

Multicenter Evaluation of Cystatin C Measurement after Assay Standardization

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BACKGROUND: Since 2010, a certified reference material ERM-DA471/IFCC has been available for cystatin C (CysC). This study aimed to assess the sources of uncertainty in results for clinical samples measured using standardized assays.

METHODS: This evaluation was performed in 2015 and involved 7 clinical laboratories located in France and Belgium. CysC was measured in a panel of 4 serum pools using 8 automated assays and a candidate isotope dilution-mass spectrometry reference measurement procedure.

uncertainty because of possible problems associated with the implementation of traceability. Although some manufacturers have clearly improved their calibration protocols relative to ERM-DA471, most of them failed to meet the criteria for acceptable CysC measurements.

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Cystatin C (CysC)¹¹ is an additional biomarker for the estimation of renal function and also for prediction of

Contexte

- Traçabilité IDMS de la créatinine
- Matériel de référence ERM-DA471/IFCC disponible pour la CysC depuis 2010
- Les fabricants sont censés utiliser ce matériel pour standardiser leurs trousse.

Etat des lieux depuis la « standardisation »

ifferences in equation performance were found between both equations.

4. Discussion

In this study, we were able to demonstrate that the current calibrated cystatin C (cysC) assays provided by Siemens (PENIA) and Roche

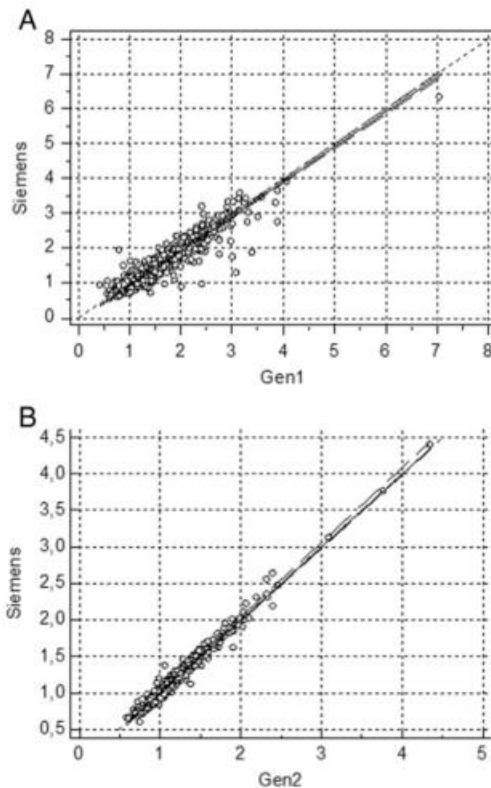
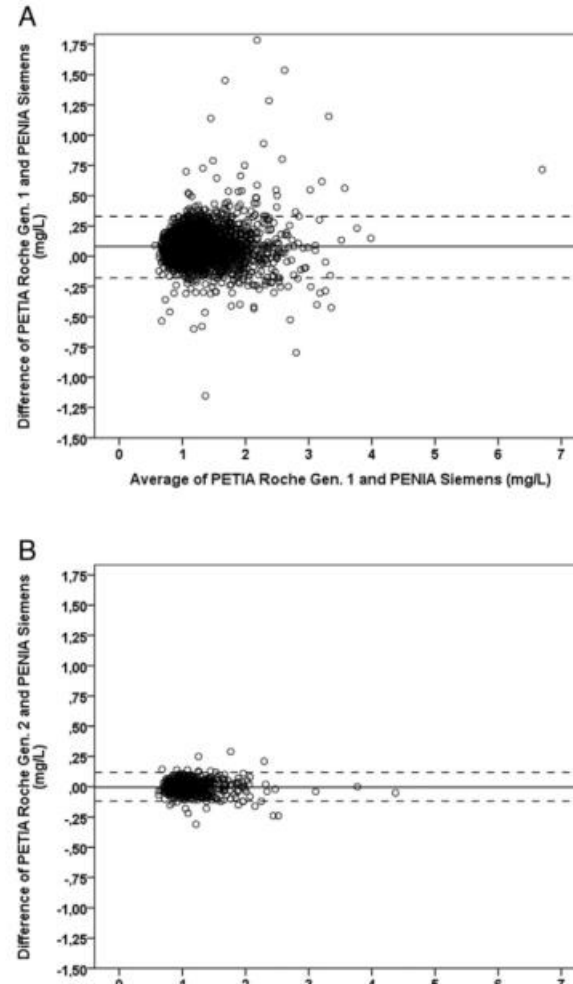
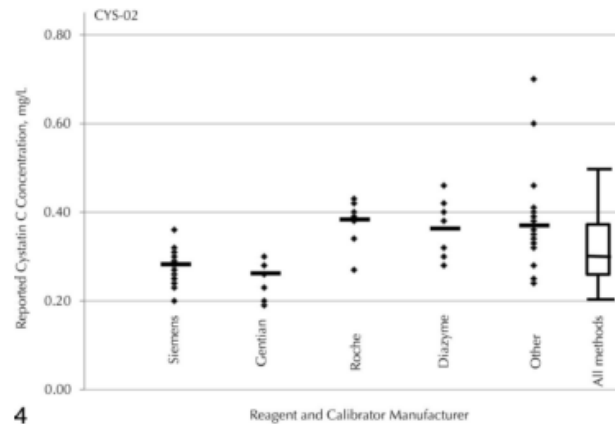
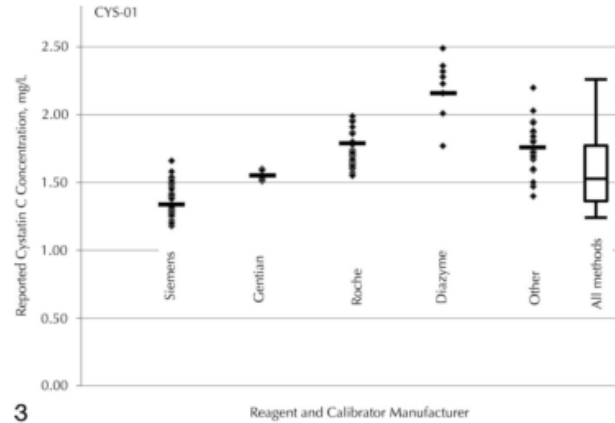


Fig. 1. A Passing Bablok correlation with details on slope, intercept, random difference and



CAP Survey Avril 2014



But de l'étude

- Evaluer la standardisation des trousse de CysC avec:
 - Une méthode IDMS de référence candidate récemment publiée (Gonzalez-Antuna, Proteomics 2015)
 - Plusieurs laboratoires
 - 4 pools sériques fraîchement préparés, dont la commutabilité a été vérifiée

Méthodes utilisées

Table 1. Main characteristics of the 8 automated CysC reagent-analyzer combinations.

Reagents/analyzer	Participating laboratories	Principle underlying the commercial assay	CE marking	Antibody to human CysC (source)	Calibrator references, names, and concentrations	Declared expanded uncertainty (k = 2)	Stated traceability
Abbott (Abbott Laboratories) Multigent Cystatin C/Architect cSystem	Lyon Lab 1/Tenon	PETIA ^a	Yes (Abbott)	Polyclonal antibodies (goat) absorbed on latex particles	Cystatin C calibrator Ref 1P93 - 10 Lot 50148Y600: 9.97 mg/L	2.9%	ERM-DA471/IFCC
DiaSys (DiaSys Diagnostic Systems) Cystatin C FS/ Abbott Architect cSystem	Lyon Lab 1/enon	PETIA	Reagent/calibrator are CE marked (DiaSys) Application proposal is for guidelines only (should be approved by the biologist)	Polyclonal antibodies (goat) bound to carboxylated polystyrene particles	TruCal Cystatin C Ref 1 7150 99 10 059 Lot 20054: 0.50 mg/L Lot 20055: 1.50 mg/L Lot 20056: 3.00 mg/L Lot 20057: 5.50 mg/L Lot 20058: 8.00 mg/L	4.6% 3.1% 3.3% 3.0% 3.3%	ERM-DA471/IFCC
DiaSys Cystatin C FS/Roche (Roche Diagnostics) Cobas c502	Avignon/Montpellier	PETIA	Reagent/calibrator are CE marked (Diasys) Application proposal is for guidelines only (should be approved by the biologist)	Polyclonal antibodies (goat) bound to carboxylated polystyrene particles	TruCal Cystatin C Ref 1 7150 99 10 059 Lot 20054: 0.50 mg/L Lot 20055: 1.50 mg/L Lot 20056: 3.00 mg/L Lot 20057: 5.50 mg/L Lot 20058: 8.00 mg/L	4.6% 3.1% 3.3% 3.0% 3.3%	ERM-DA471/IFCC
Gentian Cystatin C/Abbott Architect cSystem	Lyon Lab 1/Tenon	PETIA	Yes The entire measurement system is CE marked (Gentian)	Polyclonal antibodies (avian) attached to uniform polystyrene particles	Gentian Cystatin C Calibrator Ref 1012 Lot 1405402: 7.70 mg/L	3.0%	ERM-DA471/IFCC
Gentian Cystatin C/Roche Cobas c502	Avignon/Montpellier	PETIA	Yes The entire measurement system is CE marked (Gentian)	Polyclonal antibodies (avian) attached to uniform polystyrene particles	Gentian Cystatin C Calibrator Ref 1012 Lot 1405402: 7.70 mg/L	3.0%	ERM-DA471/IFCC
Roche Tina-Quant Cystatin C Gen.2/Cobas c502	Avignon/Montpellier	PETIA	Yes (Roche)	Polyclonal antibodies (rabbit) coated latex particles	C.f.a.s. Cystatin C Ref 04 975 901 191 Lot 61296701: 7.11 mg/L	0.2%	ERM-DA471/IFCC
Siemens (Siemens Healthcare Diagnostics) N Latex Cystatin C/BN ProSpec	Avignon/Lyon Lab 2	PENIA	Yes (Siemens)	Polyclonal antibodies (rabbit) coated latex particles	N Protein Standard UY Ref OQLV055 Lot 049865: 1.98 mg/L	5.0%	ERM-DA471/IFCC
Siemens Flex CYSC/Vista	Bichat/Sart-Tilman	PENIA	Yes (Siemens)	Polyclonal antibodies (rabbit) coated latex particles	PROT3 CAL Ref KC770C Lot 5GC081: 1.90 mg/L	2.7%	ERM-DA471/IFCC

^a PETIA, particle-enhanced turbidimetric immunoassay; PENIA, particle-enhanced nephelometric immunoassay.

Valeurs des pools déterminées @Oviedo

Pool	1	2	3	4
CysC (mg/L)	0.957±0.036	1.118±0.041	1.45±0.027	1.962±0.056

Critères d'acceptation basés sur la variabilité biologique de la CysC

	Minimum	Désirable	Optimum
Imprécision	<3.75%	<2.5%	<1.25%
Biais	<5.22%	<3.48%	<1.74%
Incertitude à 95% (U)	±7.5%	±5.0%	±2.5%

Résultats: imprécision

- Imprécision **totale** <3.75% pour tous SAUF:
 - DiaSys/Architect pour P1, 2 et 3
 - Roche/Cobas pour P1 et 3
 - Abbott/Architect pour P1
- Imprécision **intra-laboratoire**: tout <3.75%.
- Gentian/Architect meilleur que Gentian/Cobas
- Abbott/Architect: meilleurs CV: <1.25% pour tous les pools
- Imprécision inter-laboratoire de Abbott/Architect est deux fois plus élevée que la précision intra-laboratoire

Résultats: biais

- Biais optimal ($<1.74\%$) atteint:
 - Siemens/Prospect, DiaSys/Architect (P2, 3 et 4)
 - DiaSys/Cobas (P2)
 - Gentian Cobas (P1 et 2)
 - Siemens/Vista (P2 et 4)

Résultats: biais

- Biais > biais minimal (>5.2%)
 - Abbott/Architect sur les 4 pools (20.1; 19.7; 17.0; 16.3%)
 - Roche Cobas sur les 4 pools (8.3; 7.2; 5.9; 5.2%)
 - Gentian/Architect (5.2et 8.9% sur P3 et P4)

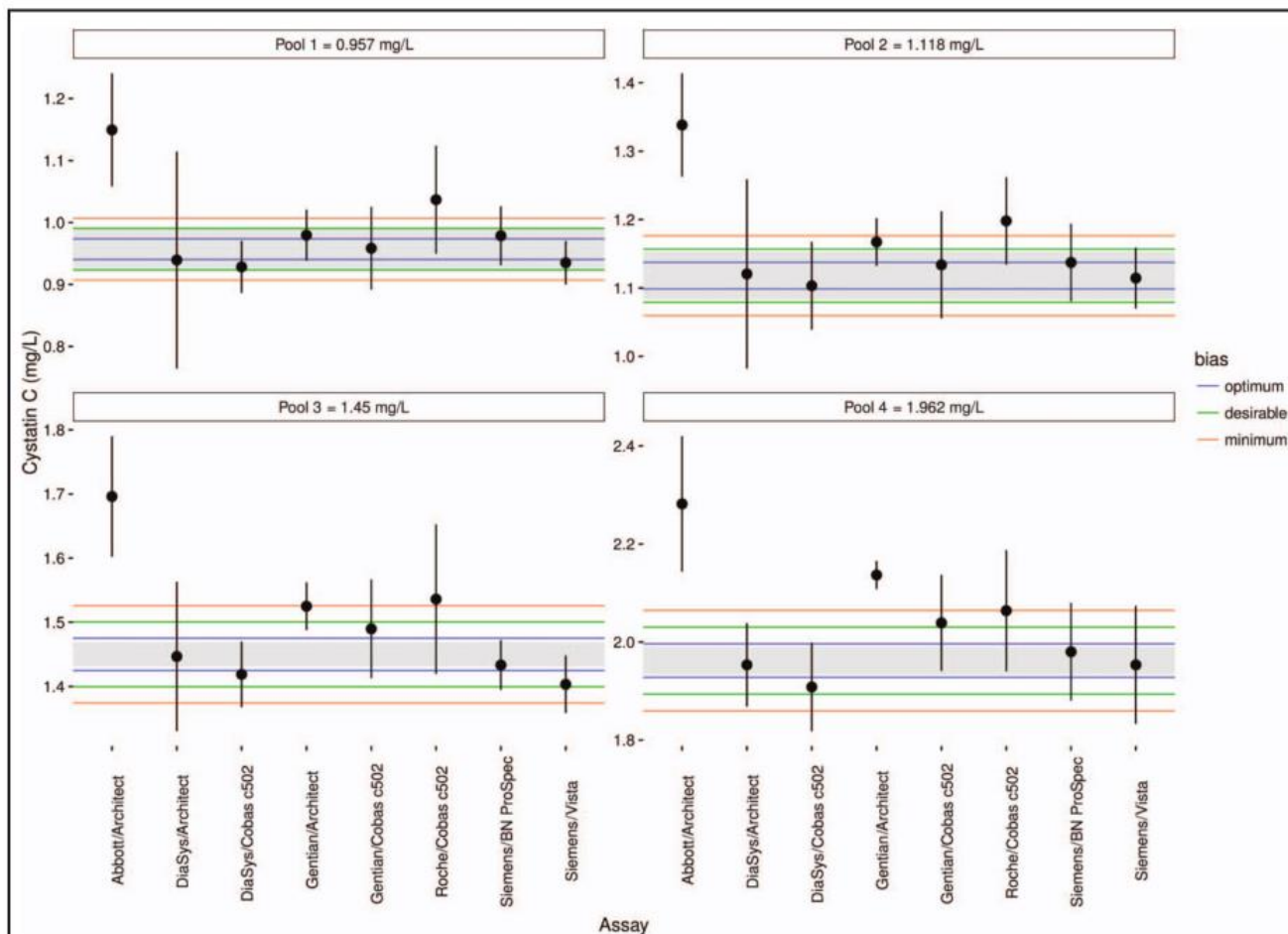
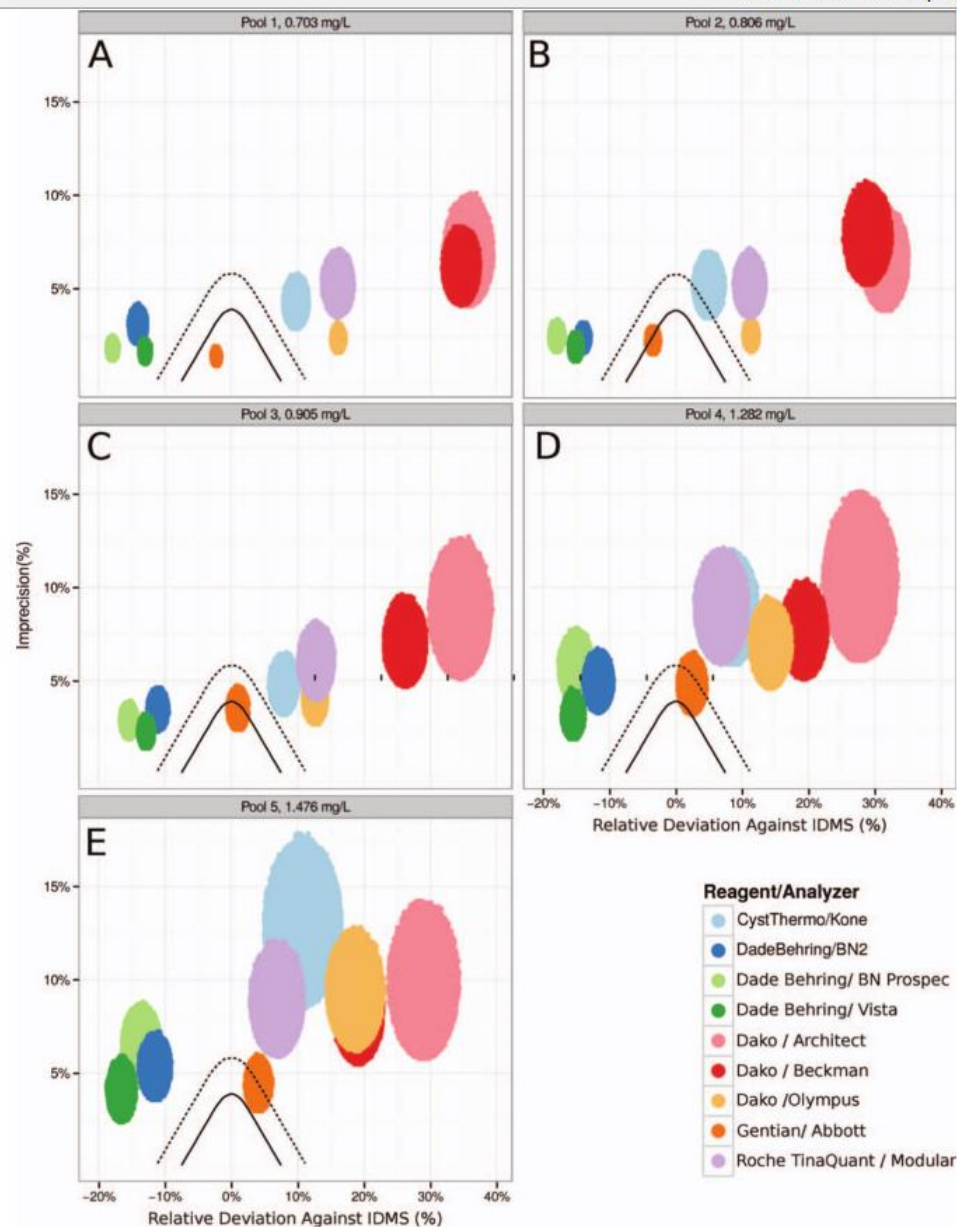


Fig. 1. Biases between the commercial assays and the IDMS target value for CysC.

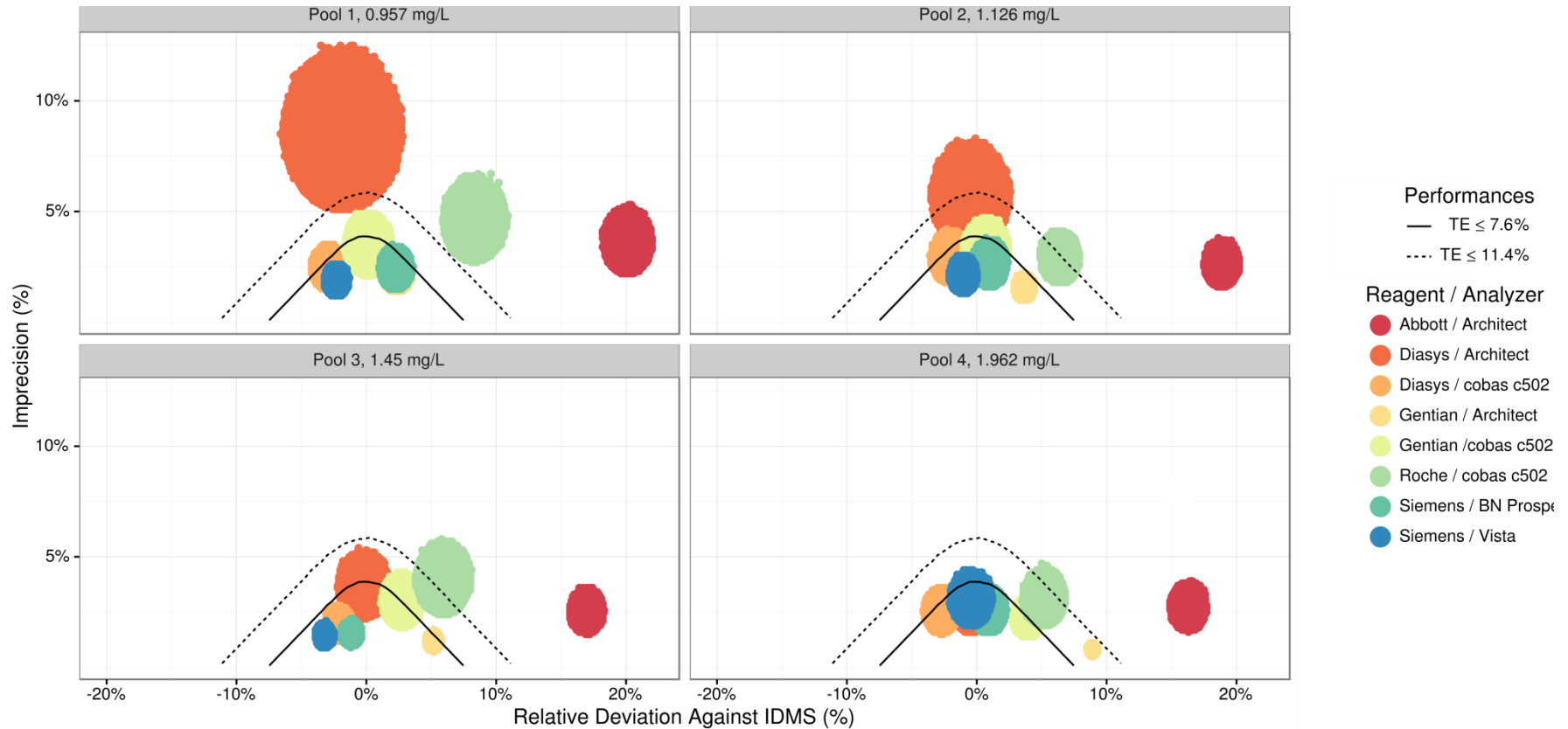
The figure shows the reference material values and the areas of their uncertainty (grey zone), the mean (SD) of the results from the evaluated systems, and lines depicting the bias specifications (red, green, and blue lines correspond to the optimal, desirable, and minimum quality levels, respectively).

Impact de la standardisation par
le standard ERM-DA471/IFCC



2008:
Standard International non
encore disponible.
Echantillons redosés en IDMS
par la suite -> biais

2016: dosages théoriquement standardisés



Conclusions

- Malgré la disponibilité d'un matériel de référence, la standardisation du dosage de la CysC reste encore à désirer, mais une amélioration nette est déjà observée
- Siemens a fortement réduit le biais par rapport à notre dernière évaluation et est la seule société à montrer des spécifications désirables
- Le couple anticorps/instrument a toute son importance