Metrological aspects and External Quality Assurance Programs

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Interlaboratory comparison

- Proficiency testing (PT)
- External quality control (EQC)
- External quality assessment (EQA)
- External quality assurance programs (EQAP)

EQA: where it started

A SURVEY OF THE ACCURACY OF CHEMICAL ANALYSES IN CLINICAL LABORATORIES*

WILLIAM P. BELK, M.D.,† AND F. WILLIAM SUNDERMAN, M.D.†

In 1946 the Committee on Laboratories of the Medical Society of the State of Pennsylvania proposed a survey‡ to check the accuracy of some of the more common chemical measurements made in hospital laboratories throughout the state. It undertook to do this by distributing solutions which had been carefully

TABLE 1

NUMBER OF DETERMINATIONS CLASSED AS SATISFACTORY, UNSATISFACTORY AND GROSS ERROR

September Analyses

SUBSTANCE TESTED	SATISFACTORY LIMITS OF RESULTS PER 100 ML.	NUMBER SATISFACTORY	NUMBER UNSATISFACTORY**	GROSS ERROR**
Hemoglobin	9.8 ± 0.3 gm.	17	34	11
Hemoglobin	15.1 ± 0.5 gm.	21	31	3
Glucose	60 ± 10 mg.	33	19	5
Glucose	375 ± 30 mg.	27	24	4
Sodium chloride	456 ± 50 mg.	30	14	2
Total protein	6.6 ± 0.4 gm.	18	29	7
Albumin	4.6 ± 0.3 gm.	9	35	7

October Analyses

Am J Clin Pathol 17: 853-861, 1947

Objectives of EQAP

- Laboratory performance evaluation for regulatory purpose (PT)
- Laboratory performance evaluation (EQA schemes)
- Method performance evaluation(EQAS/EQAP)
- Vigilance role (EQAP)
- Training & help, (EQAP)
- Contineous education (EQAP)

We focus today on:

- Promotion of interchangeability of laboratory results
- Follow-up of standardisation
- Improving laboratory service

Interchangeability of laboratory results

Why?

Patient comfort

Efficiency

Cost effectiviness

May 31st – June 1st, Mahón

The Europe of Health: Circulation of patients

Content:

Contact:

33

Harmonisation

TRACEABILITY

- “Property of the result of a measurement or the value of a standard, whereby it can be related to stated references, usually national or international standards through an unbroken chain of comparisons all having stated uncertainties”

VIM: 6.10, 1993

European parliament and council directive on in vitro diagnostic medical devices: 98/79/EC

Annex 1: Essential requirements

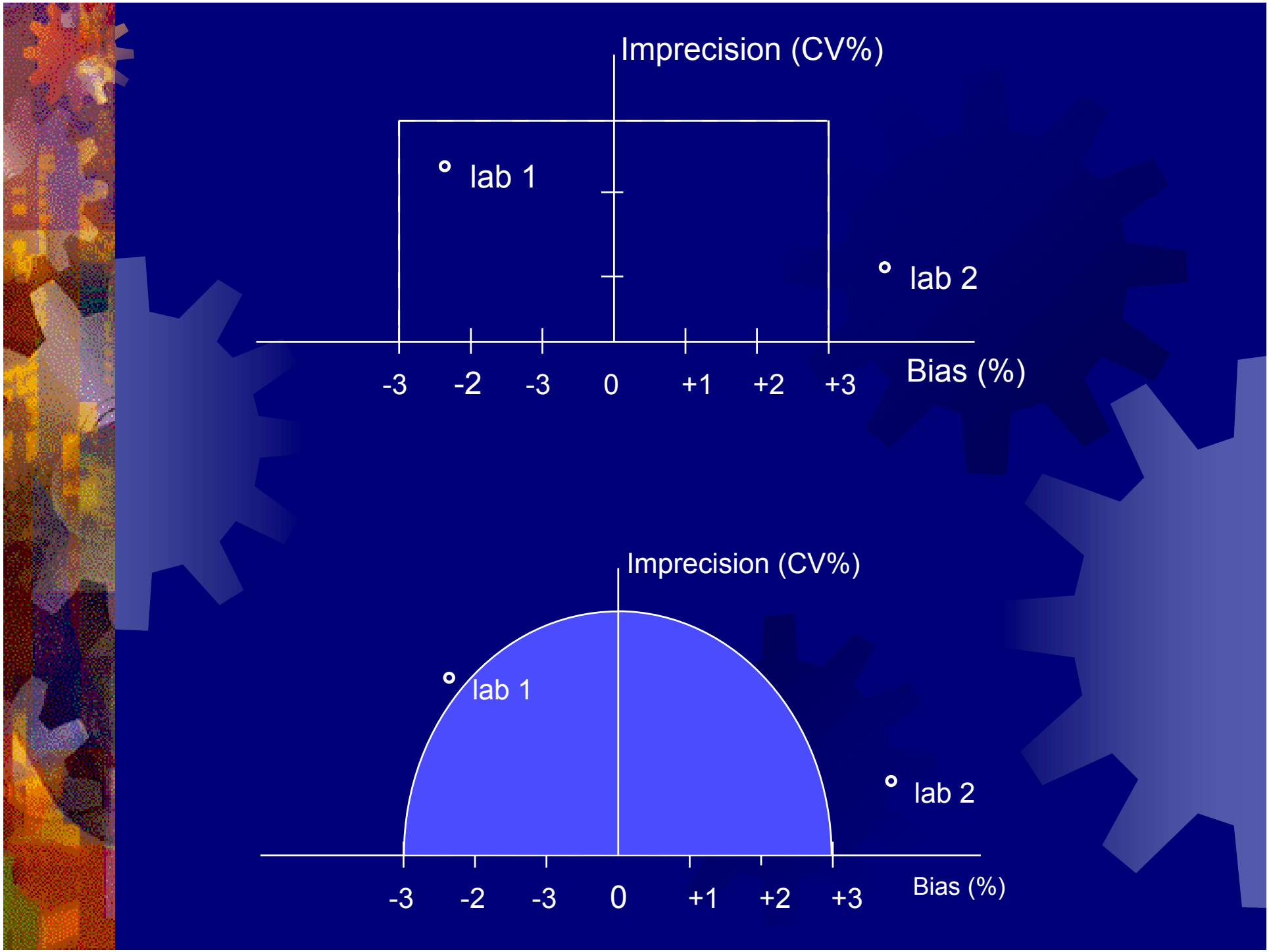
I. GENERAL REQUIREMENTS

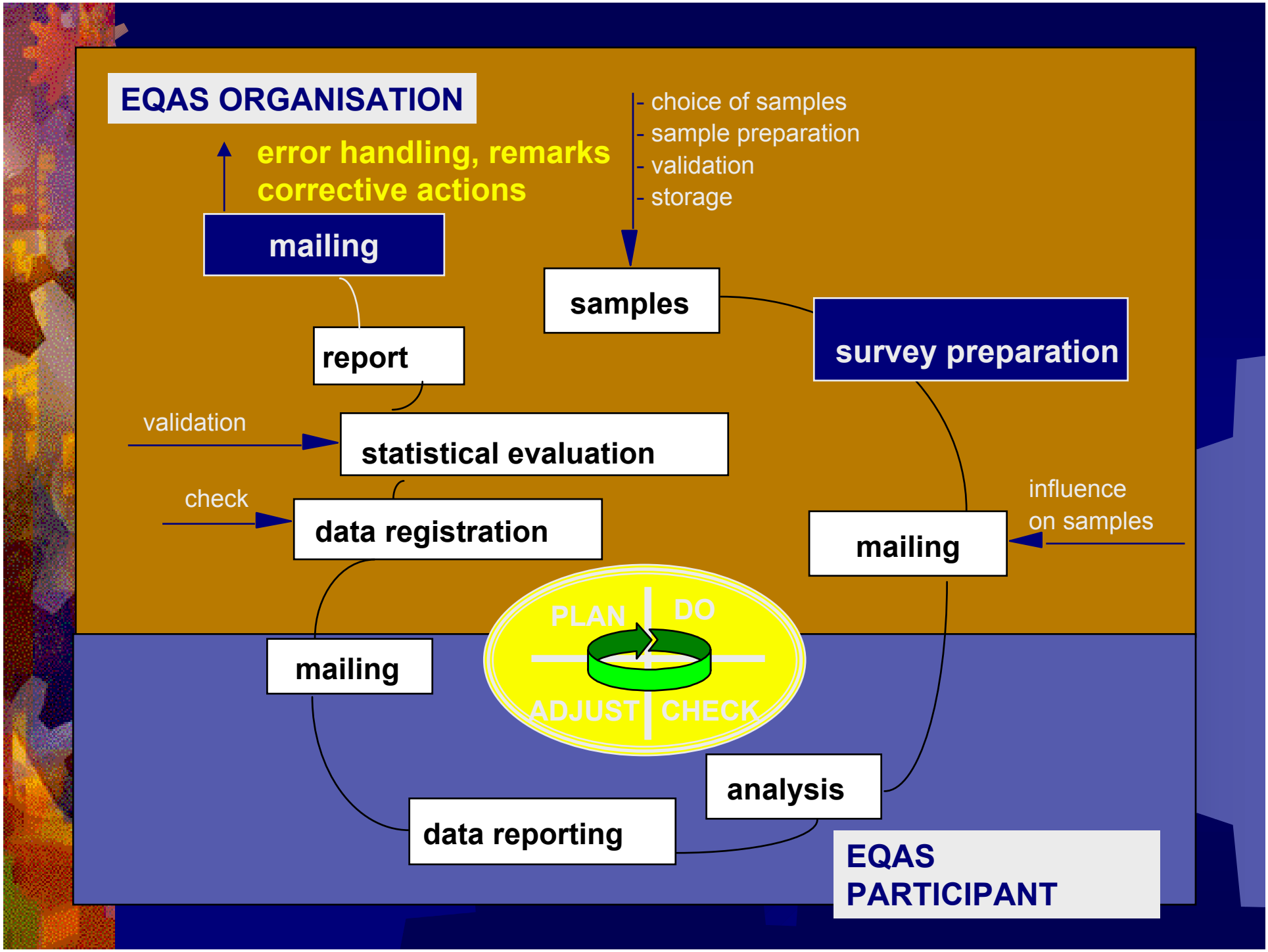
3. .....

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

Advantages of traceability

- Transferability of results between laboratories based on true values
- Possibility to use common reference intervals


Imprecision (CV%)
lab 1
lab 2
-3
-2
-3
0
+1
+2
+3
Bias (%)
Imprecision (CV%)
lab 1
lab 2
-3
-2
-3
0
+1
+2
+3
Bias (%)


EQAS ORGANISATION
error handling, remarks
corrective actions
- choice of samples
- sample preparation
- validation
- storage
mailing
samples
survey preparation
report
validation
statistical evaluation
check
data registration
influence
on samples
mailing
PLAN
DO
ADJUST
CHECK
mailing
analysis
data reporting
EQAS
PARTICIPANT

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Prerequisites

- Appropriate samples
  - Genuine material
  - Assured sample integrity
- Appropriate scheme design
- Target values with stated measurement uncertainty

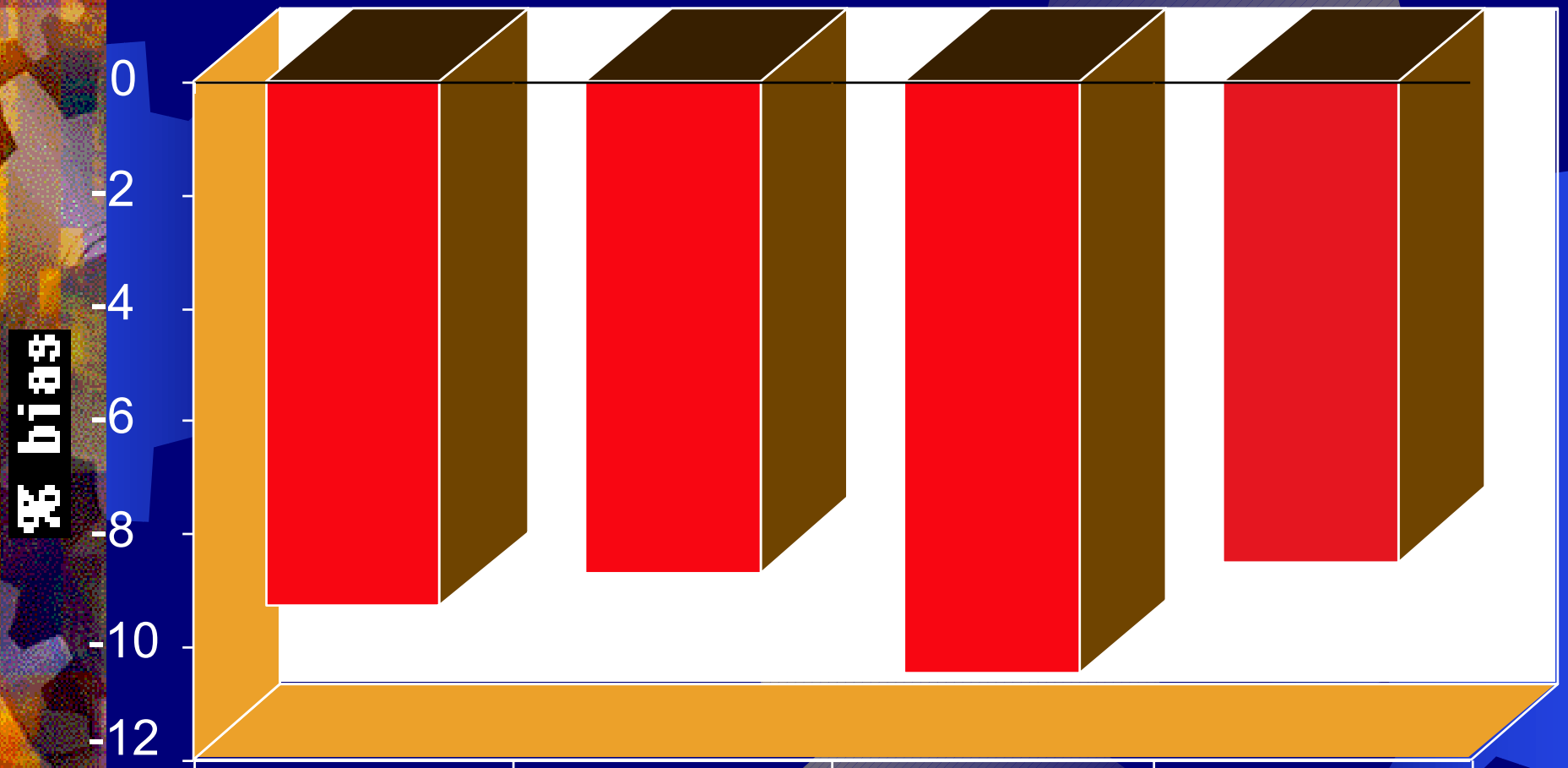
Appropriate sample material

- Fresh serum
- Frozen single donation serum
- Frozen human pool serum

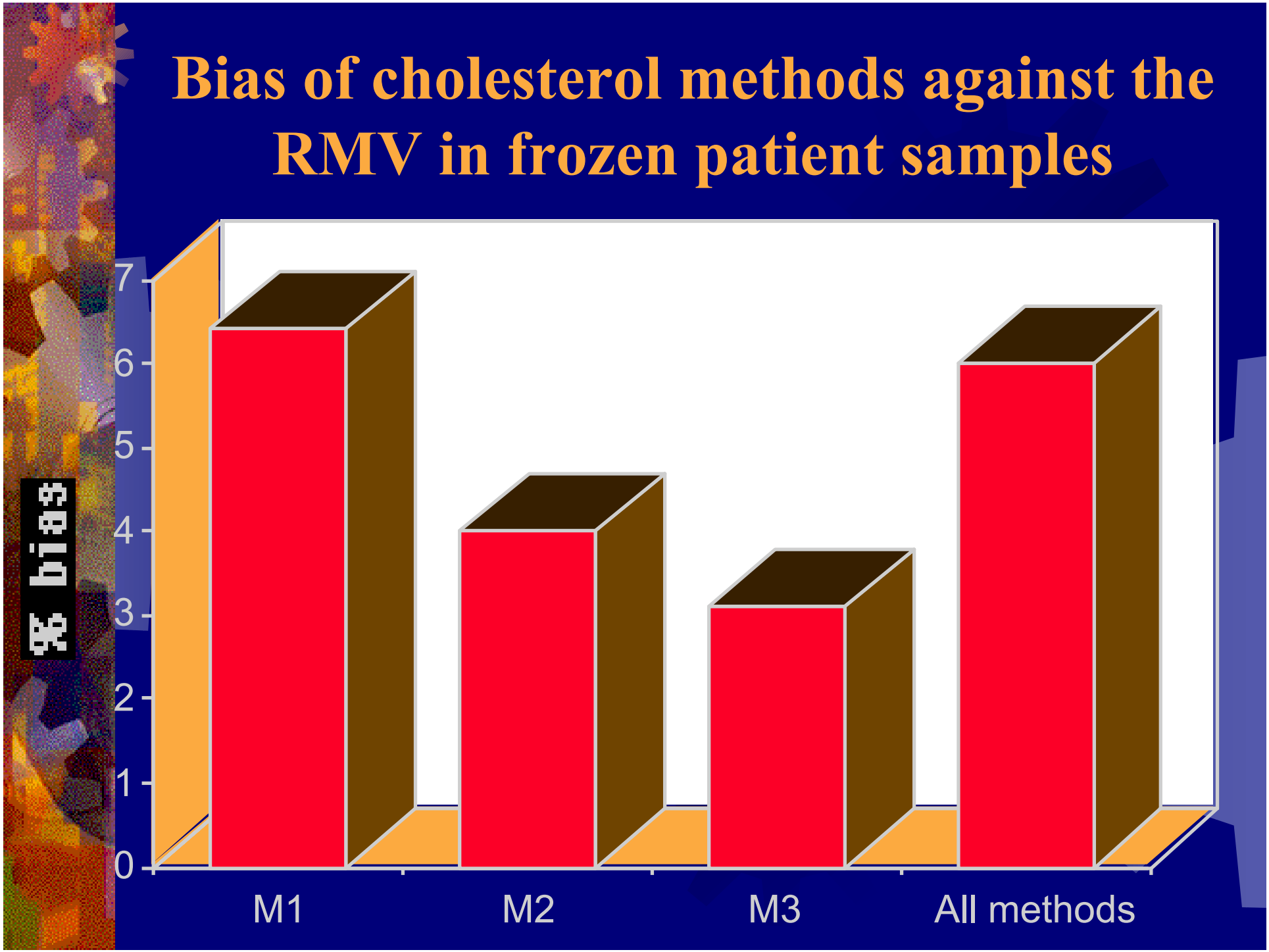
- More attention to sample integrity

Sample integrity during transport conditions

Bias of cholesterol methods against the RMV in lyophilised control samples



Bias of cholesterol methods against the RMV in frozen patient samples



Method performance evaluation

best method?

CREATININE (µmol/l)

- **Method 2: Jaffé methods**

  N = 206 M = 172.0 SD = 35 CV(%) = 20.4

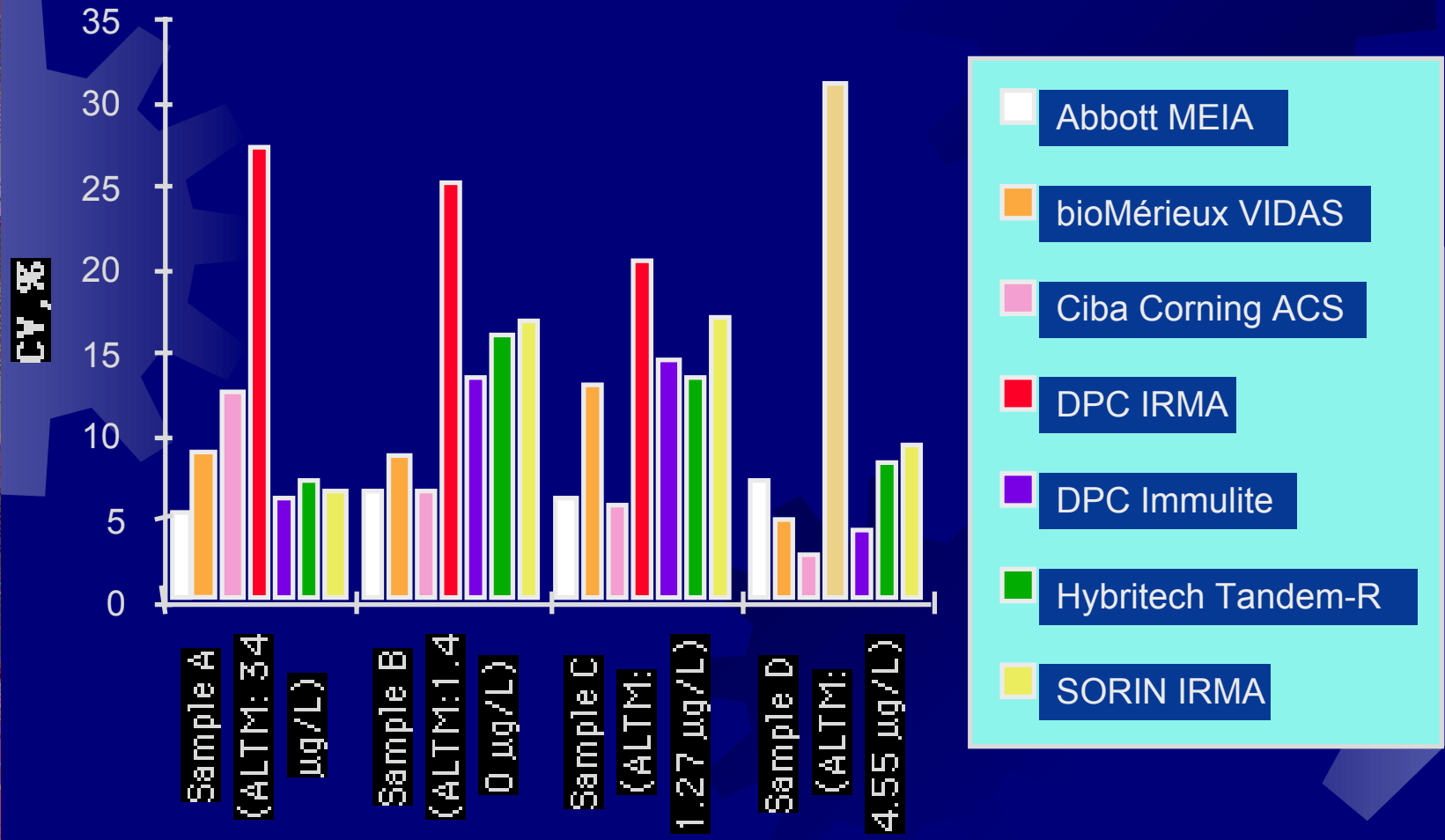
- **Method 7: Enzymatic method**

  N = 7 M = 54.9 SD = 51.7 CV(%) = 94

- **Method 9: Reflectance photometry**

  N = 54 M = 62.0 SD = 0.83 CV(%) = 1.3

Reproducibility of PSA testkits (results of BEQAS 1995)



PSA (F/T ratio)

- Patient samples:
  - Normal: 20%
  - Benign prostate hypertrophy: < 20%
- EQA control samples (spiked with semen fluid): 50 - 95%

Example of scheme design for bias

- Multiple determinations
- Homogeneous groups
  - Recommended calibrator
  - Protocol according to the recommendations of the manufacturer

Libeer J.C., Baadenhuijsen H., Fraser C.G., Hyltoft Petersen P., Ricos C., Stöckl D. Thienpont L. Characterization and classification of external quality assessment schemes (EQA) according to objectives such as evaluation of methods and participant bias and standard deviation. Eur. J. Clin. Chem. Clin. Biochem. 34: 665-678, 1996.

Reference measurement values

DRAFT INTERNATIONAL STANDARD ISO/DIS 15195

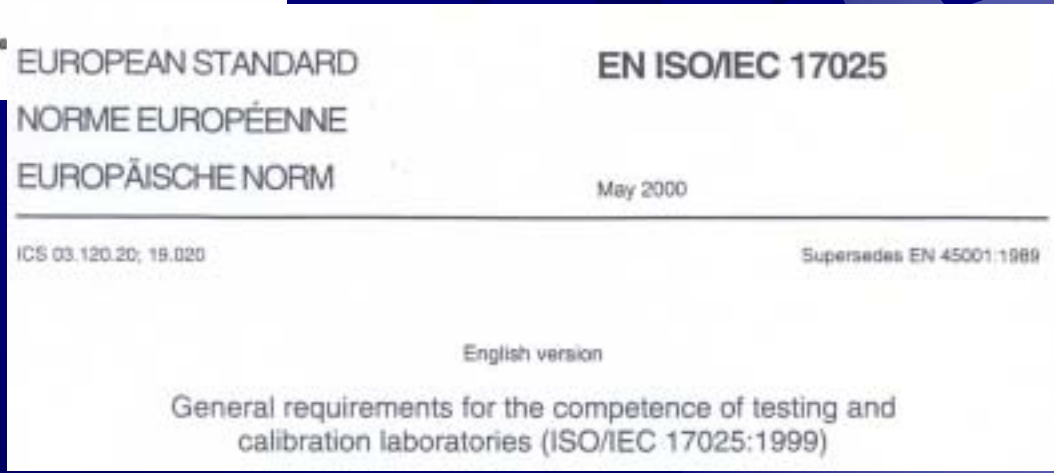
ISO/TC 212 Secretariat: ANSI

Voting begins on 2000-08-17 Voting terminates on 2000-01-17

INTERNATIONAL ORGANIZATION FOR STANDARDIZATION • МЕЖДУНАРОДНАЯ ОРГАНИЗАЦИЯ ПО СТАНДАРТИЗАЦИИ • ORGANISATION INTERNATIONALE DE NORMALISATION

Clinical laboratory medicine — Requirements for reference measurement laboratories

Laboratoires d'analyses de biologie médicale — Prescriptions pour les laboratoires mesurages de référence



EUROPEAN STANDARD
NORME EUROPÉENNE
EUROPÄISCHE NORM

EN ISO/IEC 17025

May 2000

ICS 03.120.20; 19.020

Supersedes EN 45001:1989

English version

General requirements for the competence of testing and calibration laboratories (ISO/IEC 17025:1999)

Richtlinien der Bundesärztekammer zur Qualitätsicherung quantitativer laboratoriums-medizinischer Untersuchungen
24 August 2001

Follow-up of standardisation efforts

- International
  - Specific proteins (calibration according to CRM 470)
  - HbA1c
  - NCCLS guidelines microbiology
- National
  - Common normal control plasma
- Measurement uncertainty

How to promote the use of CRM 470 for calibration?

- From survey 1996: letter to participants announcing that only acceptable results will be possible if specific proteins are calibrated against CRM 470.
- Advice to calibrate against CRM 470 even if the manufacturer still continue to give also the old calibration values
- Advice to change reference intervals

Clin Chem Lab Med 2001; 39(11):1129–1133 © 2001 by Walter de Gruyter · Berlin · New York

Commutability of Serum Protein Values: Persisting Bias among Manufacturers Using Values Assigned from the Certified Reference Material 470 (CRM 470) in the United States

Thomas B. Ledue[1] and A. Myron Johnson[2]

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[2]University of North Carolina School of Medicine, Chapel Hill, NC, USA

Clin Chem Lab Med 2001; 39(11):1123–1128 © 2001 by Walter de Gruyter · Berlin · New York

Effect of Certified Reference Material 470 (CRM 470) on National Quality Assurance Programs for Serum Proteins in Europe

A. Myron Johnson[1] and John T. Whicher[2]

[1] Departments of Pediatrics and Obstretics-Gynecology, University of North Carolina, Chapel Hill, NC, USA
[2] Rush House, Leeds, UK

ence material was expected to reduce variance and improve the commutability of results.

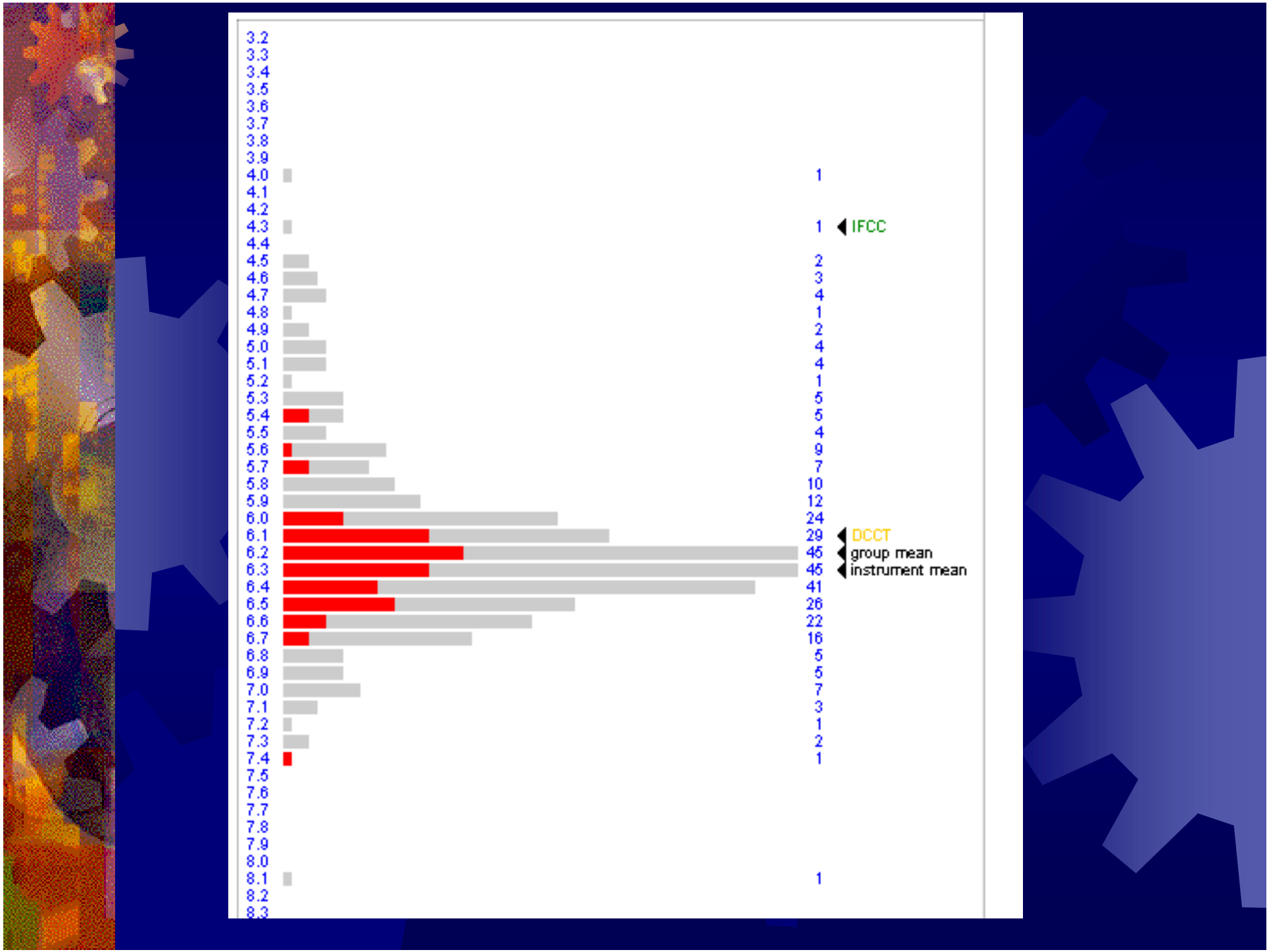
Several quality control schemes in Europe have already shown a significant improvement in among-laboratory variance (7–9). In addition, two publications

Standardization of HbA1c

- Step 1: DCCT harmonisation
- Step 2: IFCC: metrological traceability

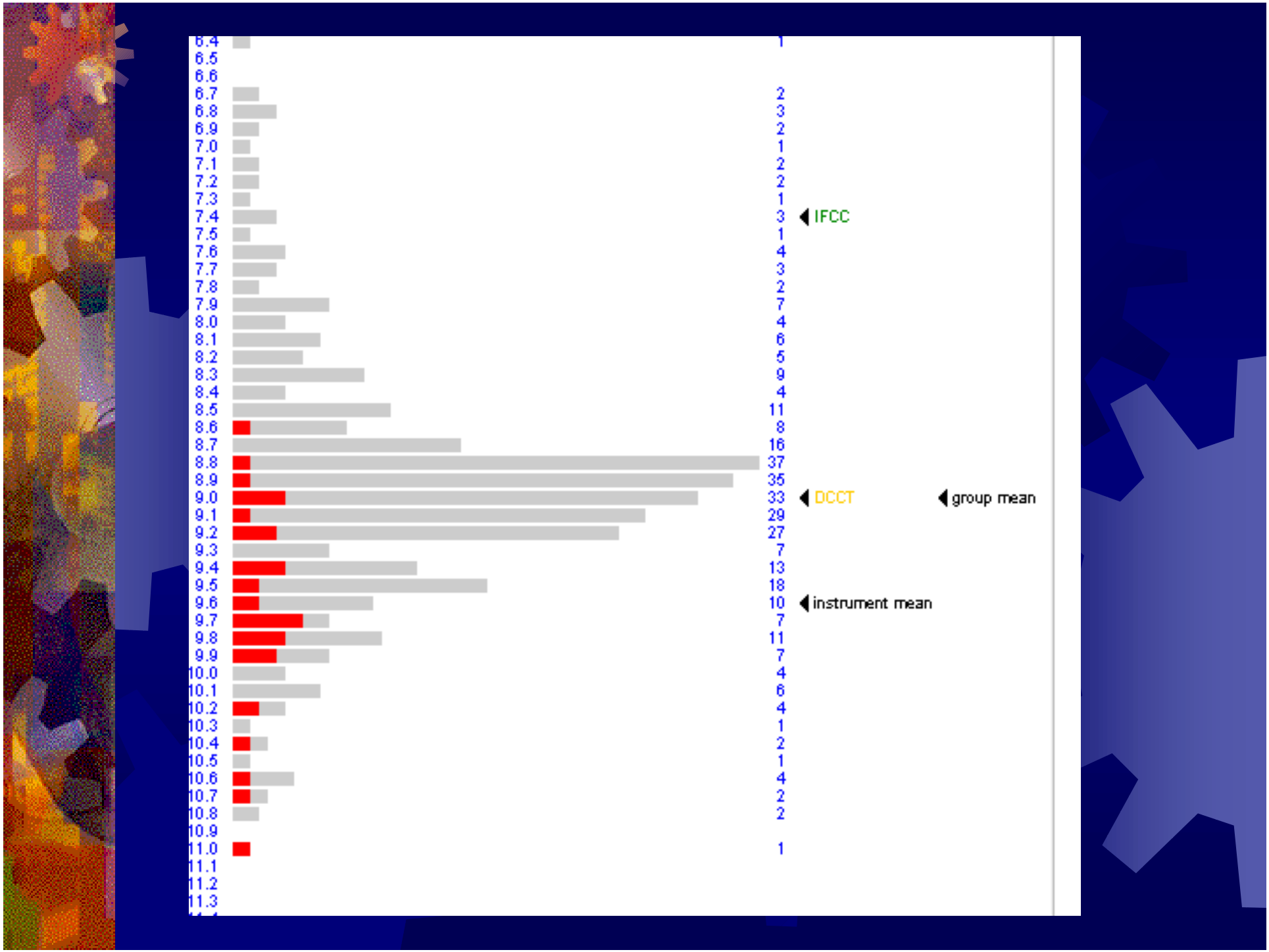
HbA1c: Menarini 8140

	selections for report	statistical results		
sample no.	EURO113		group	instrument(s)
deadline	4-4-2002	IFCC	4.3	4.3
unit	%	DCCT	6.1	6.1
group	all labs (gray bars)	your value	-	-
instrument(s)	Menarini 8140 (red bars)	mean	6.2	6.3
		n	348	77

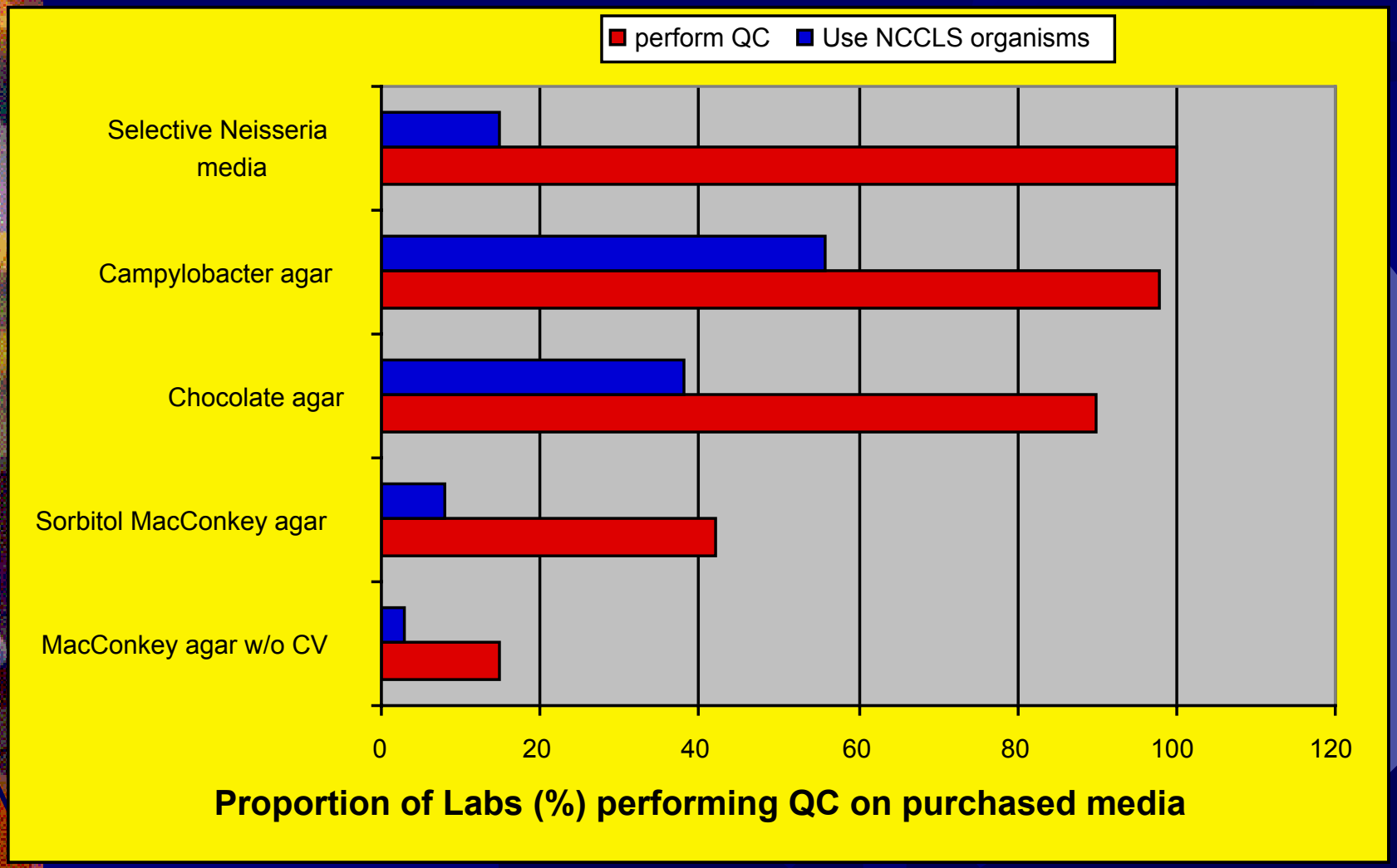

3.2
3.3
3.4
3.5
3.6
3.7
3.8
3.9
4.0 1
4.1
4.2
4.3 1 IFCC
4.4
4.5 2
4.6 3
4.7 4
4.8 1
4.9 2
5.0 4
5.1 4
5.2 1
5.3 5
5.4 5
5.5 4
5.6 9
5.7 7
5.8 10
5.9 12
6.0 24
6.1 29 DCCT
6.2 45 group mean
6.3 45 instrument mean
6.4 41
6.5 26
6.6 22
6.7 16
6.8 5
6.9 5
7.0 7
7.1 3
7.2 1
7.3 2
7.4 1
7.5
7.6
7.7
7.8
7.9
8.0
8.1 1
8.2
8.3

HbA1c: Tinaquant

	selections for report	statistical results		
sample no.	EURO109		group	instrument(s)
deadline	7-2-2002	IFCC	7.4	7.4
unit	%	DCCT	9.0	9.0
group	all labs (gray bars)	your value	-	-
instrument(s)	Tina Quant (Hitachi) (red bars)	mean	9.0	9.6
		n	359	37


6.4 1
6.5
6.6
6.7 2
6.8 3
6.9 2
7.0 1
7.1 2
7.2 2
7.3 1
7.4 3 IFCC
7.5 1
7.6 4
7.7 3
7.8 2
7.9 7
8.0 4
8.1 6
8.2 5
8.3 9
8.4 4
8.5 11
8.6 8
8.7 16
8.8 37
8.9 35
9.0 33 DCCT group mean
9.1 29
9.2 27
9.3 7
9.4 13
9.5 18
9.6 10 instrument mean
9.7 7
9.8 11
9.9 7
10.0 4
10.1 6
10.2 4
10.3 1
10.4 2
10.5 1
10.6 4
10.7 2
10.8 2
10.9
11.0 1
11.1
11.2
11.3

Promotion of standards



EUROPEAN COMMISSION
DIRECTORATE GENERAL JRC
JOINT RESEARCH CENTRE
IRMM
Institute for Reference Materials and Measurements

IRMM
Isotope Measurements

GE/R/IM/34/01
November 2001
Revised 2001-11-19

Evaluation of measurement uncertainty in clinical chemistry

Applications to determinations of total concentration of calcium and glucose in human serum

Case 3. **Uncertainty budget for c_{Gluc} with pre-analytical, analytical and patient-related contributions.**

Quantity	Value	Standard Uncertainty	Index
c_0	0.0 mmol/L		
A_s	0.152000 AU	$760 \cdot 10^{-6}$ AU	0.5 %
A_0	$-1.150 \cdot 10^{-3}$ AU	$127 \cdot 10^{-6}$ AU	0.0 %
A_{cal}	0.265650 AU	$889 \cdot 10^{-6}$ AU	0.2 %
c_{cal}	10.5000 mmol/L	0.0500 mmol/L	0.5 %
k_{intra}	1.0000	0.0650	86.4 %
k_{drift}	1.00000	$5.77 \cdot 10^{-3}$	0.7 %
k_{prc}	0.0 mmol/L	0.144 mmol/L	11.7 %
c_{gluc}	6.027 mmol/L	0.421 mmol/L	

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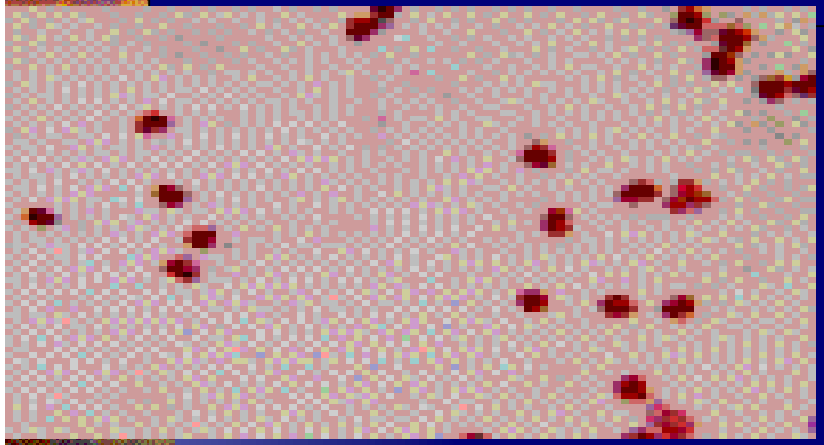
Clinical Relevancy Reporting



Smear from male urethra

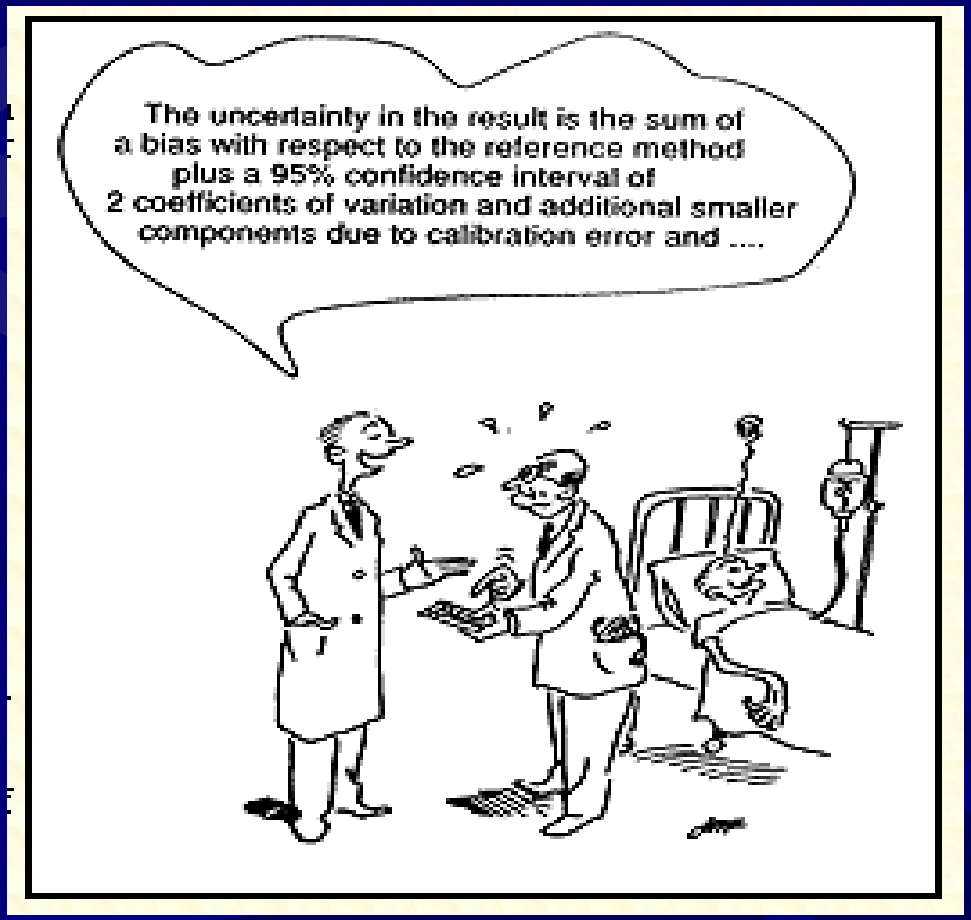
Gram: neutrophils and *H. influenzae*

Culture: *H. influenzae*

- Challenge Results

No *N. gonorrhoeae*	55%
No *N. gonorrhoeae*; *H. influenzae*	28%
H. influenzae	15%
Other	2%

From analytical result to useful information



Congratulations ma'am, according to your HCG concentration, you are a little pregnant