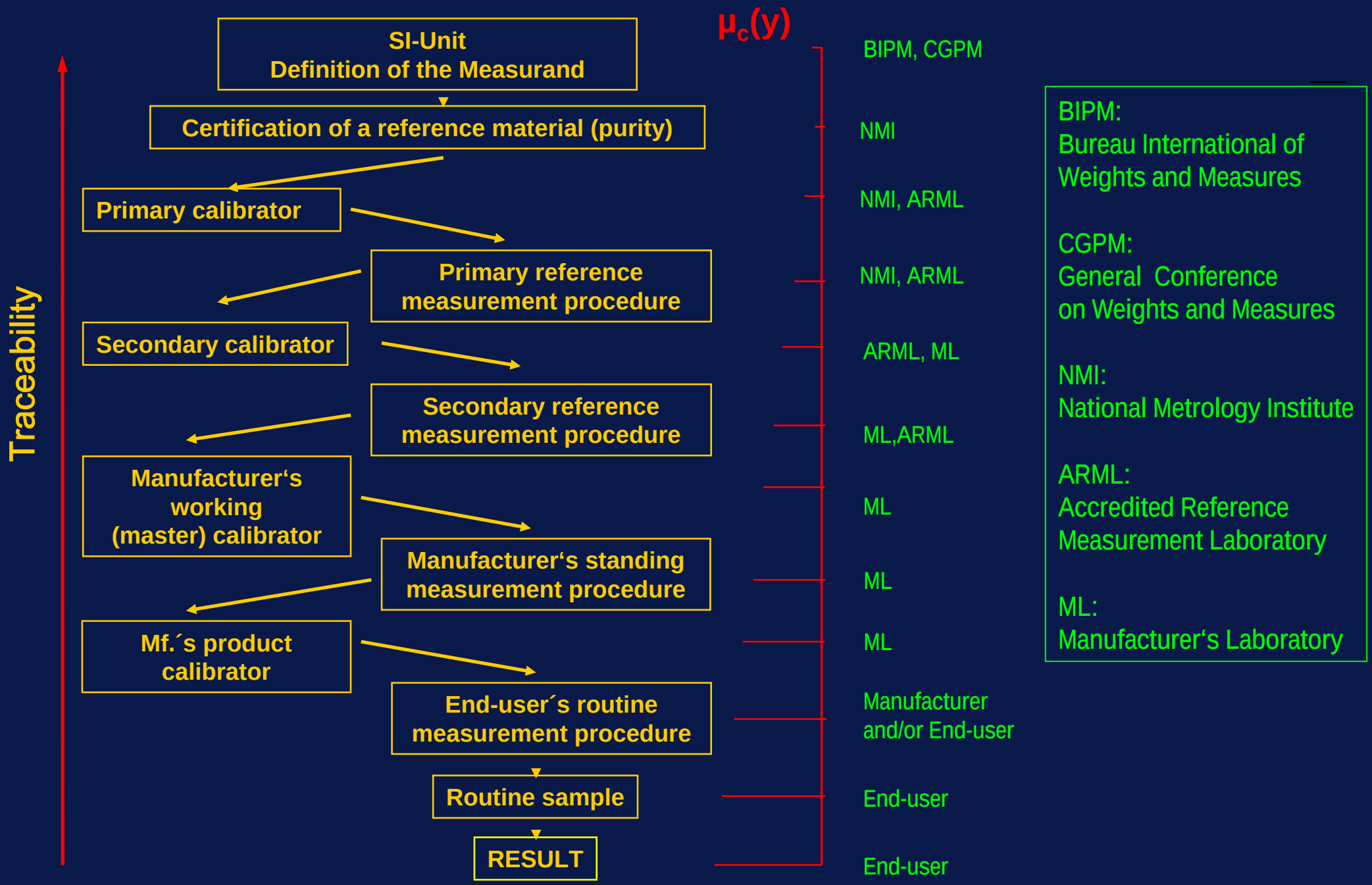
Identification of Reference Measurement Laboratories

JCTLM WG-2

Standards related to the Traceability Concept

- **ISO 17511: Metrological Traceability of Values Assigned to Calibrators and Control Materials**
- **ISO 18153: Metrological Traceability of Values for Catalytic Concentration of Enzymes Assigned to Calibrators and Control Materials**
- **ISO 15193: Presentation of Reference Measurement Procedures**
- **ISO 15194: Description of Reference Materials**
- **ISO 15195: Requirements for Reference Measurement Laboratories**


Traceability
SI-Unit
Definition of the Measurand
Certification of a reference material (purity)
Primary calibrator
Primary reference measurement procedure
Secondary calibrator
Secondary reference measurement procedure
Manufacturer‘s working (master) calibrator
Manufacturer‘s standing measurement procedure
Mf.´s product calibrator
End-user´s routine measurement procedure
Routine sample
RESULT
$\mu_c(y)$
BIPM, CGPM
NMI
NMI, ARML
NMI, ARML
ARML, ML
ML,ARML
ML
ML
ML
Manufacturer and/or End-user
End-user
End-user
BIPM:
Bureau International of Weights and Measures
CGPM:
General Conference on Weights and Measures
NMI:
National Metrology Institute
ARML:
Accredited Reference Measurement Laboratory
ML:
Manufacturer‘s Laboratory

Hierarchy of Laboratories

National Metrology Institutes

↓

Accredited Reference Laboratories
(universities, hospitals, manufacturers)

↓

Manufacturer‘s Standardisation Laboratories

↓

Routine Laboratories

ISO 15195: Requirements for Reference Measurement Laboratories

Management System Requirements

- Quality management system
- Personnel
- Documentation and records
- Contracting

Technical Requirements

- Premises and environmental conditions
- Handling of samples
- Equipment
- Reference materials
- Reference measurement procedures
- Metrological traceability – Uncertainty
- Quality assurance
- Reporting results

Identification of Reference Laboratories

Reference Measurement Laboratories will be identified

- according to the metrological level of the reference procedures applied; JCTLM listed RMPs (WG1),

- on the basis of accreditation according to ISO 17025 or ISO 15195 as calibration / reference laboratory; or CIPM-MRA peer reviewed,

- on the basis of their ability to demonstrate performance in regular inter-laboratory comparisons (ring trials) .

Reference Laboratories in Laboratory Medicine

Section 1:
Address & Identity

Reference Laboratory		Address								Status of Reference Laboratory
Organisation	Name of person responsible	Street	City	Post Co	State	Country	Phone	Fax	e-mail	indicate: Nat.Metrology Institute, EQAS Organizer, Manufacturer,
Korea Research Institute of Standards and Science	Sang-Ryoul Park	P.O.Box 102, Yuseong	Daejeon	305-600		S. Korea	82-42-868-5658	82-42-868-5042	srpark@kriss.re.kr	Nat. Metrology Institute
DGKC	Prof.Dr. L. Siekmann, Dr. Anja Kessler	Im Mühlenbach 52a	Bonn	53127	NRW	Germany	0049-228-2875911	0049-228-2875033	lothar.siekmann@ukb.uni-bonn.de	EQAS Organizer, University
LGC	John Marriott	Queens Road	Teddington	TW11 0LY	Middlesex	UK	+44 (0)20 8943 7509	+44 (0)20 8943 2767	john.marriott@lgc.co.uk	Designated Nat. Measurement Institute
Physikalisch-Technische Bundesanstalt (PTB)	Dr. Henrion	Bundesallee 100	Braunschweig	38116		Germany	+ 49 531 592-3210	+ 49 531 592-3015	andre.henrion@ptb.de	Nat. Metrology Institute
Centers for Disease Control and Prevention	Parvin P. Waymack	4770 Buford Hwy NE MS F25	Atlanta	30341	GA	USA	770-488-7976	770-488-4192	pwaymack@cdc.gov	Governmental Reference Laboratory
Diagnostica e Ricerca S. Raffaele - Laboratorio Standardizzazione	Ceriotti Ferruccio	Via Olgettina, 60	Milan	20132		Italy	+39-02-26432850	+39-02-26432640	ceriotti.ferruccio@hsr.it ferrero.carlo@hsr.it	CRMLN Member EQAS-Organizer
NIST	W. E. May	Mailstop 8390, 100 Bureau Drive	Gaithersburg	20899	MD	USA	(301)975-3108		willie.may@nist.gov	NMI

Reference Laboratories in Laboratory Medicine

Section 2:
Measurand and Procedure

Type	Measurand		Status	Reference Measurement Procedure				
of Measurand	Analyte	System (e.g.: Blood, Serum,	of Reference Procedure (a) primary (b) secondary	SI-traceable (Yes/No)	Principle of analytical procedure	Reference material(s) for calibration	Reference material(s) for trueness control	Literature Reference
M&S	Creatinine	Serum		Yes	HPLC-ID/MS	Locally proved NIST SRM - 914 a	NIST SRM 909 b	
M&S	creatinine	serum		Yes	HPLC	NIST SRM914a	L-Suitrol Ⅰ"Nissui〃 EXA Liquid 3- abnormal	
M&S	Creatinine	Serum		Yes	ID/MS	SRM 914a	SRM 909b	Anal. Chem., 58, 1681-1685 (1986)
M&S	Creatinine	Serum		Yes	ID-GC/MS	NIST SRM 914 a	NIST SRM 909 b, DGKC-Reference Sera	L. Siekmann, J. Clin. Chem. Clin. Biochem. 23 (1985) 137 - 44
M&S	Creatinine	Serum/Plasma/Urine		Yes	GC-IDMS	Creatine (Sigma) /Creatinine (NIST)	NIST-909b	

Reference Laboratories in Laboratory Medicine

Section 2:
Measurand and Procedure

Type	Measurand		Status	Reference Measurement Procedure				
of Measurand	Analyte	System (e.g.: Blood, Serum,	of Reference Procedure (a) primary (b) secondary	SI-traceable (Yes/No)	Principle of analytical procedure	Reference material(s) for calibration	Reference material(s) for trueness control	Literature Reference
M&S	Glucose	Serum		Yes	IDMS	SRM 917a		U. Hannestad and A. Lundbland. Clinical Chemistry 43:5 749-800 (1997)
M&S	Glucose	Serum		Yes	Ba(OH)2/ZnSO4 deproteinization and HK/G6PD Enzymatic	NIST SRM 917a	NIST SRM 965 (no more available)	Neese, J., Duncan, P., Bayse D., Robinson M., Development and
M&S	Glucose	Whole blood, Serum, Plasma		Yes	Glucose Oxidase Method	100 mg/dL, 200 mg/dL, 300 mg/dL	NIST SRM 965	NCCLS C30-A2 Ancillary (Bedside) Blood Glucose Testing in Acute
M&S	glucose	serum		yes	isotope dilution GC/MS	SRM 917b glucose	SRM 956 glucose in frozen human serum	Biomed Mass Spectrom 9, 395-405 (1982)
M&S	Glucose	Serum		Yes	HPLC-ID/MS, GC-ID/MS	Locally proved NIST SRM - 917 b	NIST SRM 965 b	
M&S	Glucose	Serum		Yes	ID/MS	SRM 917a	SRM 909b	Biomed. Mass Spectro., 9, 395-405, (1982)
M&S	Glucose	serum, plasma		Yes	ID-GC/MS	Calibrated with SRM 917b, high purity glucose	DGKC-sera	Clin Chem 39,1001-6 (1993) [=part II of Clin Chem 39,993-1000 (1993)]; Eur J

Reference Laboratories in Laboratory Medicine

Section 2:
Measurand and Procedure

Type	Measurand		Status	Reference Measurement Procedure				
of Measurand	Analyte	System (e.g.: Blood, Serum,	of Reference Procedure (a) primary (b) secondary	SI-traceable (Yes/No)	Principle of analytical procedure	Reference material(s) for calibration	Reference material(s) for trueness control	Literature Reference
M&S	Total cholesterol	Serum		Yes	IDMS			Clinical Chemistry 43:10 pp 1896-1903 (1997)
M&S	Total cholesterol	Serum, Plasma		Yes	Abell-Kendall	SRM 911b	CDC quality control serum	Abell,et al., JBC 1952
M&S	Total cholesterol	Serum		Yes	1. Spectrophotometric; 2. HPLC	NIST SRM 911b	CDC Reference Materials	1. Duncan IW, et al. Procedure for the Proposed Cholesterol Reference Method, Atlanta, GA: Centers for Disease Control; 1982. 2. Chen W, et al. Clin Chem
M&S	Total cholesterol	Serum		Yes	IDMS	CRM: GBW09203b		Anal Chem 61, 1718-1723 (1989)
M&S	Total cholesterol	Serum		Yes	Abel-Kendall (hidrolysis of cholesterol esters and extraction with	SRM 911b (NIST)	CDC reference materials	
M&S	Total Cholesterol	Serum		Yes	Abell Kendall	NIST SRM 911	CDC Reference Materials	Duncan IW, Mather A, Cooper GR, The Procedure for the proposed cholesterol reference method. Atlanta, GA 30333: Centers for Disease Control, 1982
M&S	Total cholesterol	serum		yes	isotope dilution GC/MS	SRM 911b cholesterol	SRM 1951a lipids in fresh-frozen human serum	

Reference Laboratories in Laboratory Medicine

Section 2:
Measurand and Procedure

Type	Measurand		Status	Reference Measurement Procedure				
of Measurand	Analyte	System (e.g.: Blood, Serum, Plasma,	of Reference Procedure (a) primary (b) secondary	SI-traceable (Yes/No)	Principle of analytical procedure	Reference material(s) for calibration	Reference material(s) for trueness control	Literature Reference
M&S	Urea	serum		yes	isotope dilution GC/MS	SRM 912a urea	SRM 909b human serum	Anal Chem 56, 713-719 (1984)
M&S	Urea	Serum		Yes	HPLC-ID/MS	Locally proved NIST SRM - 912 a	NIST SRM 909 b	
M&S	Urea	serum, plasma			enzymatic - colorimetric	SRM 912a	SRM 909b	Sampson EJ et al. J. Clin Chem 26/7, 816-826 (1980)
M&S	Urea	Serum		Yes	ID-GC/MS	NIST SRM 912 a	NIST SRM 909 b, DGKC-Reference Sera	A. Kessler, L. Siekmann, J. Clin. Chem. 45 (1999) 9 1523 - 9
M&S	Urea	Urine		Yes	ID-GC/MS	NIST SRM 912 a	NIST SRM 909 b, DGKC-Reference Sera	A. Kessler, L. Siekmann, J. Clin. Chem. 45 (1999) 9 1523 - 9
M&S	Urea	Serum/Plasma/ Urine		No*	GC-IDMS	Urea - NIST	NIST-909b	
M&S	Urea	serum		Yes	spectrophotometry	SRM912a		Clin Chem 26:816(1980)

Reference Laboratories in Laboratory Medicine

Section 2:
Measurand and Procedure

Type	Measurand		Status	Reference Measurement Procedure				
of Measurand	Analyte	System (e.g.: Blood, Serum, Plasma,	of Reference Procedure (a) primary (b) secondary	SI-traceable (Yes/No)	Principle of analytical procedure	Reference material(s) for calibration	Reference material(s) for trueness control	Literature Reference
M&S	Uric Acid	Serum		Yes	290 nm reading after TCA Precipitation and Uricase	NIST SRM 913	NIST 909	Duncan, P., Cochman, N., Cooper, T., at al: Development and evaluation of a candidate reference Method for uric acid in serum, 1979. U.S. Department of Health
M&S	uric acid	serum		yes	isotope dilution GC/MS	SRM 913a uric acid	SRM 909b human serum	Anal Chem 62, 2173-2177 (1990)
M&S	Uric acid	Serum		Yes	HPLC-ID/MS	Locally proved NIST SRM - 913 a	NIST SRM 909 b	
M&S	uric acid	serum		Yes	HPLC	NIST SRM913a	L-Suitrol I "Nissui 〃 EXA Liquid 3- abnormal	
M&S	Uric Acid	Serum		Yes	ID/MS	SRM 913	SRM 909b	Anal. Chem., 62, 2173-2177 (1990)
M&S	Uric acid	serum, plasma		Yes	ID-GC/MS	Calibrated with SRM 913a, high purity uric acid	SRM 909b & DGKC-sera	Clin Chem 39,1001-6 (1993) [=part II of Clin Chem 39,993-1000 (1993)]; Eur J Clin Chem
M&S	Uric acid	Serum		Yse	HPLC of JSCC reference method	NIST SRM913a		JSCC reference method
M&S	Uric Acid	Serum		Yes	ID-GC/MS	NIST SRM 913	NIST SRM 909 b, DGKC-Reference Sera	L. Siekmann, J. Clin. Chem. Clin. Biochem. 23 (1985) 129-35
M&S	Uric Acid	Urine		Yes	ID-GC/MS	NIST SRM 913	NIST SRM 909 b, DGKC-Reference Sera	L. Siekmann, J. Clin. Chem. Clin. Biochem. 23 (1985) 129-35
M&S	Uric Acid	Serum/Plasma/ Urine		Yes	GC-IDMS	Uric Acid - NIST	NIST-909b	
M&S	uric acid	serum		Yes	spectrophotometry	SRM 913a		Clin Chem 28:284-90(1982).

Reference Laboratories in Laboratory Medicine

Section 2:
Measurand and Procedure

Type	Measurand		Status	Reference Measurement Procedure				
of Measurand	Analyte	System (e.g.: Blood, Serum, Plasma, Urine)	of Reference Procedure (a) primary (b) secondary (c) intern.conventional (d) no	SI-traceable (Yes/No)	Principle of analytical procedure	Reference material(s) for calibration	Reference material(s) for trueness control	Literature Reference
Enzyme	ALT	Blood serum		Yes	Kinetic spectrophotometry		IRMM-454	Schumann G et al., Clin Chem Lab Med 2002; 40:718-24
Enzyme	ALT	Serum		Yes?*	L-Alanine+2-Oxoglutarate (ALT)-> Pyruvate+L-Glutamate		IRMM-IFCC 454	Schumann G et al., IFCC Primary Reference Procedures for the Measurement of Catalytic Activity Concentrations of Enzymes at 37°C Part 4. Reference Procedure for the Measurement of Catalytic
Enzyme	ALT	Serum		Yes	Spectrophotometry		IRMM/IFCC 454	IFCC Clin Chem Lab Med 2002; 40(4):718-724 IFFC Clin Chem Lab
Enzyme	ALT	Serum		(Yes)	IFCC-Methods Roche Hitachi	Roche csaf	Precinorm U, Precipath U	
Enzyme	ALT	Serum		katal per cubic metre	JSCC reference method	JC-ERM		
Enzyme	ALT	Serum		katal per cubic metre	JSCC reference method	JC-ERM		
Enzyme	ALT	Blood serum, Control material		Yes	IFCC-Ref.Procedure, Kinetic light absorption measurement	not applicable	Certfied reference material IRMM/IFCC-454, DGKC reference materials	Schumann G et al, Clin Chem Lab Med 2002; 40:718-724
Enzyme	ALT	Serum, Plasma			IFCC Reference Methods		IFCC/IRMM calibrators	

Reference Laboratories in Laboratory Medicine

Section 2:
Measurand and Procedure

Type	Measurand		Status	Reference Measurement Procedure				
of Measurand	Analyte	System (e.g.: Blood, Serum, Plasma, Urine)	of Reference Procedure (a) primary (b) secondary (c) intern.conventional (d) no	SI-traceable (Yes/No)	Principle of analytical procedure	Reference material(s) for calibration	Reference material(s) for trueness control	Literature Reference
Electrolyte	Na	Lyophilized Human Serum		Yes	ICP-AES,AAS	CRM:GBW06103a		
Electrolyte	Na	Serum		Yes	Flame Emission Reference Method	NIST SRM 919a	NIST 956a	A reference Method for the determination of Sodium in Serum - NBS Special Publication 260-60
Electrolyte	Na	serum		yes	Gravimetry or ICP/MS	SRM 919a sodium chloride	SRM 956a Electrolytes in Frozen Human Serum	J. Anal. At. Spectrom. 17, 1589-1594 (2002)
Electrolyte	Na	Serum, Plasma, Urine		yes	Flame atomic emission spectrometry	SRM 919a	SRM 909 b	NBS-Special Public. 260-60
Electrolyte	Na	Serum		Yes	Gravimetry	SRM 919a or JCSS Standard (NMIJ Primary Standard)	SRM 909b	NIST Spec. Pub. 260-60
Electrolyte	Na	serum, plasma		Yes	Ion chromatography	Calibrated with SRM 919a, high purity sodium chloride	SRM 909b & DGKC-sera	J Chromatogr A 706,443-50 (1995); Clin Biochem 29, 501-8 (1996); J Chromatogr A 789, 557-
Electrolyte	Na	Serum		Yes	Atomic absorption spectrometry	NIST SRM 919	NIST SRM 909	
Electrolyte	Na	serum, plasma			flame atomic emission spectrophotometer	SRM 919a	SRM 956a	Velapoldi RA, NBS special publication 260-60, (1978)
Electrolyte	Na	Serum		Yes	Atomic Emission Spectrometry	Sodium Chloride, 99.999% pure (Aldrich Cat. no. 20,443-9)	SRM 909b	Thienpont et al., Validation of Candidate Reference Methods Based on Ion
Electrolyte	Na	serum		Yes	flame atomic emission spectroscopy	SRM 919		NBS Special Publication 260-60. Clin Chem 27:1824-8(1981).
Electrolyte	Na	serum		yes	gravimetry, ionchromatography (IC)	NaCl CRM from BAM, NIST SRM 919	SRM 909b	J.R.Moody, T.W.Vetter, Journal of research of the NIST 101,155(1996)

Type	Measurand		Status	Reference Measurement Procedure				
of Measurand	Analyte	System (e.g.: Blood, Serum, Plasma, Urine)	of Reference Procedure (a) primary (b) secondary (c) intern.conventional (d) no	SI-traceable (Yes/No)	Principle of analytical procedure	Reference material(s) for calibration	Reference material(s) for trueness control	Literature Reference
Hormones	cortisol	serum		yes	isotope dilution LC/MS	SRM 921 cortisol		in press
Hormones	Cortisol	serum, plasma		Yes	ID-GC/MS	Calibrated with SRM 921, high purity cortisol	BCR CRM 192 & 193 & DGKC-sera	Anal Biochem 234, 204-9 (1996); Clin Chem 41, 1781-3 (1995); Eur J Clin Chem Clin Biochem 34, 853-60 (1996)
Hormones	Cortisol	Serum		Yes	ID-GC/MS or ID-HPLC/MS	NIST SRM 921	IRMM CRM 192, 193, DGKC-Reference Sera	L. Siekmann, H. Breuer, J. Clin. Chem. Clin. Biochem. 20 (1982) 883 - 92
Hormones	Cortisol	Serum		Yes	Gas Chromatography Mass Spectrometry	Cortisol, 98.7% pure (Sigma cat. no.	BCR-192, BCR-193	1 Siekmann L. Determination of Steroid hormones by the use of isotope dilution-mass spectrometry: a definitive
Hormones	Cortisol	Serum		Yes	HPLC-ID/MS	Locally proved NIST SRM - 921	NIST SRM 909 b	

Identification of Reference Laboratories

Reference Measurement Laboratories will be identified

- according to the metrological level of the reference procedures applied; JCTLM –listed → WG1,

- on the basis of accreditation according to ISO 17025 or ISO 15195 as reference/calibration laboratory; or CIPM-MRA peer reviewed,

- on the basis of their ability to demonstrate performance in regular inter-laboratory comparisons (ring trials) .

Reference Laboratories in Laboratory Medicine

Section 3:
Status of Accreditation

Status	Accreditation			Compliance
of Laboratory Accreditation (a) calibration (b) testing (c) no	based on ISO standard (e.g. 17025):	as calibration laboratory (Yes/No)	as testing laboratory (Yes/No)	with National/ International Standards please indicate:
	NMI Peer Review (Novem, 2002)			NMI itself
		Yes	Yes	
	17025			National
	ISO/IEC 17025	Yes	No	
	ISO-17025	Yes	No	According to RiliBÄK-2002
	ISO17025	No	Yes	
	ISO 17025 (self declaration)			
	ISO/IEC 17025	Yes	No	

ISO 15195: Requirements for Reference Measurement Laboratories

Management System Requirements

- Quality management system
- Personnel
- Documentation and records
- Contracting

Technical Requirements

- Premises and environmental conditions
- Handling of samples
- Equipment
- Reference materials
- Reference measurement procedures
- Metrological traceability – Uncertainty
- Quality assurance
- Reporting results

Reference Laboratories in Laboratory Medicine

Section 4:
Frequency of Measurements

Frequency of Measurements			Remarks
in 2000	in 2001	in 2002	
14	10	8	
3 analytical batches / year	3 analytical batches / year	3 analytical batches / year	CRMs certification - Assignment of Target Values to EQA materials, *(*) the measurement system is compliant with EN ISO 18153
> 8000	> 8000	> 8000	Frequency for each enzyme except LDH where frequency is > 2000 per year

Identification of Reference Laboratories

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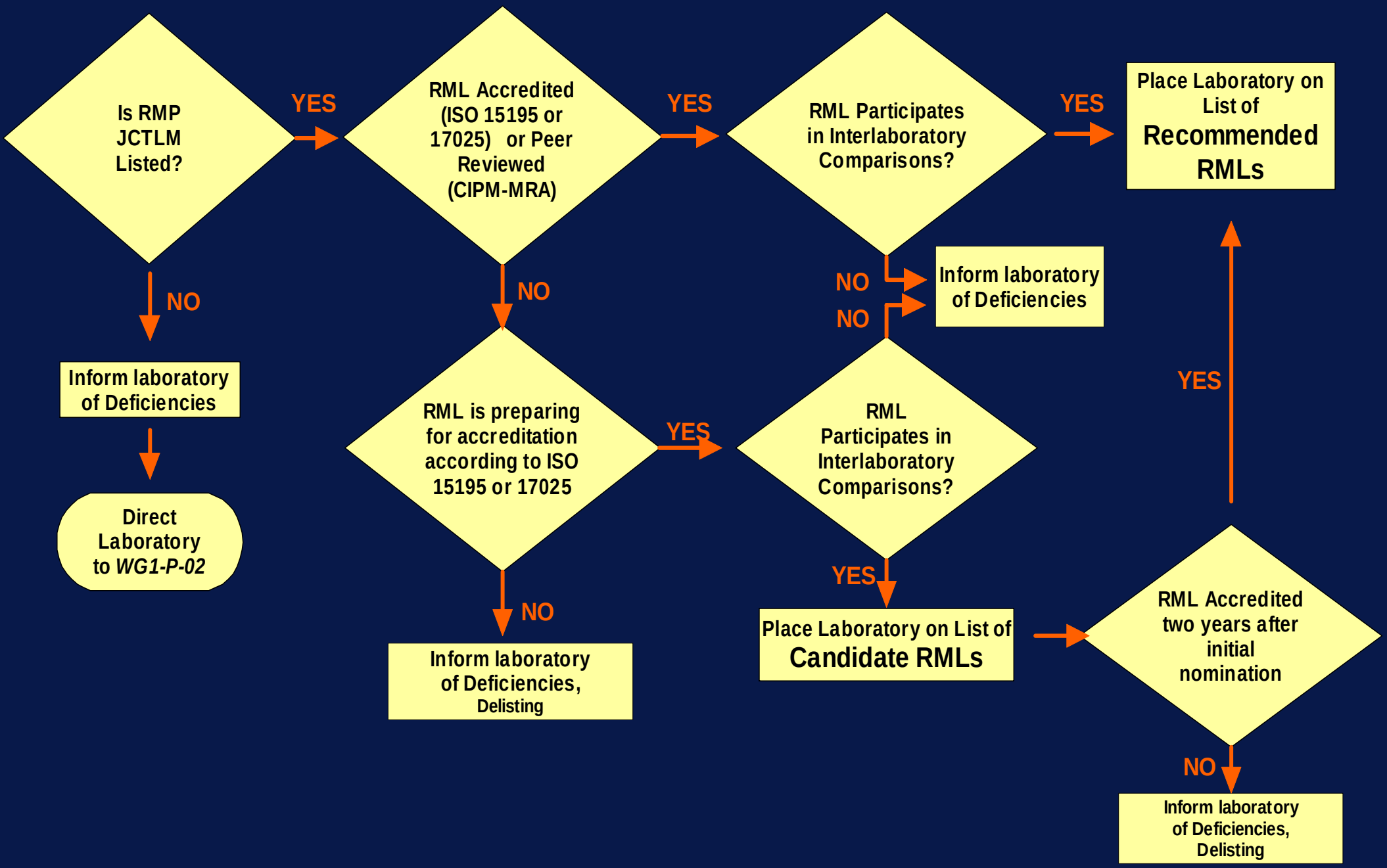
- on the basis of their ability to demonstrate performance in regular inter-laboratory comparisons (ring trials) .

Reference Laboratories in Laboratory Medicine

Section 5:
Network Membership - Ring Trials

Status	Network Membership		Ring Trials	
of Comparative Measurements e.g. in a network (a) regular (b) occasionally (c) no	Organisation	Name of Network	Participation in: Ring Trials, Certification Campaigns, Key Comparisons	Frequency of participation (months):
	CCQM	Organic W.G.	KC of CCQM Organic Working Group - KC12	
			Survey hosted by Japan Medical Association, Survey hosted by Japanese	Once a year Once a year Twice a year
	PTB	National Reference Network	National Reference Network, Key Comparison Pilot Study (BIPM)	18
			Certification of values for EQAS	4x per annum
	BIPM	CCQM	CCQM-P9, CCQM-K12	
	BIPM	CCQM	CCQM-P9, CCQM-K12 (IMEP 17)	18


Is RMP JCTLM Listed?
YES
NO
Inform laboratory of Deficiencies
Direct Laboratory to *WG1-P-02*
RML Accredited (ISO 15195 or 17025) or Peer Reviewed (CIPM-MRA)
YES
NO
RML is preparing for accreditation according to ISO 15195 or 17025
YES
NO
Inform laboratory of Deficiencies, Delisting
RML Participates in Interlaboratory Comparisons?
YES
NO
NO
Inform laboratory of Deficiencies
Place Laboratory on List of **Candidate RMLs**
RML Accredited two years after initial nomination
YES
NO
Inform laboratory of Deficiencies, Delisting
RML Participates in Interlaboratory Comparisons?
YES
Place Laboratory on List of **Recommended RMLs**