JCTLM Working Group on Traceability Education & Promotion

Commutability : why it matters

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MEASUREMENT & STANDARDS
Keys to COMPETITIVENESS and A SAFER WORLD

Reliability of medical tests is a major public health challenge

- 60 to 70% of medical decisions are based on an in vitro diagnostic test
- Results are not always traceable to internationally recognized references

→ Results will not always be comparable depending on what method is used!

1) Health point of view : risk of inappropriate medical decisions

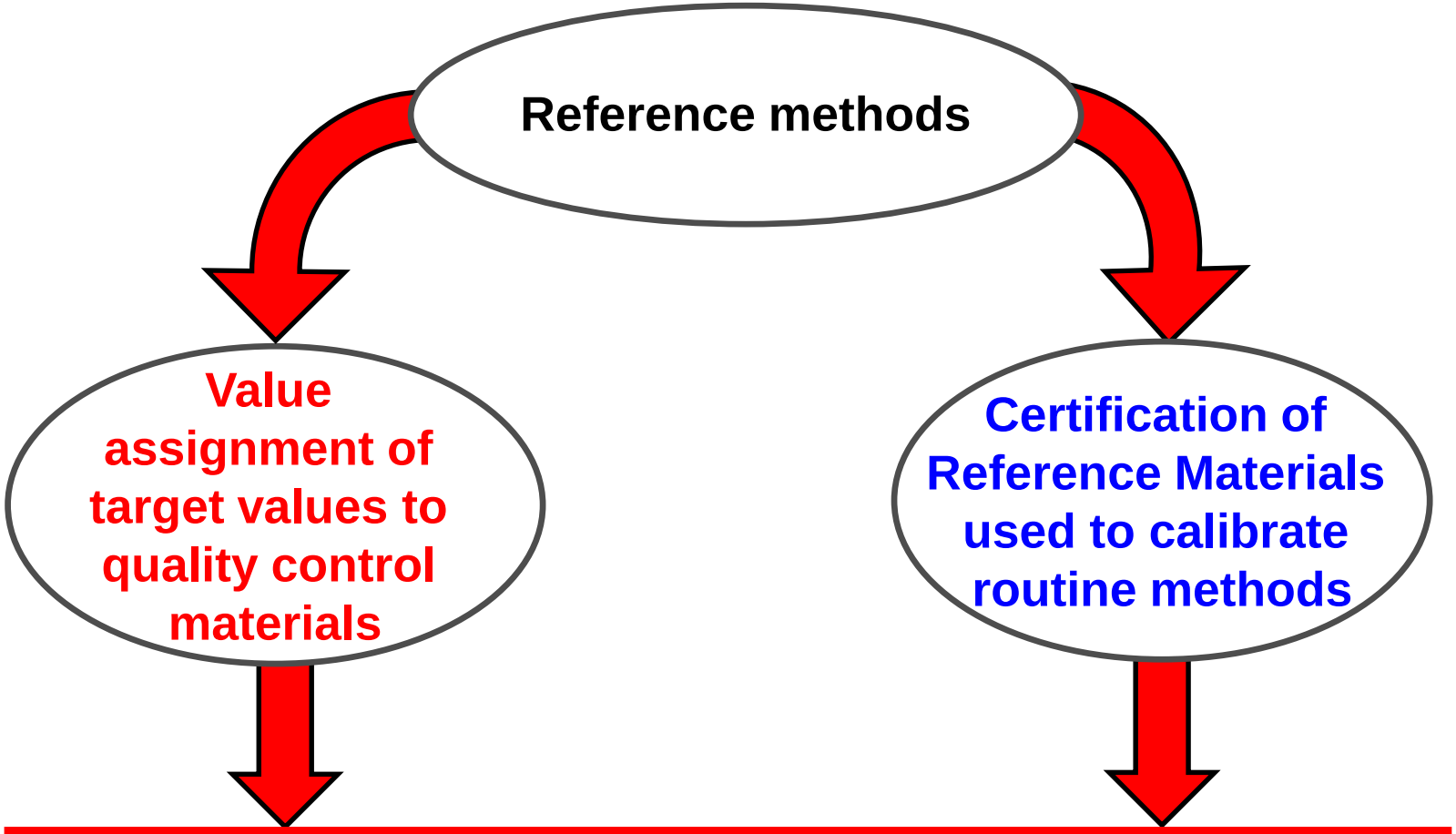
2) Economic point of view : repetition of measurements = waste of money

25 to 30% of costs are due to test repetitions, prevention and error detection instead of diagnostic itself (15-30 billion $ / year in the US)

3) Science point of view : lack of reliable data for epidemiological studies and clinical trials hampers understanding of pathologies & discovery of new treatments

How to assess and improve reliability and comparability of clinical measurements?

Importance of reference methods



Assessing and improving reliability and comparability of medical tests

Regulatory drivers

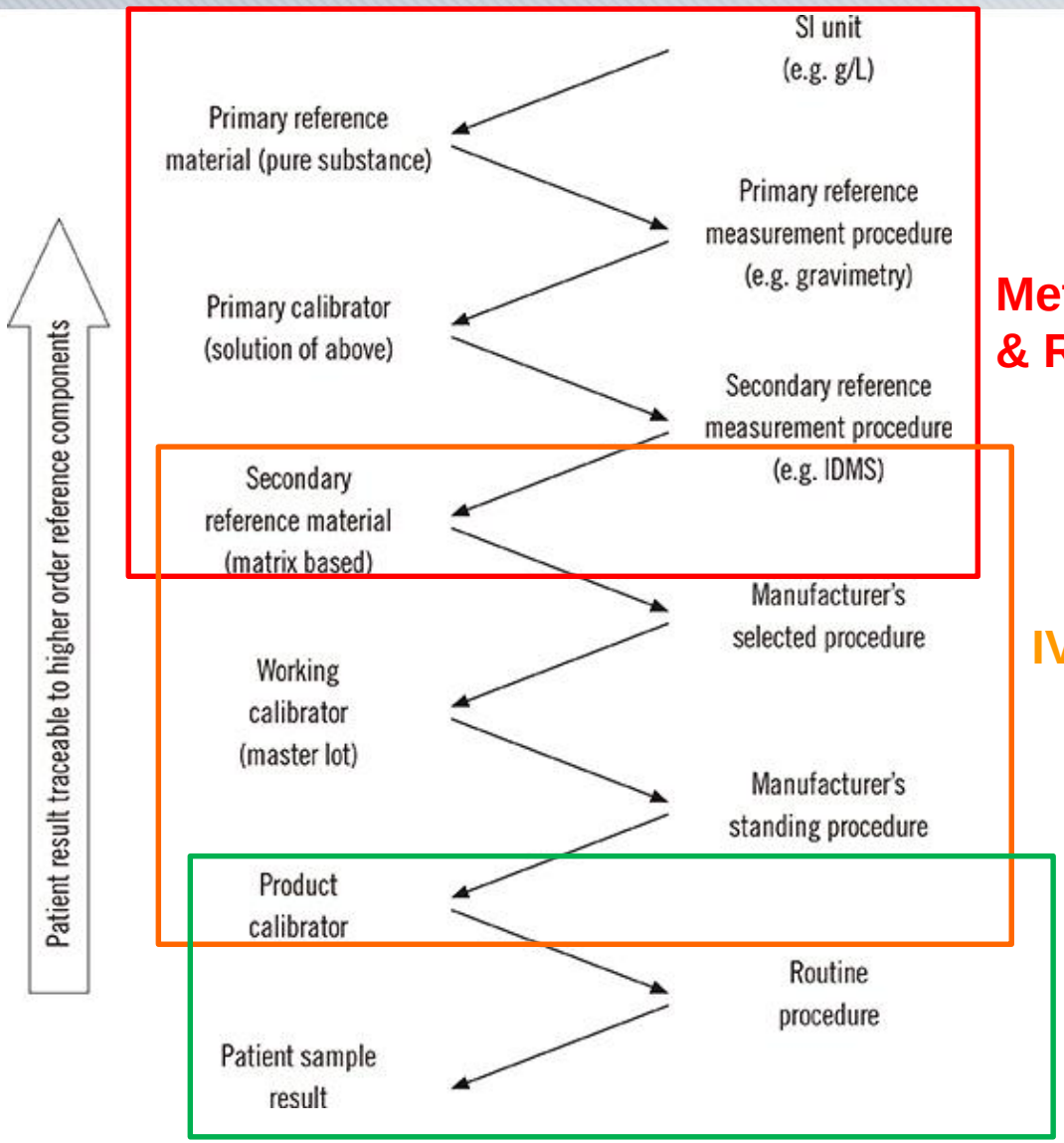
In vitro diagnostic medical devices Directive 98/79/EC

« The traceability of values assigned to calibrators and/or control materials must be assured through available reference measurement procedures and/or available reference materials of a higher order »

According to ILAC (*International Laboratory Accreditation Cooperation*) elements needed to confirm metrological traceability of results include:

- **an unbroken metrological traceability chain to an international measurement standard or a national measurement standard,**
- **a documented measurement uncertainty,**
- **a documented measurement procedure,**
- **accredited technical competence,**
- **metrological traceability to the SI,**
- **calibration intervals**

Traceability chains in laboratory medicine



Metrology Institutes & Reference Labs

IVD Manufacturers

Medical laboratories

Miller et al. Ann Lab Med. 2014;34(3):187-197.

JCTLM

- JCTLM = Joint Committee for Traceability in Laboratory Medicine
- Review teams of experts regularly review Reference Materials, Reference Methods and Reference Laboratories for entry into a public database

http://www.bipm.org/jctlm/

BIPM
Bureau International des Poids et Mesures

Database of higher-order reference materials, measurement methods/procedures and services

JCTLM
JCTLM Database
Laboratory medicine and *in vitro* diagnostics

> You are here : JCTLM-DB

JCTLM database: Laboratory medicine and *in vitro* diagnostics

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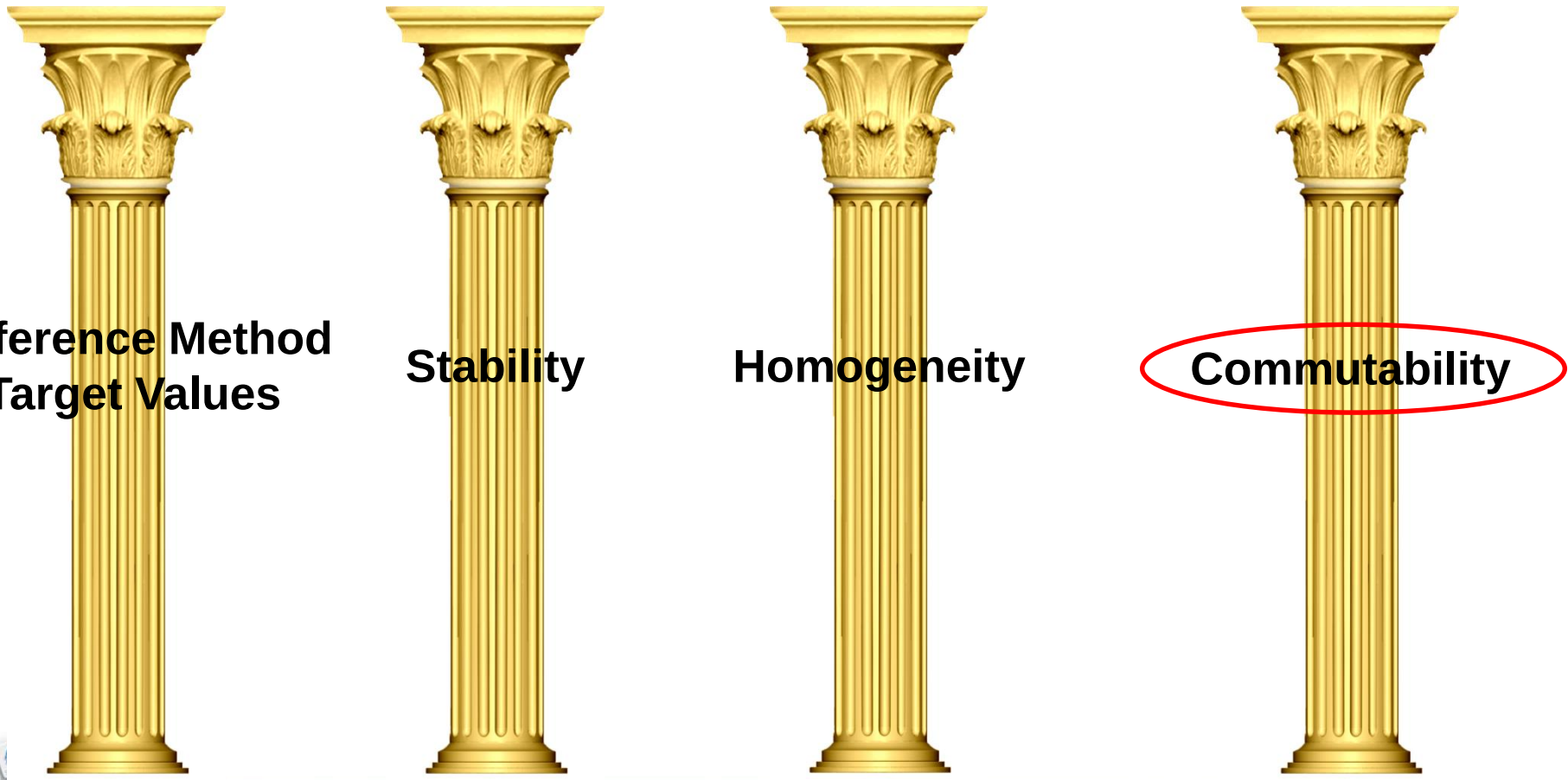
Analyte	total cholesterol
Material or matrix	blood serum, calibration solution
Applicable material or matrix	lyophilized, fresh, or frozen human serum, calibration solution
Quantity	Amount-of-substance concentration
Service measurement range	1 mmol/L to 10 mmol/L
Expanded uncertainty (level of confidence 95%)	3 % to 1 % The expanded uncertainty is relative.
Interlaboratory comparison results	RELA - IFCC External Quality assessment scheme for Reference Laboratories in Laboratory Medicine at http://www.dqkl-rfb.de:81/index.shtml
Measurement principle	ID-GC/MS

Reference methods & CRMs are available only for a limited number of biomarkers

Pillars of standardization

Certified Reference Materials for standardization

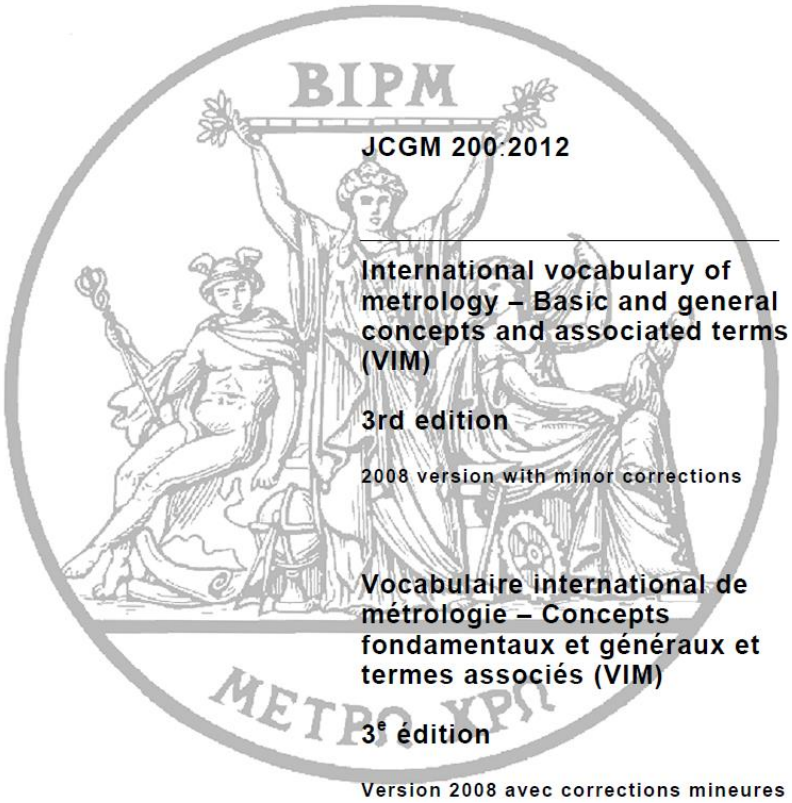


What is commutability?

❖ VIM definition

5.15
commutability of a reference material

property of a **reference material**, demonstrated by the closeness of agreement between the relation among the **measurement results** for a stated **quantity** in this material, obtained according to two given **measurement procedures**, and the relation obtained among the measurement results for other specified materials



❖ Simplified definition

Property of a RM that indicates how well it mimics the characteristics of (a set of) typical clinical specimens for a given method and for a stated measurand

Non commutability of calibrators breaks traceability chains!

Clinical Chemistry 59:9
1322–1329 (2013)

The Importance of Commutability of Reference Materials Used as Calibrators: The Example of Ceruloplasmin

Ingrid Zegers,[1*] Robert Beetham,[2] Thomas Keller,[3] Joanna Sheldon,[4] David Bullock,[5] Finlay MacKenzie,[5] Stefanie Trapmann,[1] Hendrik Emons,[1] and Heinz Schimmel[1]

BACKGROUND: Different methods for ceruloplasmin tend to give different results in external quality assessment schemes. During the production of the certified reference material ERM-DA470k/IFCC discrepant measurement results were also found for ceruloplasmin measured with different methods, and consequently the protein could not be certified in the material.

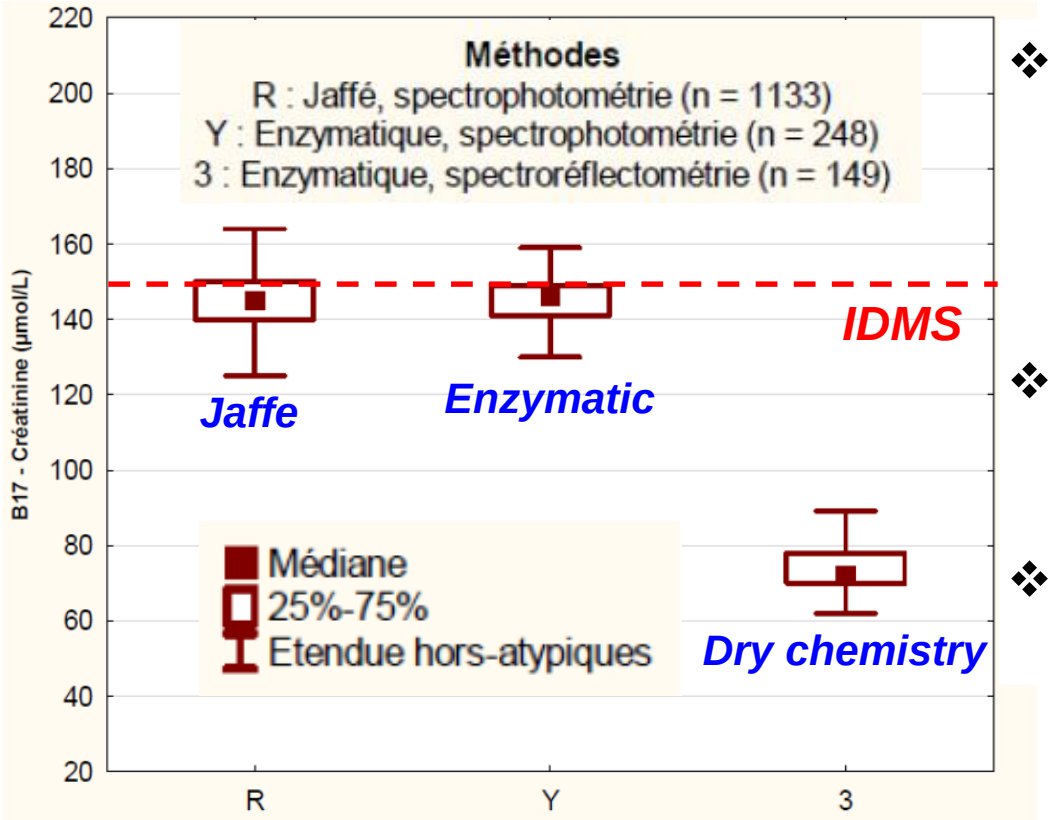
METHODS: We performed a commutability study with 30 serum samples and the reference materials ERM-DA470, ERM-DA470k/IFCC, and ERM-DA472/IFCC, using 6 different methods. Data were analyzed according to the CLSI Guideline C53-A to assess whether the reference materials had the same behavior as the serum samples with respect to measurement results obtained with combinations of the methods used.

RESULTS: Measurement results from different methods showed a good linear correlation for the serum samples. ERM-DA470 showed marked noncommutability for certain combinations of methods. ERM-DA470k/IFCC and ERM-DA472/IFCC were commutable for more combinations of methods. The lack of commutability of ERM-DA470 for certain combinations of methods correlates with results from the UK National External Quality Assessment Service showing discrepancies between results from these methods. For serum stored in the presence of sodium azide the results from different methods are essentially equivalent.

CONCLUSIONS: Ceruloplasmin in ERM-DA470 is a fully documented example of a situation in which, due to lack of commutability, the use of a common material for calibration did not lead to harmonization .

Non commutability of EQA materials skews trueness assessment !

ansm
Agence nationale de sécurité du médicament et des produits de santé



- Use of a non-commutable control material lead to the conclusion that dry chemistry (used by 149 laboratories) had a bias of -50% agaist IDMS reference method !
- Agreement between results of the different peer groups could not be accurately estimated
- Fully independant post-market vigilence could not be performed

Commutable EQA materials are needed to evaluate standardization effectiveness and monitor methods' trueness

Commutability of EQA materials

European standard

French standard

NF EN ISO 15189
August 2007

Classification index: **S 92-060**

Medical laboratories

Particular requirements for quality and competence

5 Technical requirements

5.6 Assuring quality of examination procedures

5.6.4 The laboratory shall participate in interlaboratory comparisons such as those organized by external quality assessment schemes. Laboratory management shall monitor the results of external quality assessment and participate in the implementation of corrective actions when control criteria are not fulfilled. Interlaboratory comparison programmes shall be in substantial agreement with ISO/IEC Guide 43-1.

External quality assessment programmes should, as far as possible, provide clinically relevant challenges that mimic patient samples and have the effect of checking the entire examination process, including pre- and post-examination procedures.

Different types of External Quality Assessment Schemes

Miller et al.
Clin Chem 2011;57:1670-80

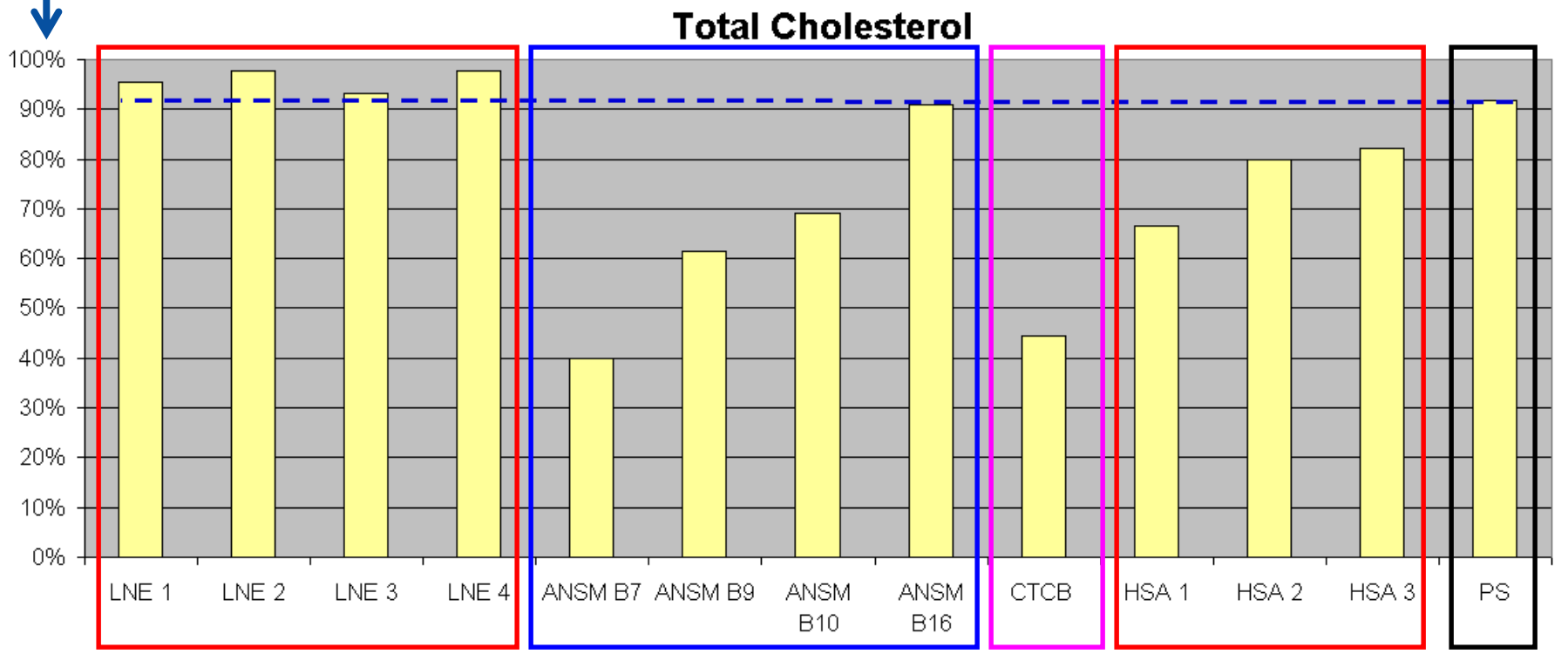
Table 3. Evaluation capabilities of PT/EQA related to scheme design.

	Sample characteristics			Evaluation capability: Accuracy: Individual laboratory: Absolute vs RMP or CRM	Evaluation capability: Accuracy: Individual laboratory: Relative to participant results		Evaluation capability: Reproducibility		Evaluation capability: Standardization or harmonization[b]: Measurement procedure calibration traceability	
Category	Commutable	Value assigned with RMP[a] or CRM	Replicate samples in survey	Absolute vs RMP or CRM	Overall	Peer group	Individual laboratory intralab CV	Measurement procedure interlab CV	Absolute vs RMP or CRM	Relative to participant results
1	Yes	Yes	Yes	X	X	X	X	X	X	X
2	Yes	Yes	No	X	X	X		X	X	X
3	Yes	No	Yes		X	X	X	X		X
4	Yes	No	No		X	X		X		X
5	No	No	Yes			X	X	X		
6	No	No	No			X		X		

- EQAS relying on non-commutable materials don't make it possible to assess comparability of results among different peer groups
- EQAS relying samples which target values have not been value assigned with a reference method don't make it possible to assess absolute bias

Commutability total cholesterol

% of pairwise comparisons in which each material was found commutable



LNE CRMs frozen sera CLSI C37A

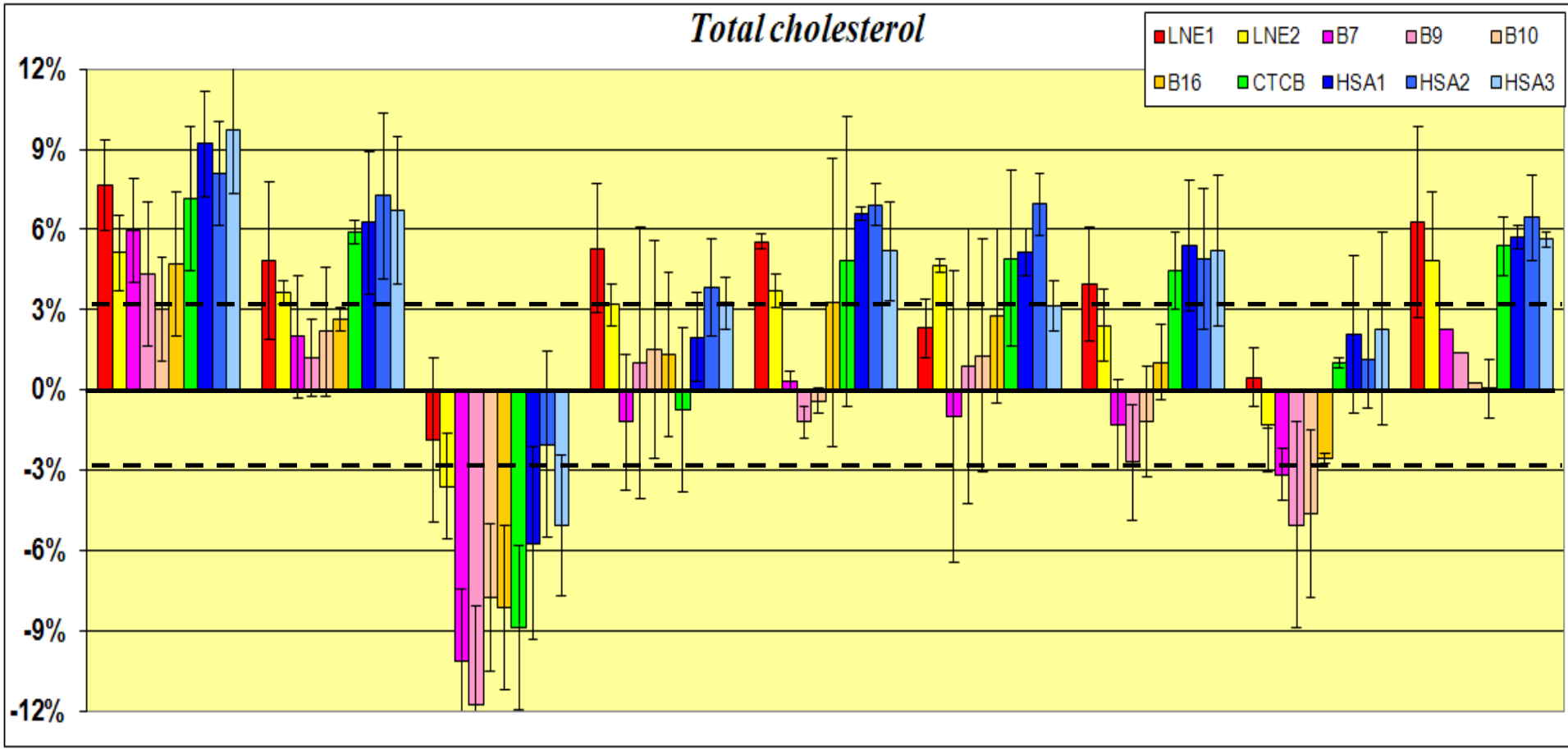
ANSM EQA samples lyophilized sera

CTCB Frozen sera « Home made »

frozen sera CLSI C37A

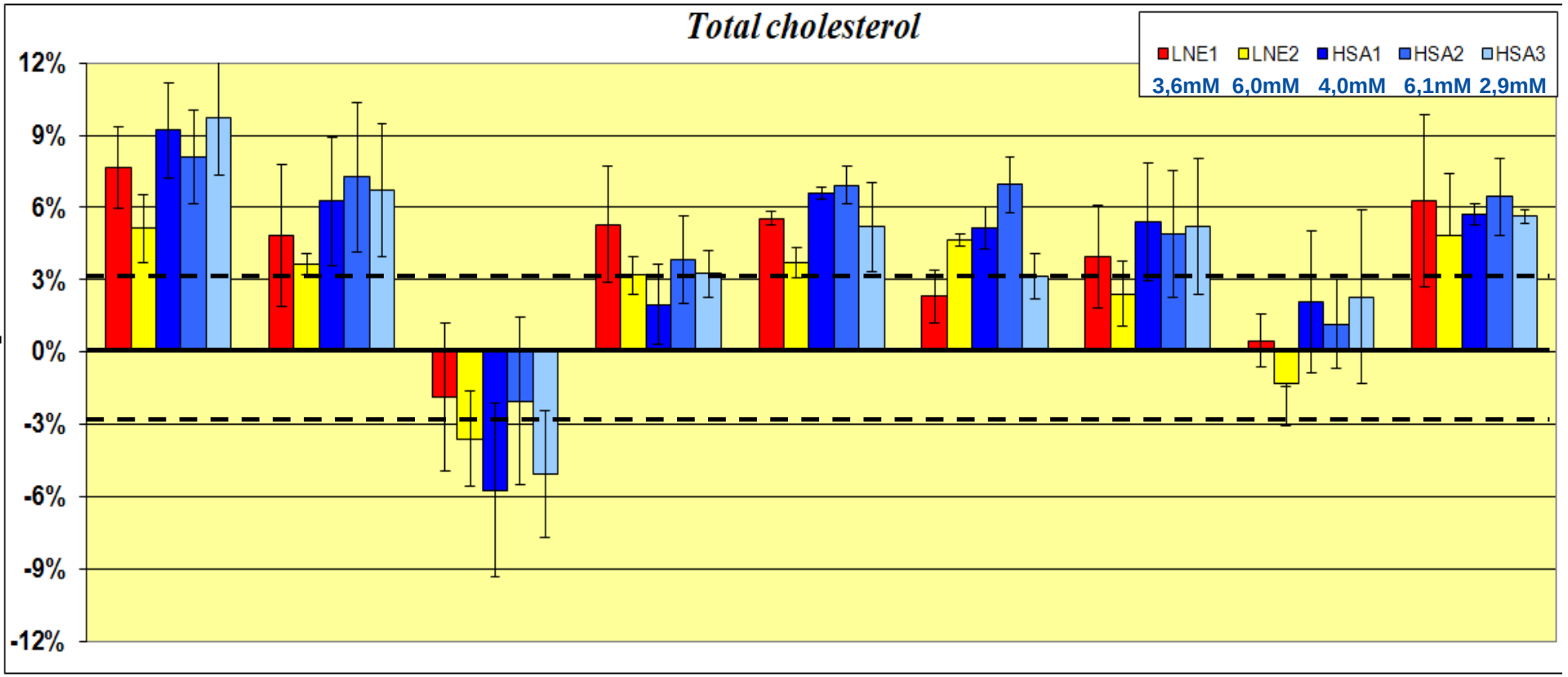
Control Fresh patient samples

Trueness total cholesterol



Measured bias depend on the quality (commutability) of control materials!

Trueness total cholesterol



Much better agreement when commutable materials are used

LNE-LABAC 2013 commutability study

Objectives : Assess commutability of 7 CRMs and 9 EQA materials for 6 parameters : glucose, creatinine, TCh, LDLc, HDLc, TG

✓ LNE CRM BIO 101a

→ 2 pools of Human Frozen Serum (CLSI C37A)
→ Certified for Glucose, Creatinine, TCh, LDLc, HDLc & TG
→ Recognized as higher order RM by the JCTLM

✓ 9 control materials from various EQAS

- 5 EQA materials from the French mandatory EQAS (Lyophilized sera)
- 3 EQA materials from an EQAS in Singapore (Frozen sera - CLSI C37-A)
- 1 EQA material from a French EQA Provider (Frozen serum, « home made »)

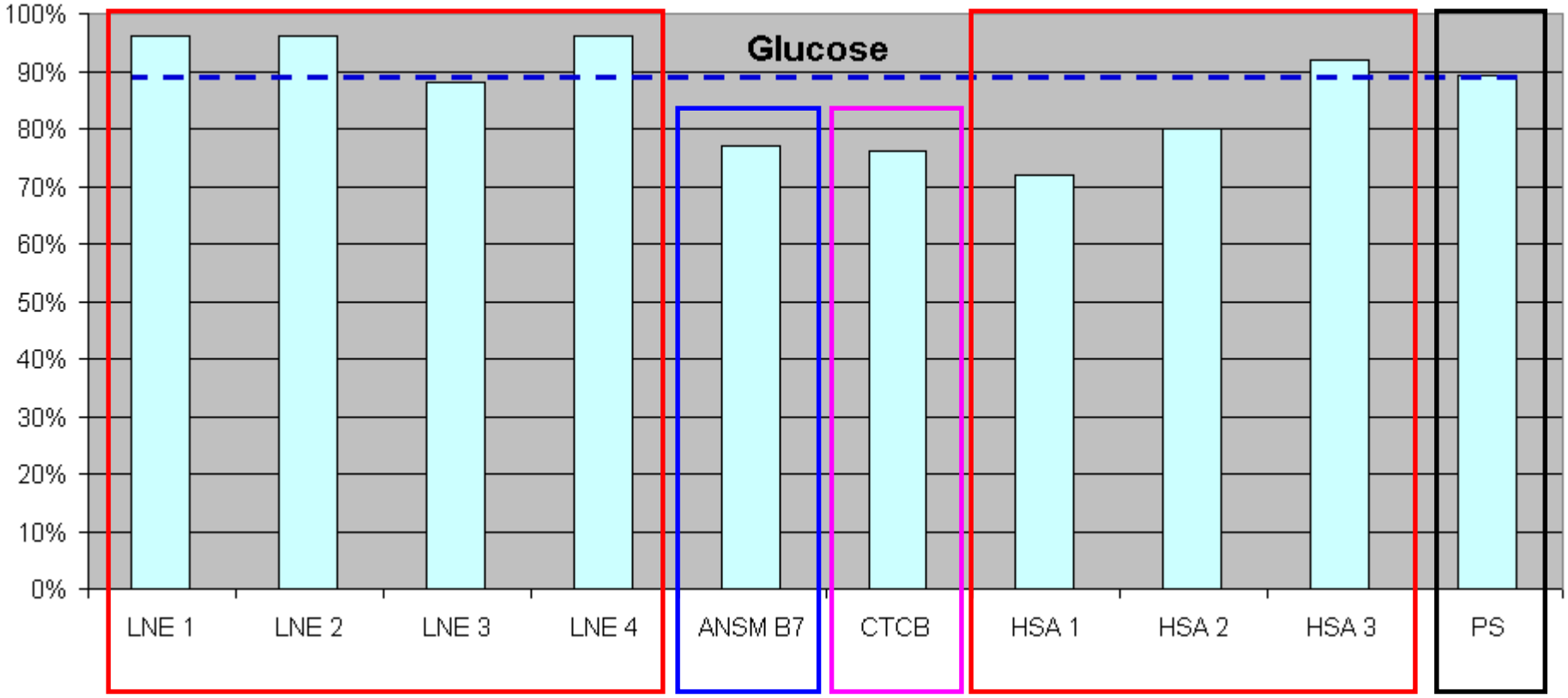
A material could be commutable for a given method but not for another one!

→ Commutability assessed for all (most popular) methods

→ 37 medical labs involved : 7 Roche Cobas, 6 Siemens Vista, 6 Abbott Architect, 5 Beckman DxC, 3 Beckman AU, 2 Siemens Advia, 3 Ortho-CD Vitros, 2 Roche Modular, 2 Thermo KoneLab

Commutability glucose

% of pairwise comparisons in which each material was found commutable



LNE CRMs
frozen sera
CLSI C37A

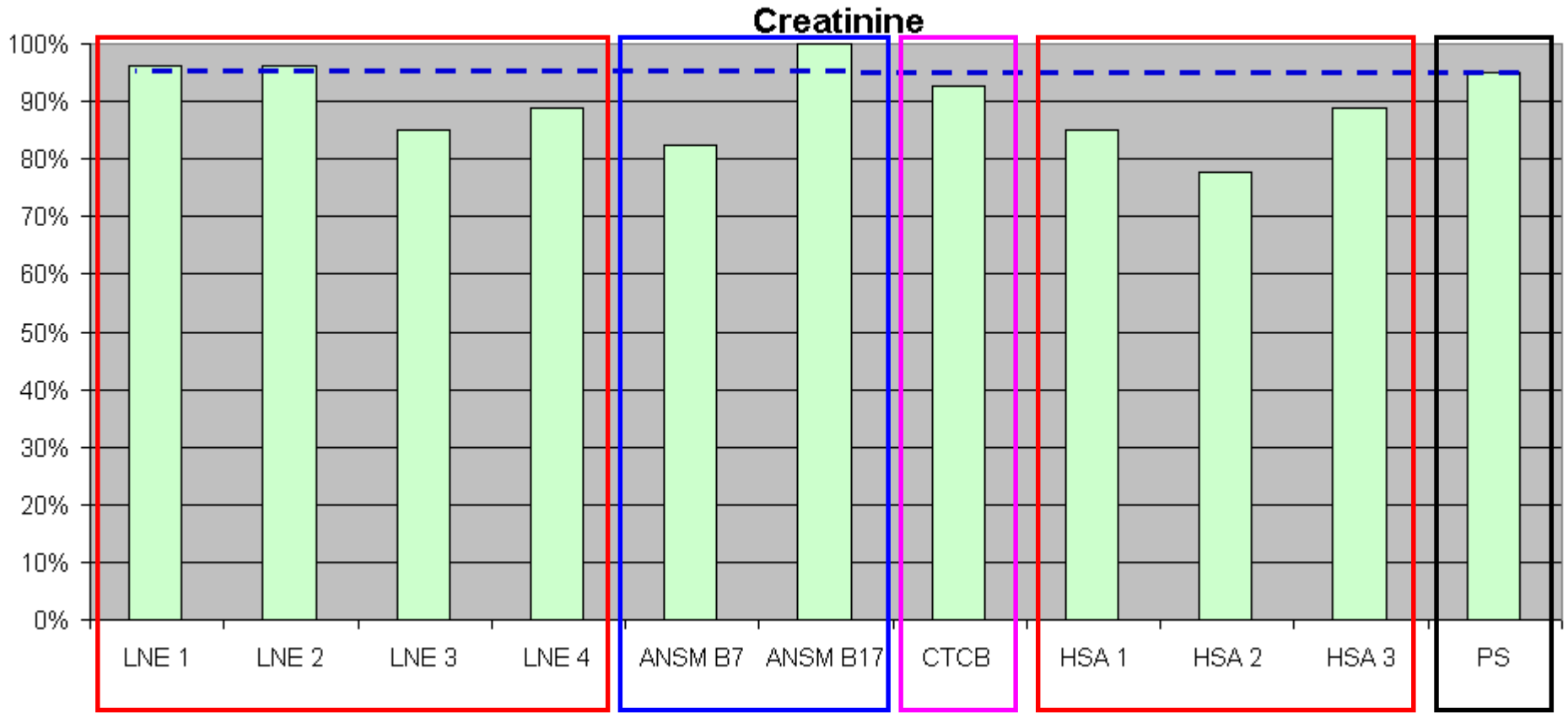
ANSM
EQA samples
lyophilized sera

CTCB
Frozen sera
"Home made"

frozen sera
CLSI C37A

Control
Fresh
patient
samples

Commutability creatinine



LNE CRMs frozen sera CLSI C37A

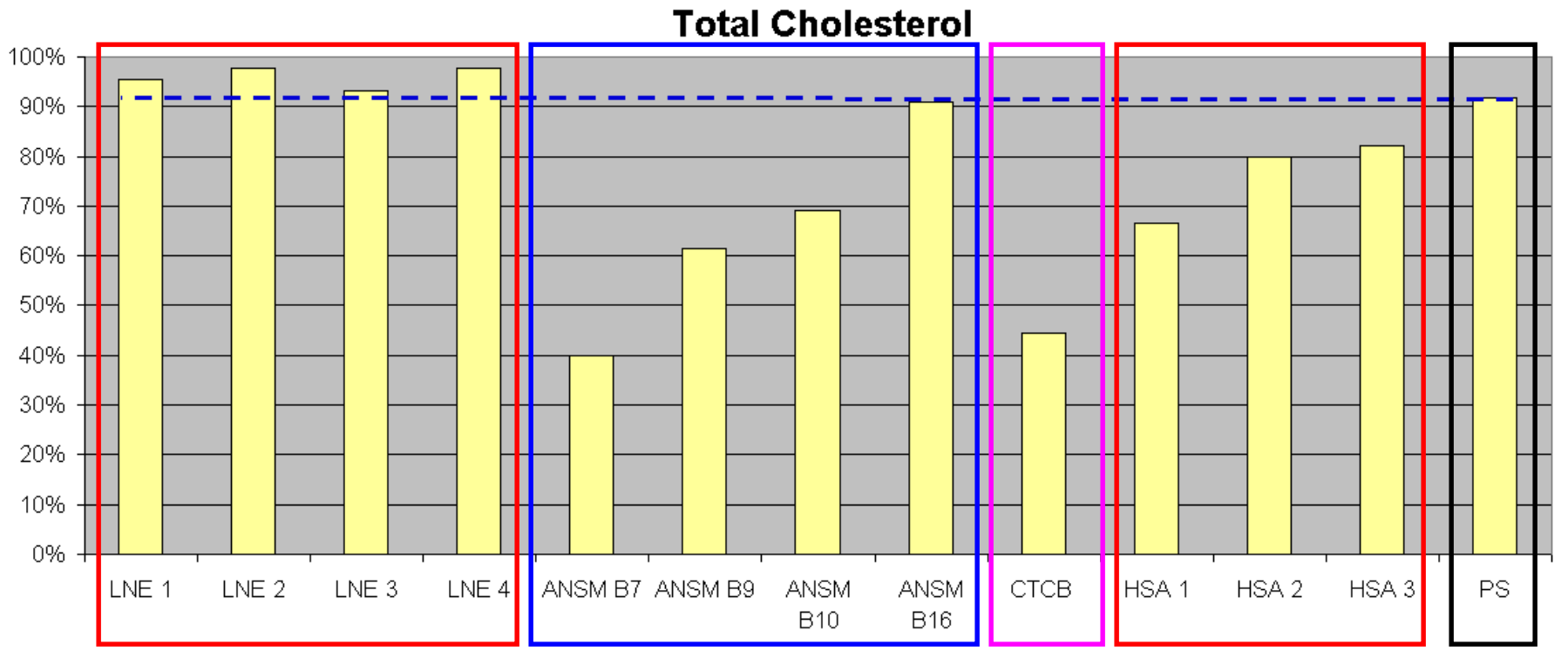
ANSM EQA samples lyophilized sera

CTCB Frozen sera "Home made"

frozen sera CLSI C37A

Control Fresh patient samples

Commutability total cholesterol



LNE CRMs frozen sera CLSI C37A

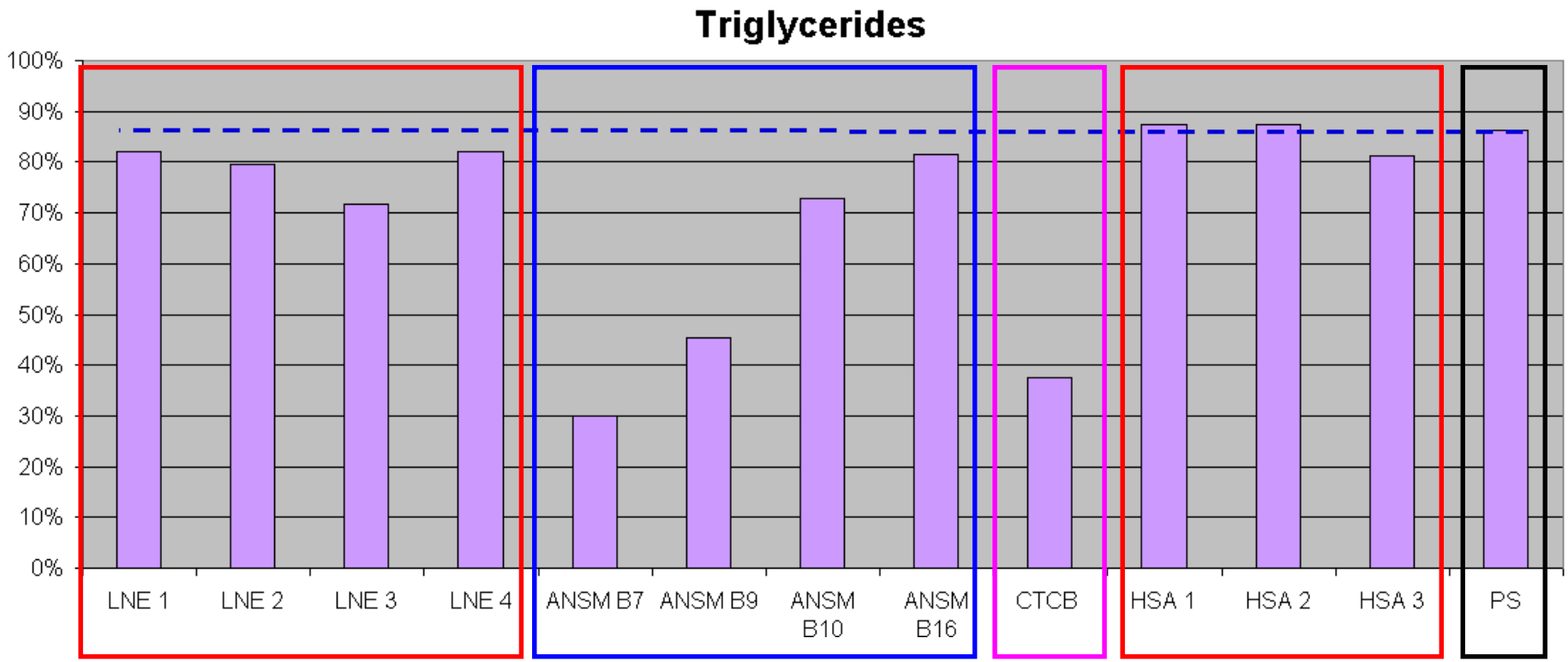
ANSM EQA samples lyophilized sera

CTCB Frozen sera « Home made »

frozen sera CLSI C37A

Control Fresh patient samples

Commutability TG



LNE CRMs
Frozen sera
CLSI C37A

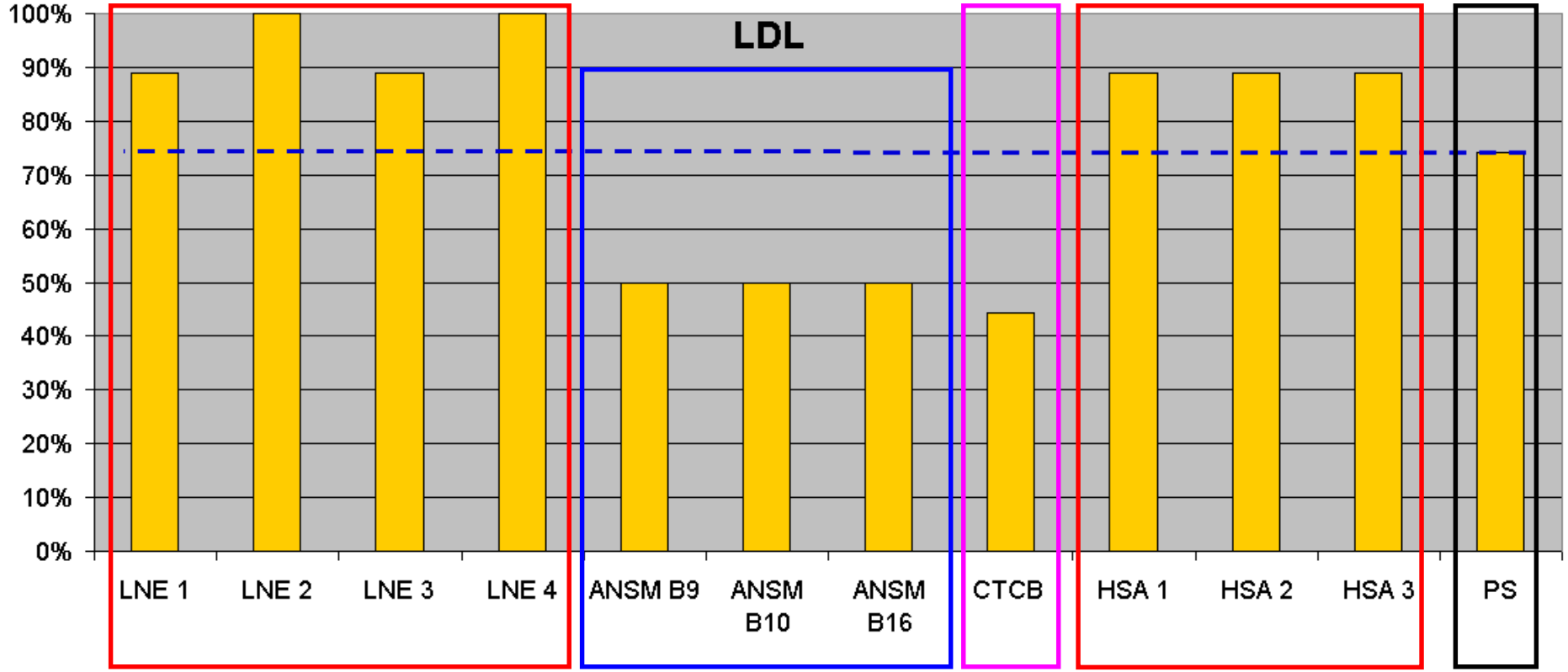
ANSM
EQA samples
lyophilized sera

CTCB
Frozen sera
« Home made »

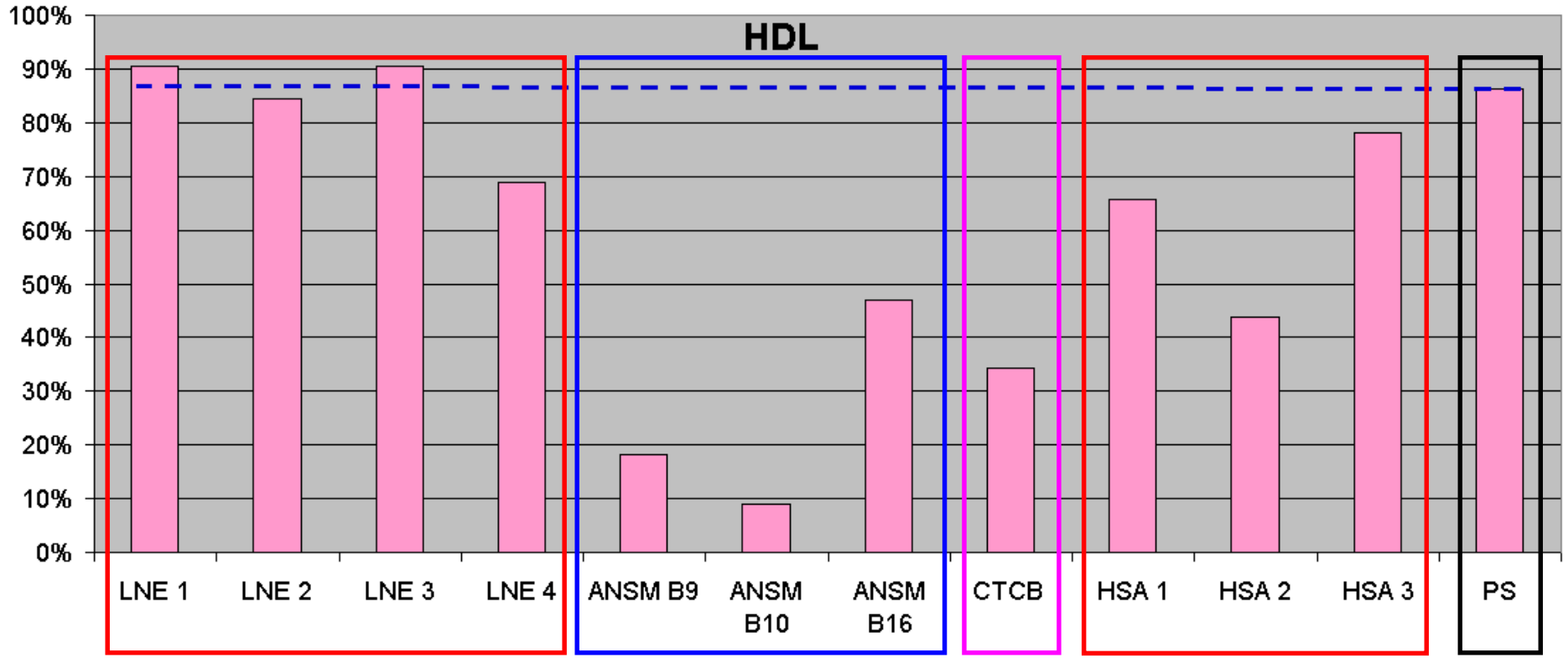
Frozen sera
CLSI C37A

Control
Fresh
patient
samples

Commutability direct LDL-C



Commutability HDL-C



2016 French National Quality Control

ansm
Agence nationale de sécurité du médicament et des produits de santé

MARCHE PUBLIC DE FOURNITURES ET SERVICES

Cahier des Clauses Techniques Particulières

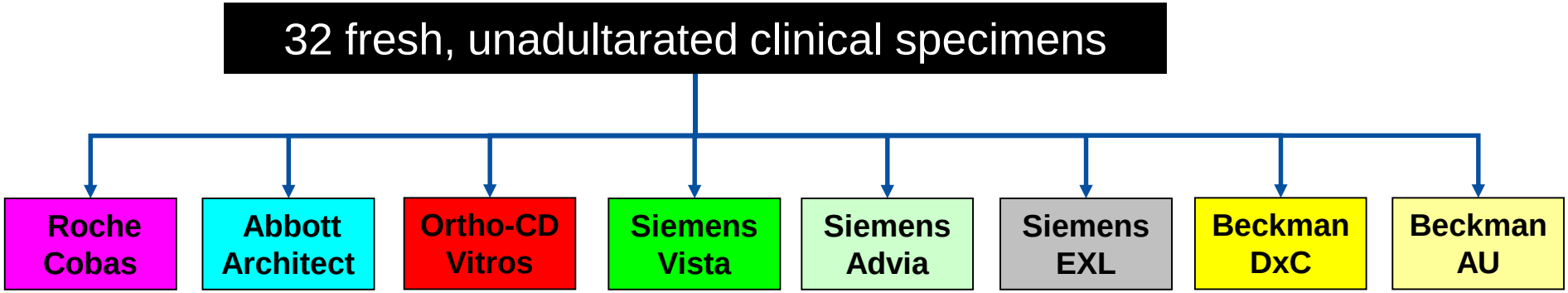
Etabli en application du Code des marchés publics relatif à :

LA FABRICATION D'ECHANTILLONS BIOLOGIQUES POUR LE CONTROLE NATIONAL DE QUALITE DES LABORATOIRES DE BIOLOGIE MEDICALE POUR LE COMPTE DE L'ANSM

- **For the first time in France, the mandatory National Quality Control organized by ANSM relied on Certified Reference Materials of proven commutability**
- **2 pools of frozen human serum produced according to CLSI C37A guidelines**
- **6 parameters : glucose, creatinine, TCh, LDLc, HDLc, TG**
- **Target values assigned in LNE using higher order reference methods listed in JCTLM database**
- **Samples distribued to all 1100 French medical laboratories in Nov. 2016**
- **Results available later by Summer 2017**

LNE-LABAC 2016 commutability study

GOAL : Assess commutability of 8 CRMs (C37A) and 22 EQA materials (6 frozen + 16 lyophilized) for 14 parameters : glucose, creatinine, TCh, LDLc, HDLc, TG, uric Acid, urea, Ca, Na, Cl, K, Fe, albumin



- **30-33 FRESH, unadulterated clinical specimens selected so as to bracket concentration of CRMs & EQA samples whose commutability is assessed**
- **Clinical specimens collected and aliquoted into 8 fractions on Monday, shipped on Tuesday and measured in triplicate on Wednesday / Thursday in the same analytical sequence as CRMs & EQA materials**
- **Commutability assessed for the 8 most popular methods in France : Roche Cobas, Siemens Vista, Abbott Architect, Ortho CD Vitros, Beckman AU, Beckman DxC, Siemens Advia, Siemens EXL**

Commutability of ANSM samples

ANSM B24	Glc	Creat	TC	TG	HDL	LDL	Uric Acid	Urea	Ca	Na	Cl	K	Fe	Alb
Siemens Vista	C	C	C	C	C	C	C	I	C	C	C	C	C	C
Roche Cobas	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Beckman DxC	C	C	C	I	C	NA	C	C	I	I	C	C	C	NA
Ortho CD Vitros	I	C	C	C	C	C	C	I	C	C	I	C	NA	NA
Abbott Architect	C	C	C	C	C	NA	C	C	C	C	C	C	C	C
Siemens Advia	C	C	C	C	C	C	C	C	C	C	C	C	I	C
Beckman AU	C	C	C	C	C	NA	C	C	C	C	C	C	C	C
Siemens EXL	C	C	C	C	C	NA	C	C	NA	NA	NA	NA	NA	NA

ANSM B25	Glc	Creat	TC	TG	HDL	LDL	Uric Acid	Urea	Ca	Na	Cl	K	Fe	Alb
Siemens Vista	C	C	C	C	I	C	C	C	C	C	C	C	C	C
Roche Cobas	C	C	C	C	C	C	C	C	C	C	C	C	C	I
Beckman DxC	C	I	C	I	C	NA	NA	C	C	C	C	C	C	NA
Ortho CD Vitros	I	I	C	C	C	C	C	C	NC	I	I	I	NA	NA
Abbott Architect	C	C	C	C	C	NA	C	C	C	C	C	C	C	C
Siemens Advia	C	C	C	C	C	C	C	I	C	C	C	C	C	C
Beckman AU	C	C	C	C	C	NA	C	C	C	C	C	C	C	C
Siemens EXL	C	C	C	C	C	NA	C	C	NA	NA	NA	NA	NA	NA

ANSM materials found commutable for most methods and parameters

→ **Possibility to assess comparability between the different methods**

→ **Possibility to assess trueness of the different methods, bearing in mind that 2 samples are probably not enough to evaluate trueness, especially for HDLc and LDLc (trueness should be evaluated using panels of commutable samples)**

Commutability metabolites (glucose, creatinine, uric Acid & urea)

Glucose	CRM 1	CRM 2	CRM 3	CRM 4	CRM 5	CRM 6	CRM 7	CRM 8	EQA F1	EQA F2	EQA F3	EQA F4	EQA F5	EQA F6	EQA L1	EQA L2	EQA L3	EQA L4	EQA L5	EQA L6	EQA L7	EQA L8	EQA L9	EQA L10	EQA L11	EQA L12	EQA L13	EQA L14	EQA L15	EQA L16
Siemens Vista	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C	NC	C	NC	NC	I	I	I	NC	C	I	C	NC	C	C	C
Roche Cobas	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Beckman DxC	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	I	I	C	C	C	C	C	C	C	C	C
Ortho CD Vitros	I	I	C	I	NC	I	NC	NC	C	C	C	NC	NC	NC	C	NC	C	NC	NC	NC	NC	I	NC	NC	NC	NC	C	C	C	C
Abbott Architect	C	C	NC	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Siemens Advia	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	I	C	C	C	C	C	C	C	C	C
Beckman AU	C	C	C	C	C	C	C	C	NA	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Siemens EXL	C	C	C	C	C	C	C	C	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Creatinine	CRM 1	CRM 2	CRM 3	CRM 4	CRM 5	CRM 6	CRM 7	CRM 8	EQA F1	EQA F2	EQA F3	EQA F4	EQA F5	EQA F6	EQA L1	EQA L2	EQA L3	EQA L4	EQA L5	EQA L6	EQA L7	EQA L8	EQA L9	EQA L10	EQA L11	EQA L12	EQA L13	EQA L14	EQA L15	EQA L16
Siemens Vista	C	C	C	I	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	C	C	C	I	I
Roche Cobas	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	C	C	C	C	C
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Siemens EXL	C	C	C	C	C	C	C	C	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Uric acid	CRM 1	CRM 2	CRM 3	CRM 4	CRM 5	CRM 6	CRM 7	CRM 8	EQA F1	EQA F2	EQA F3	EQA F4	EQA F5	EQA F6	EQA L1	EQA L2	EQA L3	EQA L4	EQA L5	EQA L6	EQA L7	EQA L8	EQA L9	EQA L10	EQA L11	EQA L12	EQA L13	EQA L14	EQA L15	EQA L16
Siemens Vista	C	C	C	NC	I	C	NC	NC	C	NC	NC	NC	I	NC	C	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC
Roche Cobas	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	C	C	C	C	C
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Siemens Advia	C	C	I	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	C	C	C	C	C
Beckman AU	C	C	C	C	C	C	C	C	NA	C	C	NC	I	C	C	C	C	C	C	NA	I	C	C	C	C	C	C	C	C	C
Siemens EXL	C	C	C	NC	C	C	I	I	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Urea	CRM 1	CRM 2	CRM 3	CRM 4	CRM 5	CRM 6	CRM 7	CRM 8	EQA F1	EQA F2	EQA F3	EQA F4	EQA F5	EQA F6	EQA L1	EQA L2	EQA L3	EQA L4	EQA L5	EQA L6	EQA L7	EQA L8	EQA L9	EQA L10	EQA L11	EQA L12	EQA L13	EQA L14	EQA L15	EQA L16
Siemens Vista	I	C	C	C	I	C	C	I	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	C	C	C	C	C
Roche Cobas	C	C	C	C	I	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	C	C	C	C	C
Beckman DxC	C	C	C	C	I	C	C	C	C	C	C	I	I	I	I	NC	I	C	C	NC	C	C	NC	C	C	C	C	C	I	C
Ortho CD Vitros	I	C	C	I	C	I	I	I	C	NC	NC	C	NC	NC	NC	NC	NC	NC	NC	NA	C	C	NC	NC	NC	NC	NC	NC	NC	NC
Abbott Architect	C	C	I	C	C	C	C	C	C	NC	C	C	C	C	C	C	I	C	C	NC	C	C	C	C	C	C	C	C	C	C
Siemens Advia	C	I	C	I	C	I	I	I	C	C	C	C	C	C	C	C	C	C	I	NC	C	C	C	C	C	C	I	I	C	I
Beckman AU	C	C	C	C	I	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	C	C	C	C	C
Siemens EXL	C	C	C	C	C	C	C	C	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Commutability lipids (TC, TG, LDLc, HDLc)

Total Cholesterol	CRM 1	CRM 2	CRM 3	CRM 4	CRM 5	CRM 6	CRM 7	CRM 8	EQA F1	EQA F2	EQA F3	EQA F4	EQA F5	EQA F6	EQA L1	EQA L2	EQA L3	EQA L4	EQA L5	EQA L6	EQA L7	EQA L8	EQA L9	EQA L10	EQA L11	EQA L12	EQA L13	EQA L14	EQA L15	EQA L16
Siemens Vista	C	C	C	C	C	C	C	C	C	C	C	C	C	C	I	I	I	NC	C	NC	NC	I	C	NC	NC	NC	NC	C	NC	NC
Roche Cobas	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Beckman DxC	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	I	C	C	C	C	I	C	C	NC	NC	C	NC	C	NC	NC
Ortho CD Vitros	C	C	C	C	C	NC	I	C	C	NA	C	C	C	C	C	C	NC	NC	C	NA	I	C	I	NC	C	C	NC	C	C	C
Abbott Architect	C	C	NC	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Siemens Advia	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C
Beckman AU	C	C	C	C	C	C	C	C	NA	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	C	C	C	C	C
Siemens EXL	C	C	I	C	C	C	C	C	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Triglycerides	CRM 1	CRM 2	CRM 3	CRM 4	CRM 5	CRM 6	CRM 7	CRM 8	EQA F1	EQA F2	EQA F3	EQA F4	EQA F5	EQA F6	EQA L1	EQA L2	EQA L3	EQA L4	EQA L5	EQA L6	EQA L7	EQA L8	EQA L9	EQA L10	EQA L11	EQA L12	EQA L13	EQA L14	EQA L15	EQA L16
Siemens Vista	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Roche Cobas	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Beckman DxC	I	I	C	C	C	C	NC	I	C	C	C	C	NA	NA	NA	NA	NA	C	C	I	NC	NC	C	C	I	I	I	C	NC	NC
Ortho CD Vitros	C	C	C	C	I	C	C	C	NC	NC	C	NC	C	NC	I	C	NC	NC	C	NC	NC	C	NC	NC	C	C	NC	NC	NC	NC
Abbott Architect	C	C	NC	C	C	C	C	C	C	C	C	C	C	C	C	C	I	C	C	C	C	C	C	C	C	C	C	C	C	C
Siemens Advia	C	C	C	I	C	C	C	I	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Beckman AU	C	C	C	C	C	C	C	C	NA	C	C	C	C	C	I	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Siemens EXL	C	C	I	I	C	I	I	C	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

LDLc	CRM 1	CRM 2	CRM 3	CRM 4	CRM 5	CRM 6	CRM 7	CRM 8	EQA F1	EQA F2	EQA F3	EQA F4	EQA F5	EQA F6	EQA L1	EQA L2	EQA L3	EQA L4	EQA L5	EQA L6	EQA L7	EQA L8	EQA L9	EQA L10	EQA L11	EQA L12	EQA L13	EQA L14	EQA L15	EQA L16
Siemens Vista	C	C	C	C	C	C	C	C	C	C	C	C	I	C	NC	C	NC	NC	NC	C	C	C	C	C	I	C	C	I	C	C
Roche Cobas	C	C	C	C	C	C	C	C	I	C	I	I	NC	C	NC	NC	NC	NC	NC	C	I	I	I	I	I	I	C	I	C	C
Beckman DxC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Ortho CD Vitros	C	C	C	C	C	C	C	C	I	C	C	C	NC	C	NA	C	NC	NC	NC	NC	C	C	C	C	I	C	C	I	C	C
Abbott Architect	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Siemens Advia	C	C	C	C	C	C	C	C	C	C	C	C	I	C	NC	C	NC	NC	NC	NC	C	C	C	C	I	C	C	I	C	C
Beckman AU	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Siemens EXL	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

HDLc	CRM 1	CRM 2	CRM 3	CRM 4	CRM 5	CRM 6	CRM 7	CRM 8	EQA F1	EQA F2	EQA F3	EQA F4	EQA F5	EQA F6	EQA L1	EQA L2	EQA L3	EQA L4	EQA L5	EQA L6	EQA L7	EQA L8	EQA L9	EQA L10	EQA L11	EQA L12	EQA L13	EQA L14	EQA L15	EQA L16
Siemens Vista	C	I	NC	C	C	C	C	NC	C	NC	NC	NC	I	NC	C	I	NC	I	NC	NC	I	NC	NC	C	NC	C	NC	NC	NC	NC
Roche Cobas	C	C	C	C	C	C	C	C	NC	NC	NC	NC	NC	NC	C	NC	NC	NC	NC	NC	I	NC	NC	C	NC	C	NC	NC	NC	NC
Beckman DxC	C	C	NC	NC	C	C	C	I	I	NC	NC	NC	NC	NC	C	NC	NC	C	I	NC	NC	NC	NC	I	NC	C	NC	NC	NC	NC
Ortho CD Vitros	C	C	I	C	NC	C	NC	NC	NC	C	NC	NC	I	NC	C	I	NC	I	NC	NC	I	NC	NC	C	NC	C	NC	NC	NC	NC
Abbott Architect	C	C	C	NC	C	C	I	NC	I	NC	NC	NC	NC	NC	C	NC	NC	C	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC
Siemens Advia	C	C	C	I	C	C	NC	C	I	I	NC	NC	I	NC	NC	I	NC	NC	NC	NC	I	NC	NC	NC	NC	NC	NC	NC	NC	NC
Beckman AU	C	C	C	I	C	C	C	C	NA	I	NC	NC	I	NC	C	I	NC	C	I	NC	NC	NC	NC	C	NC	C	NC	NC	NC	NC
Siemens EXL	C	C	C	C	C	C	C	C	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Commutability electrolytes (Na, Cl, K, Ca)

Na	CRM 1	CRM 2	CRM 3	CRM 4	CRM 5	CRM 6	CRM 7	CRM 8	EQA F1	EQA F2	EQA F3	EQA F4	EQA F5	EQA F6	EQA L1	EQA L2	EQA L3	EQA L4	EQA L5	EQA L6	EQA L7	EQA L8	EQA L9	EQA L10	EQA L11	EQA L12	EQA L13	EQA L14	EQA L15	EQA L16
Siemens Vista	C	C	C	C	NC	C	NC	C	C	NC	C	C	I	C	C	C	C	C	I	NC	C	C	C	C	C	C	C	C	I	C
Roche Cobas	C	C	C	C	I	C	I	C	C	C	C	C	I	C	C	C	C	C	I	NC	C	C	C	C	C	C	C	C	C	C
Beckman DxC	I	C	C	C	I	C	I	C	C	C	C	C	C	C	C	C	C	C	I	NC	C	C	C	C	C	C	C	C	C	C
Ortho CD Vitros	C	I	NC	I	NC	C	NC	I	C	NC	C	I	C	NC	C	C	I	NC	I	NC	NC	I	NC	I	C	NC	I	I	I	I
Abbott Architect	C	C	C	C	I	C	C	C	C	C	C	I	C	C	C	C	C	C	I	NC	I	C	C	C	C	C	C	C	C	C
Siemens Advia	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	C	C	C	C	C
Beckman AU	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	C	C	C	C	C
Siemens EXL	NA	NA	C	C	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Cl	CRM 1	CRM 2	CRM 3	CRM 4	CRM 5	CRM 6	CRM 7	CRM 8	EQA F1	EQA F2	EQA F3	EQA F4	EQA F5	EQA F6	EQA L1	EQA L2	EQA L3	EQA L4	EQA L5	EQA L6	EQA L7	EQA L8	EQA L9	EQA L10	EQA L11	EQA L12	EQA L13	EQA L14	EQA L15	EQA L16
Siemens Vista	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	NC	C	C	C	C	C	C	C	C	C	C
Roche Cobas	C	C	C	C	C	C	C	C	C	C	I	C	C	C	C	C	C	C	C	NC	I	I	I	C	C	C	C	I	I	C
Beckman DxC	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	I	C	C	NC	C	C	C	C	C	C	C	C	C	C
Ortho CD Vitros	I	I	NC	NC	NC	NC	NC	I	C	C	C	NC	I	I	C	I	NC	NC	NC	NC	I	I	NC	NC	C	C	C	C	C	C
Abbott Architect	C	C	C	C	I	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	C	I	I	C	C
Siemens Advia	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	C	I	NC	NC	NC
Beckman AU	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	C	C	C	C	C
Siemens EXL	NA	NA	C	C	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

K	CRM 1	CRM 2	CRM 3	CRM 4	CRM 5	CRM 6	CRM 7	CRM 8	EQA F1	EQA F2	EQA F3	EQA F4	EQA F5	EQA F6	EQA L1	EQA L2	EQA L3	EQA L4	EQA L5	EQA L6	EQA L7	EQA L8	EQA L9	EQA L10	EQA L11	EQA L12	EQA L13	EQA L14	EQA L15	EQA L16
Siemens Vista	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	NC	C	C	C	C	C	C	C	C	C
Roche Cobas	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	C	C	C	C	C
Beckman DxC	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	C	C	NC	C	C	NC	NC	C	NC	C	C	C	C	C	C	C
Ortho CD Vitros	C	I	I	I	I	I	NC	I	C	C	C	NC	C	C	C	C	C	NC	C	NC	NC	NC	NC	NC	C	NC	NC	I	C	C
Abbott Architect	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	C	C	C	C	C	C	C	C
Siemens Advia	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	I	C	C	C	C	C	C	C	C	C
Beckman AU	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	I	C	C	C	C	C	C	C	C	C
Siemens EXL	NA	NA	C	C	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Ca	CRM 1	CRM 2	CRM 3	CRM 4	CRM 5	CRM 6	CRM 7	CRM 8	EQA F1	EQA F2	EQA F3	EQA F4	EQA F5	EQA F6	EQA L1	EQA L2	EQA L3	EQA L4	EQA L5	EQA L6	EQA L7	EQA L8	EQA L9	EQA L10	EQA L11	EQA L12	EQA L13	EQA L14	EQA L15	EQA L16
Siemens Vista	C	C	I	C	C	C	C	C	C	C	C	C	C	I	I	I	I	C	I	I	C	C	C	C	C	C	C	C	NC	I
Roche Cobas	C	C	C	C	C	I	C	C	C	I	C	C	C	C	I	I	C	C	I	I	C	C	C	C	C	C	I	I	I	C
Beckman DxC	I	C	NC	I	I	C	I	I	C	I	C	C	I	C	C	I	I	C	I	I	C	C	C	C	C	C	I	C	C	C
Ortho CD Vitros	C	NC	NC	NC	NC	NC	NC	NC	C	NC	NC	NC	I	I	NC	NC	NC	NC	NC	NC	C	NC	NC	NC	I	NC	NC	C	C	C
Abbott Architect	C	C	C	C	C	C	C	C	C	I	C	C	C	C	C	C	C	C	I	I	C	C	C	C	C	C	C	C	C	C
Siemens Advia	C	C	C	C	C	I	C	I	I	I	C	C	C	C	C	I	I	I	I	I	C	C	C	I	I	C	C	C	C	C
Beckman AU	C	C	C	C	C	C	C	C	C	C	C	I	C	C	C	C	C	I	NC	NC	C	I	C	C	C	C	C	I	C	C
Siemens EXL	NA	NA	C	C	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Commutability Serum Iron & Albumin

Fe	CRM 1	CRM 2	CRM 3	CRM 4	CRM 5	CRM 6	CRM 7	CRM 8	EQA F1	EQA F2	EQA F3	EQA F4	EQA F5	EQA F6	EQA L1	EQA L2	EQA L3	EQA L4	EQA L5	EQA L6	EQA L7	EQA L8	EQA L9	EQA L10	EQA L11	EQA L12	EQA L13	EQA L14	EQA L15	EQA L16
Siemens Vista	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	I	I	C	C	C	C	C	C	C	C
Roche Cobas	C	C	C	C	C	C	C	C	C	C	I	C	C	C	C	I	I	C	I	NC	I	I	C	C	I	C	C	C	C	I
Beckman DxC	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	I	I	C	C	C	C	C	C	C	C
Ortho CD Vitros	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	C	NC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Abbott Architect	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	NC	I	NC	C	C	C	I	NC	I	C	C
Siemens Advia	I	C	C	C	C	I	C	C	C	C	C	C	C	C	C	C	C	I	C	NC	I	I	C	C	C	C	C	C	C	C
Beckman AU	C	C	I	I	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	I	I	C	C	C	C	C	C	C	C
Siemens EXL	NA	NA	I	C	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Albumin	CRM 1	CRM 2	CRM 3	CRM 4	CRM 5	CRM 6	CRM 7	CRM 8	EQA F1	EQA F2	EQA F3	EQA F4	EQA F5	EQA F6	EQA L1	EQA L2	EQA L3	EQA L4	EQA L5	EQA L6	EQA L7	EQA L8	EQA L9	EQA L10	EQA L11	EQA L12	EQA L13	EQA L14	EQA L15	EQA L16
Siemens Vista	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	I	C	C	C	C	C	C	I	C	C	C	C	C
Roche Cobas	C	I	I	I	C	C	C	C	C	C	C	I	I	I	NC	C	C	I	I	I	C	C	C	I	I	C	C	C	I	C
Beckman DxC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	C	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Ortho CD Vitros	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Abbott Architect	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	I	I	I	C	C	C	I	NC	C	C	I	C	C
Siemens Advia	C	C	I	I	C	C	C	C	C	C	C	C	C	C	NC	C	C	NC	NC	NC	C	C	NC	NC	NC	C	C	C	C	C
Beckman AU	C	C	C	C	C	C	C	C	C	C	C	C	C	C	NC	C	C	I	C	NA	C	C	C	C	C	C	C	C	C	C
Siemens EXL	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Conclusions

- **Commutable calibrators** are needed to improve agreement between the different available methods
- **Commutable EQA materials** are needed to assess standardization effectiveness and monitor methods' trueness
- Commutability of frozen materials and especially those produced according to CLSI C37A guidelines is generally better that that of lyophilized materials, especially for HDLc
- HOWEVER, all frozen materials are not always commutable for all methods and for all parameters while some lyophilized materials behave very well!

Commutability can't be assumed a priori!

- Very few materials were found commutable for all analytes: some are more appropriate for given groups of parameters (electrolytes, lipids, metabolites)
- Very few materials were found commutable for all methods, which makes it difficult to rigorously estimate agreement between the different peer-groups
- Some methods seem to be more affected than others by matrix effects → commutable materials are needed to evaluate trueness of these methods

Perspectives

Predicting non-commutability

- **Preparation of pools** : number, properties and storage of single donations (inclusion of « atypical » single donations?)
- **Manufacturing process** : freezing / lyophilization, addition of preservatives and/or exogenous substances (spiking), …
- **Sample properties** : pH, turbidity, presence of interfering substences, concentration of some compounds (eg. TG, total protein?)

Upcoming / ongoing commutability studies organised by LNE

- **HbA1c** : commutability assessment of 31 CRMs & EQA materials (frozen & lyophilized haemolysates) against 24 clinical specimens (fresh whole blood)
- **Glucose meters** : commutability assessment of calibrators & EQA materials (stabilized whole blood) Vs clinical specimens (fresh CAPILLARY whole blood)
- **Tau :** commutability assessment of calibrators and EQA materials
- **Procalcitonin :** commutability assessment of calibrators and EQA materials

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- **Production of C37A CRMs :** Solomon Park Research Laboratories
- **Collection of the fresh clinical specimens :** Jacques Rostoker (BIO-VSM LAB), Anne Boutten & Tiphaine Robert (Hopital Bichat)
- **Measurements:** Jean-Marc Giannoli (Néolab), Jacques Rostoker (Bio-VSM LAB), Florian Scherrer (LBM de l'Avenue), JP Bouilloux & Marc Baynat (LX Bio), Jean-Louis Galinier, Thierry Belleau & Nadine Courtiols (Clinique Pasteur), Elisabeth Lasnier (Hopital Saint Antoine), Ivan Monneret (Laboratoire Unibio), Didier Tayac (CHU Toulouse), Vincent Sapin & Laurence Roszyk (CHU Clermont), Mouloud Hammad & Vanessa Decool (Laboratoire Biocentre), Benoit Vedie (HEGP), Patrick Gaillat (LBM Roanne), Laurence Duvillard (CHU Dijon)
- **Assignement of Reference Method Target Values** : Catherine Perrot, Gustavo Martos, Julie Cabillic, Carine Fallot (LNE), Hubert Vesper & Uliana Danilenko (CDC)
- **Statistical designs for commutability assessment :** IFCC WG on commutability

IFCC WG on commutability

IFCC International Federation of Clinical Chemistry and Laboratory Medicine

IFCC WG-C Chair : Greg Miller

- **TF1: Selecting patient specimens for inclusion in a commutability study;** Vincent Delatour (chair), Chris Burns, Angie Caliendo, Neil Greenberg.
- **TF2: Qualification of measurement procedures for inclusion in a commutability study**

  Ingrid Zegers & Heinz Schimmel (co-chairs), Mauro Panteghini.
- **TF3: Criteria to make a determination that a RM is commutable**

  Bob Rej (chair), Ferruccio Ceriotti, Cas Weykamp, Göran Nilsson.
- **TF4: Statistical designs to assess commutability**

  Göran Nilsson (chair), Jeff Budd, Ramon Durazo, Greg Miller

Commutability (WG-C)

Membership

Name	Position	Country
G. Miller	Chair	US
H. Althaus	Member	DE
J. Budd	Member	US
C. Burns	Member	UK
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C. Cobbaert	Member	NL
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IFCC WG on commutability : upcoming recommendations

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Complete List of Authors: W Greg Miller, Heinz G Schimmel, Robert Rej, Neil Greenberg, Ferruccio Ceriotti, Chris John Burns, Jeffrey R Budd, Cas Weykamp, Vincent DELATOUR, Göran Nilsson, Finlay MacKenzie, Mauro Panteghini, Thomas Keller, Johanna Eltz Camara, Ingrid Zegers, and Hubert W Vesper

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Keywords: Commutability; Standardization; Traceability

Thank you for your attention!

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