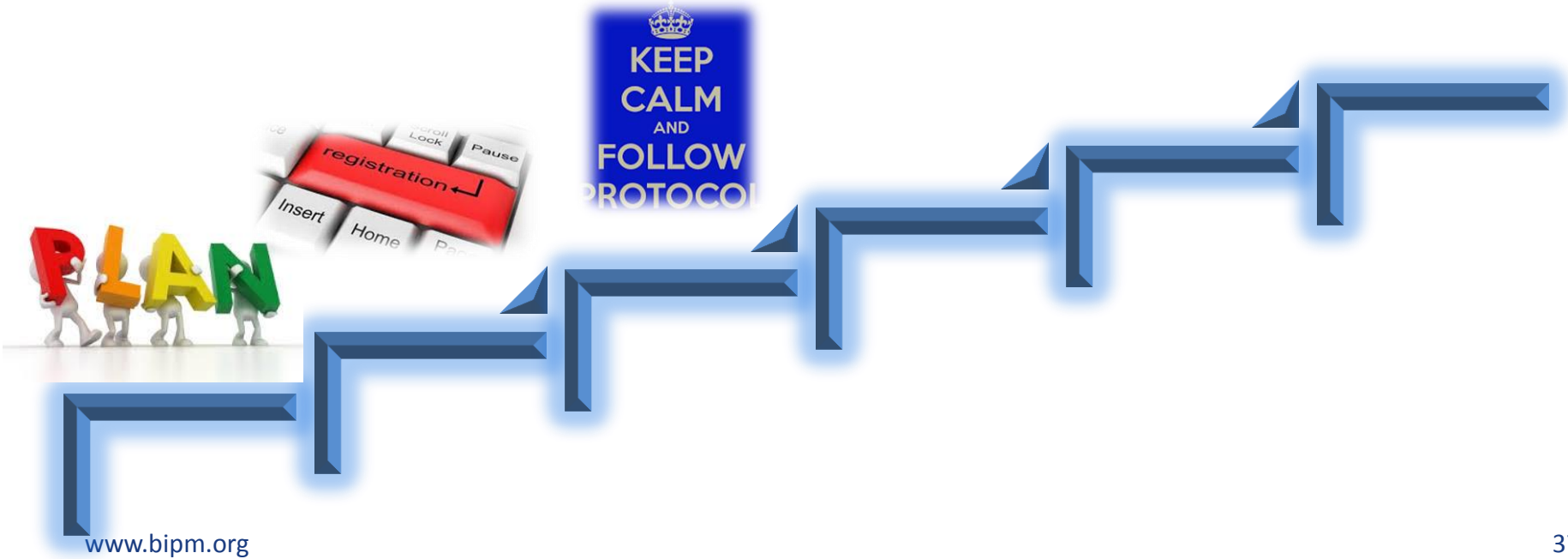
Organisation of CCQM key comparisons



Organisation of CCQM key comparisons



Organisation of CCQM key comparisons

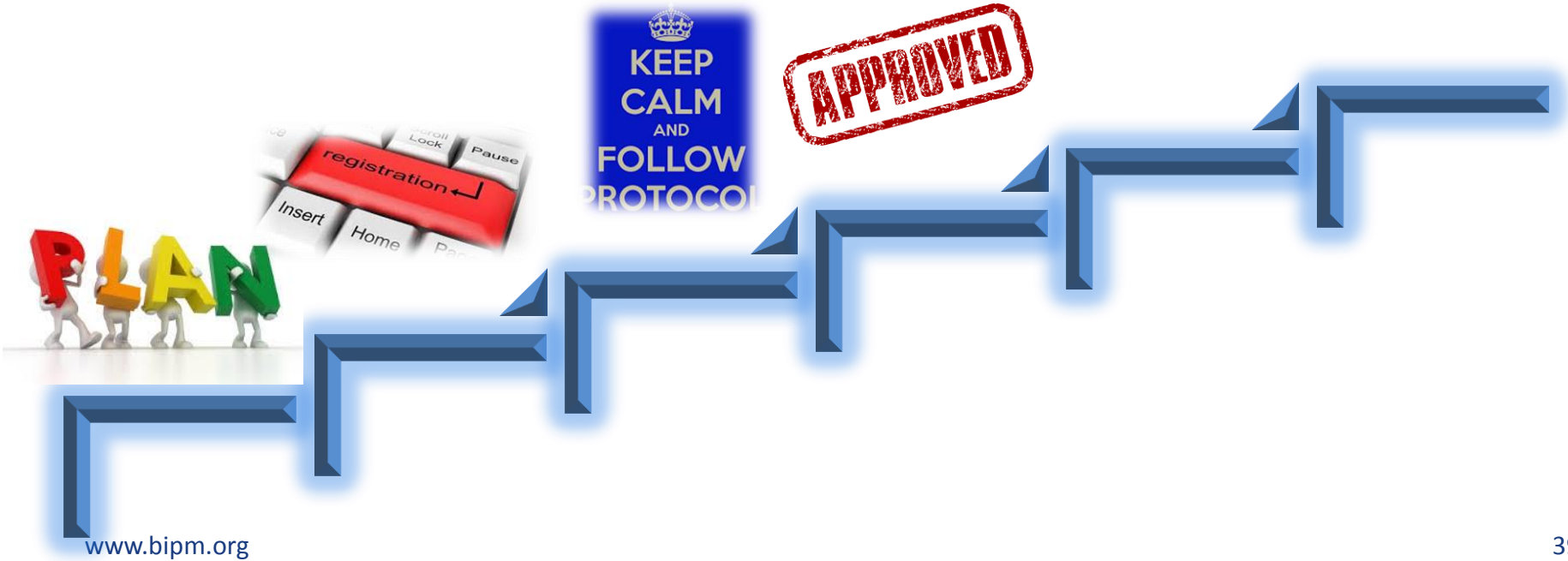


Technical protocol

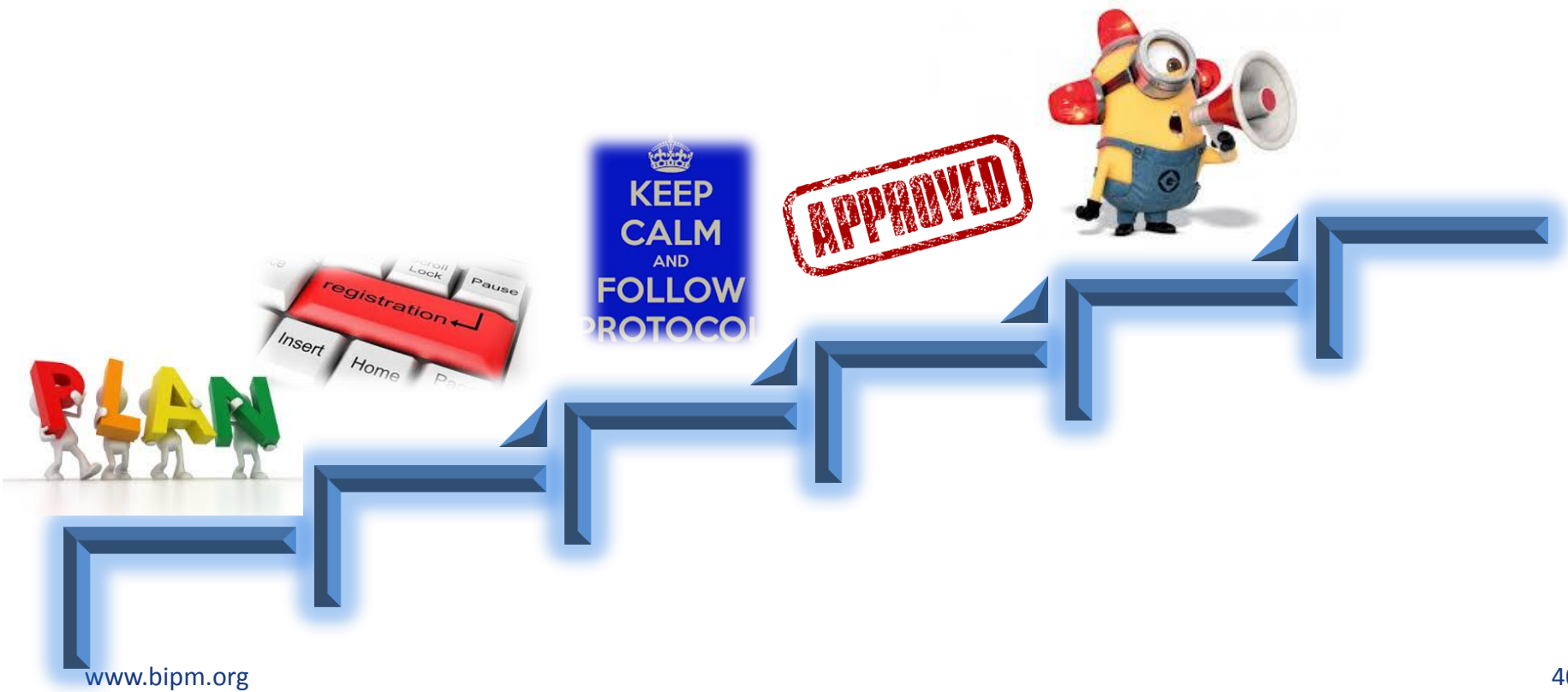
- ✓ Instructions for the handling of the sample
  - ✓ Storage
  - ✓ Re-constitution
  - ✓ Determination of moisture content
  - ✓ Sub-sampling
  - ✓ Minimum sample intake
- ✓ Information
  - ✓ Preparation of the comparison samples
  - ✓ Assessment of homogeneity
  - ✓ Assessment of stability
- ✓ Measurement methods
- ✓ Schedule
- ✓ Requirements for reporting of data
- ✓ Registration form
- ✓ Reporting form

Bureau International des Poids et Mesures

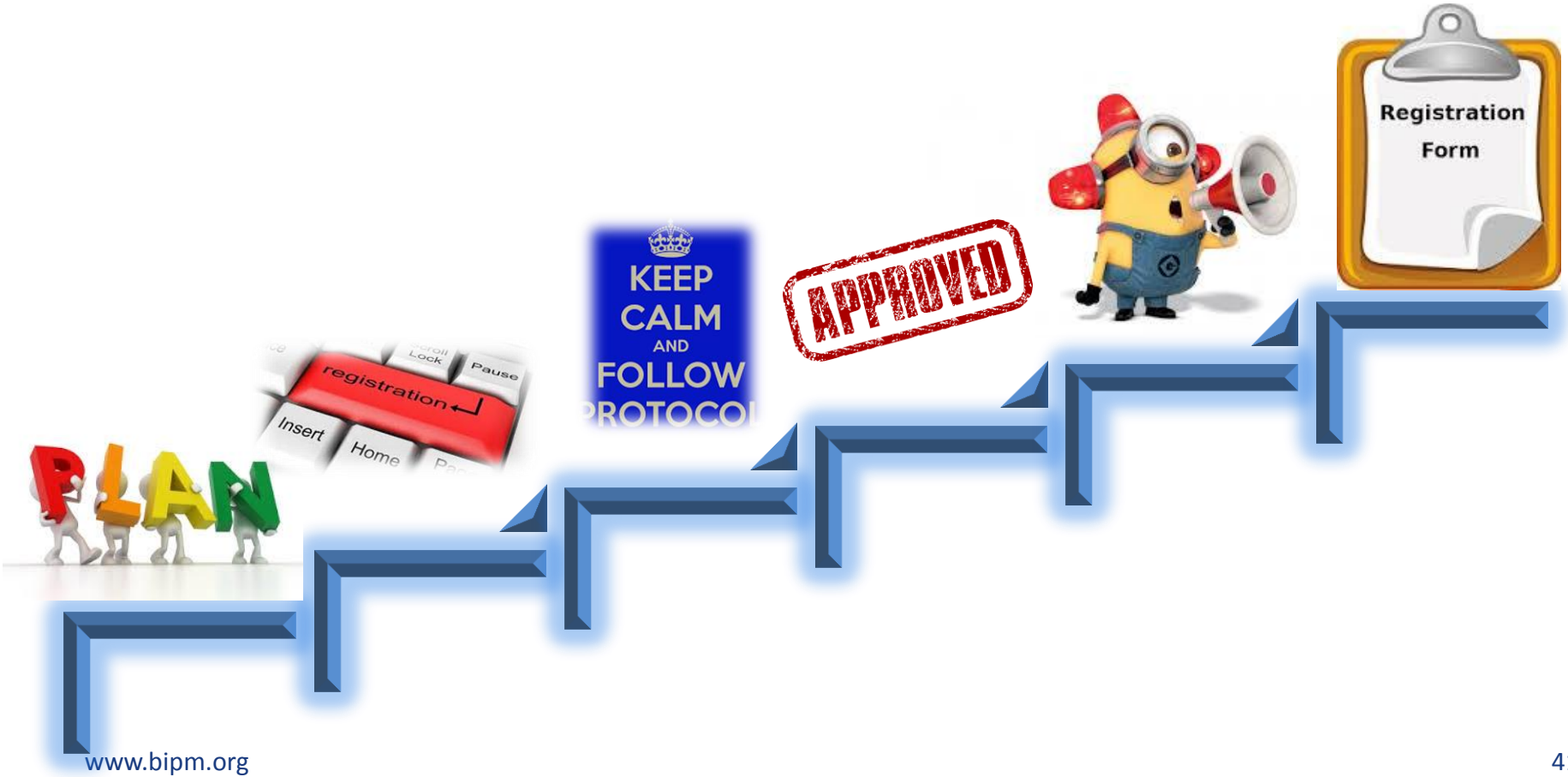
Organisation of CCQM key comparisons



Organisation of CCQM key comparisons



Organisation of CCQM key comparisons

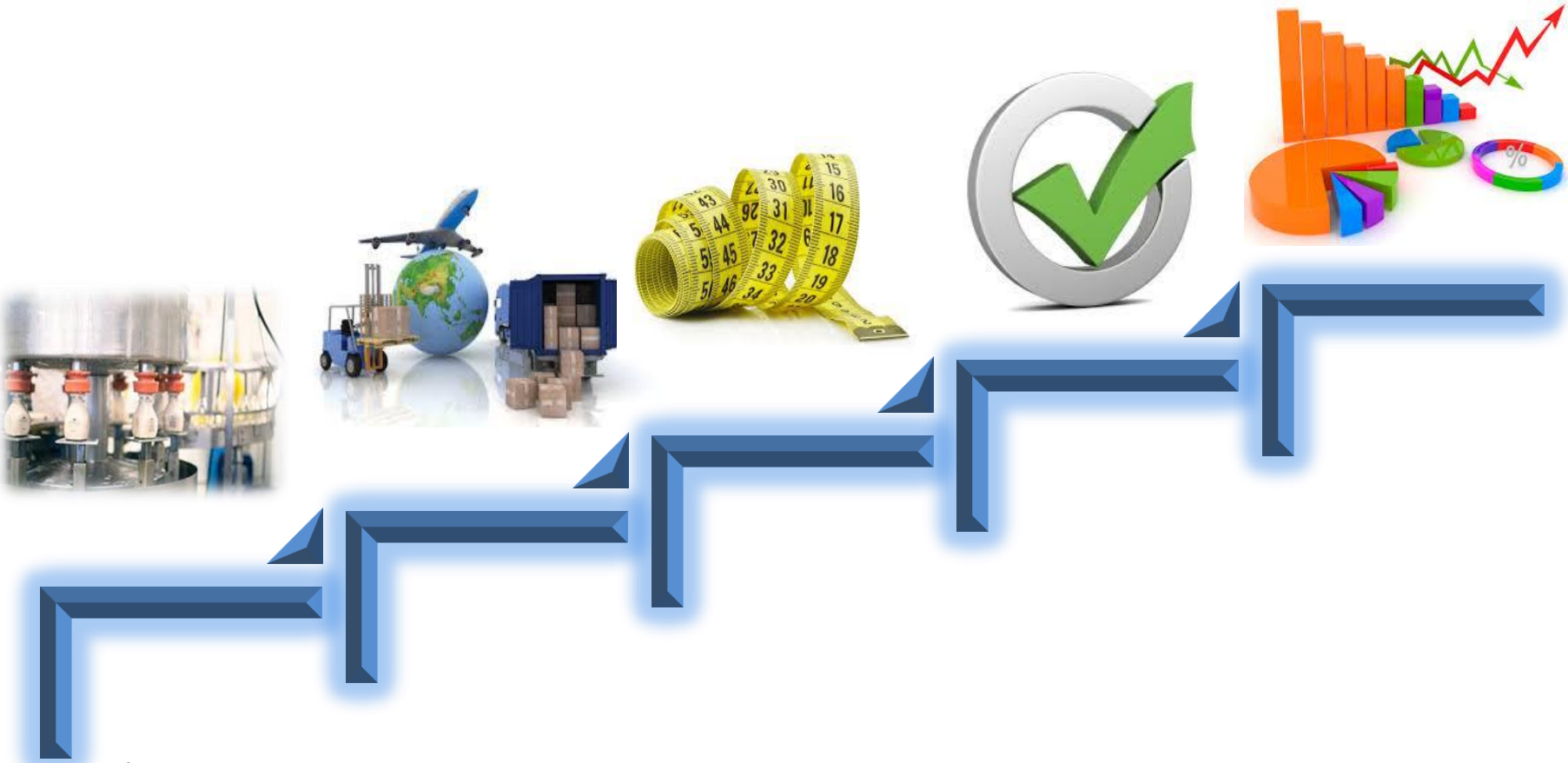


Organisation of CCQM key comparisons (cont.)

Organisation of CCQM key comparisons (cont.)

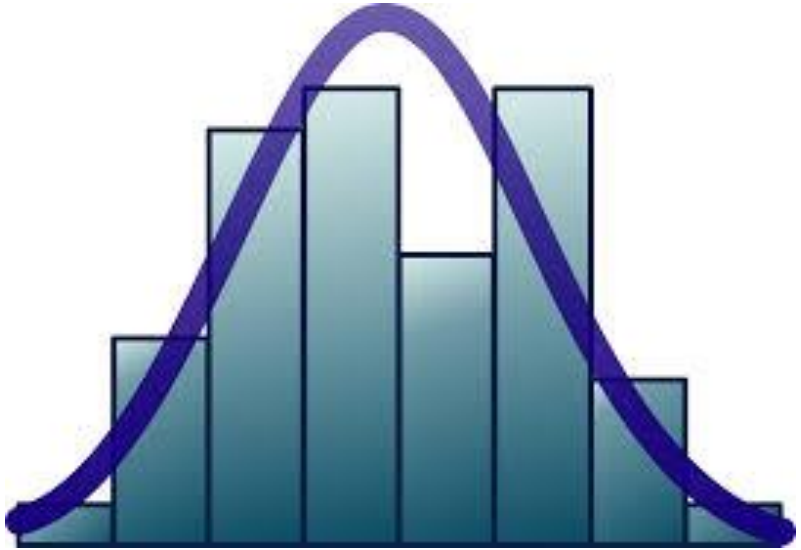
Organisation of CCQM key comparisons (cont.)

Organisation of CCQM key comparisons (cont.)

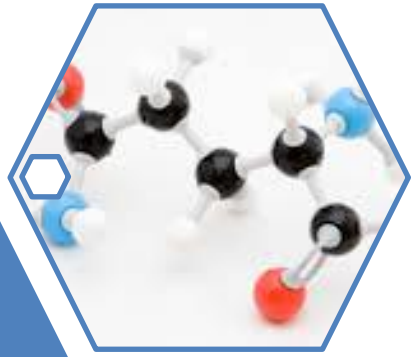


Key comparison reference value

- ✓ Unique reference value
- ✓ Independent reference value
- ✓ Consensus value
  - ✓ Different statistical models
  - ✓ Mean
  - ✓ Weighted mean
  - ✓ Largest consistent subset
  - ✓ Robust statistics



HFTLS



analyte

matrix

concentration

Bureau International des Poids et Mesures

Coordinating laboratory

- ✓ Capability
  - ✓ Preparation/distribution of the samples
  - ✓ Assessment of homogeneity
  - ✓ Assessment of stability
  - ✓ Data evaluation
- ✓ Responsibility
  - ✓ Technical protocol
  - ✓ Registration of participants
  - ✓ Distribution
  - ✓ Verification
  - ✓ Reporting

Bureau International des Poids et Mesures

CMC review process

KCWG

NMIs

Responsibilities of the KCWG

- ✓ Manage CCQM interregional CMC review process
- ✓ Focus on process and policy issues
- ✓ Resolve technical issues
  - ✓ With assistance from the CCQM WGs
- ✓ Monitor the support for CMC claims by comparison studies
  - ✓ Identify gaps and report to CCQM WG Chairs
- ✓ Manage the re-review of existing CMC claims

Structure of the KCWG

- ✓ Chair
- ✓ Vice-Chair
- ✓ Rapporteur
- ✓ RMO TCQM Chairs
- ✓ Technical experts from the CCQM WGs
- ✓ Technical experts from the RMOs
- ✓ Quota: 5 representatives from each RMO

Bureau International des Poids et Mesures

Specific requirements for CMCs

Country	NMI or Designated Service Provider	NMI Service Identifier	Meas. Serv. Cat. No.	Meas. Serv. Sub-Category No.	Meas. Serv. Category	Matrix

Bureau International des Poids et Mesures

Specific requirements for CMCs

Measurand				Dissemination Range of Measurement Capability			Range of Expanded Uncertainties as Disseminated					
Analyte Group Identifier	Analyte or Component	CAS Number	Quantity	From	To	Unit	From	To	Unit	Cov. factor	Lev. of confid.	Is the expanded uncertainty a relative one?

Bureau International des Poids et Mesures

Specific requirements for CMCs

Range of Certified Values in Reference Materials			Range of Expanded Uncertainties for Certified Value					
From	To	Unit	From	To	Unit	Cov. factor	Lev. of confid.	Is the expanded uncertainty a relative one?

Bureau International des Poids et Mesures

Specific requirements for CMCs

Mechanism(s) for Measurement Service Delivery	Source of Traceability	Measurement Technique(s) Used	Link(s) to Appendix B (Formal Comp. Name(s))	Comment(s) of Service Provider	Comments (to be published via the database)	Uncertainty Convention	RMO Services Administration	
							Review Code/ Status	Review Comments

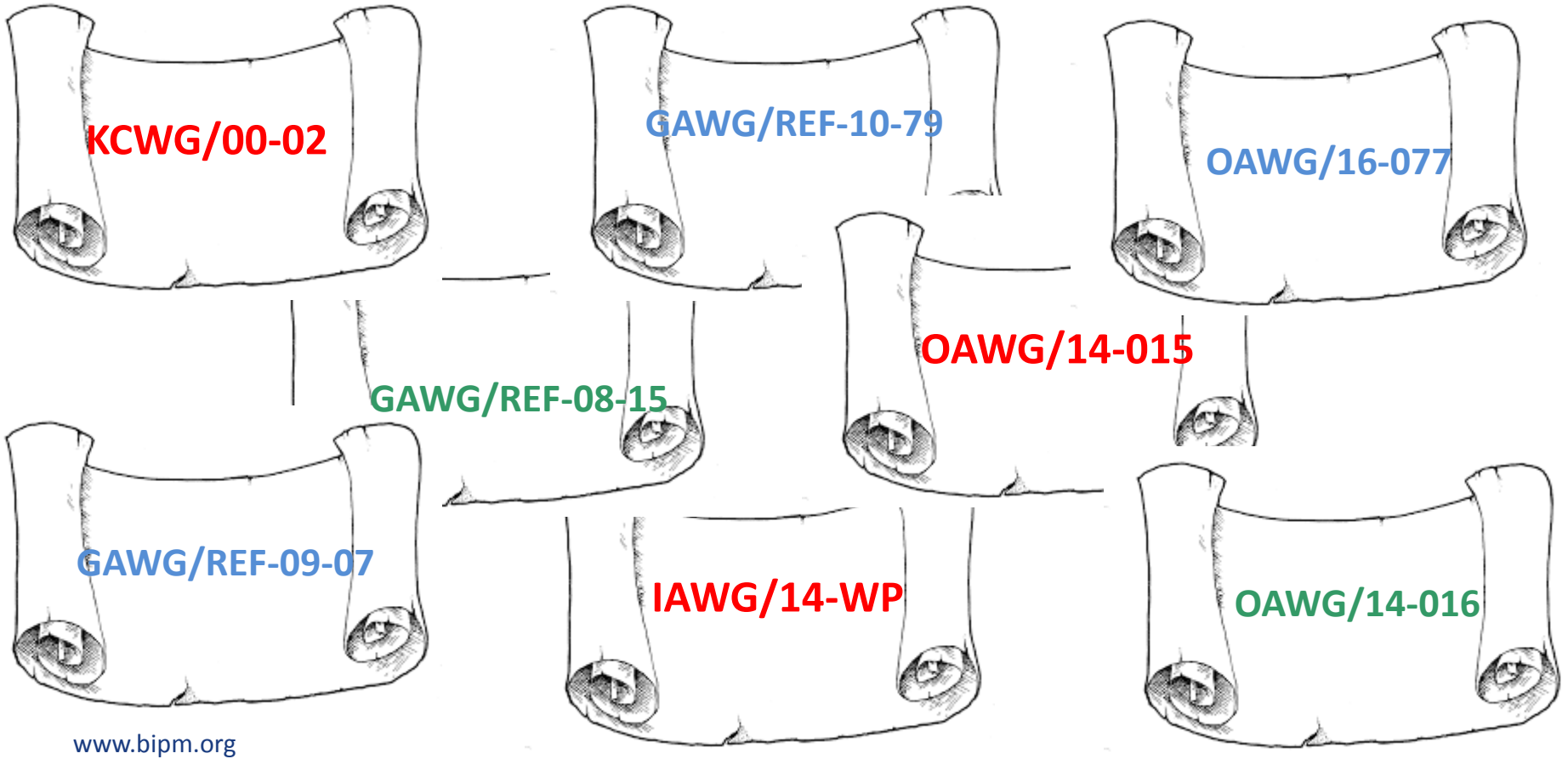
Bureau International des Poids et Mesures

Specific requirements for CMCs

New or Revised claim?	Exact nature of service delivered	Details of calibrants used and assessment of their purity/certification	Clear description of supporting evidence for this claim

Bureau International des Poids et Mesures

Guidance documents for CMC review



Capacity Building & Knowledge Transfer

Thank you

abotha@nmisa.org

Bureau International des Poids et Mesures