JCTLM
15/11/2005
Sevres, Paris

Laboratory Medicine Standardization Activity in Japan

National Institute Metrology of Japan (NMIJ)
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Japanese Committee of Clinical Laboratory Standards (JCCLS)

JCCLS

Since 1985

Government Agencies: 8

METI, MHLW, NMIJ/AIST, etc

Professional Societies: 32

JSCC (Japan Society of Clinical Chemistry)

JSLM (Japan Society of Laboratory Medicine)

Other Clinical Societies

Industries: 52

Organizations; JACRI*, JAIMA**

IVD Manufacturers

*JACRI: Japanese Association of Clinical Reagents Industry

**JAIMA: Japanese Analytical Instrument Manufacturers Association

Activities in JCCLS

1. Recommendation of Measurement Methods
2. Development of Matrix Reference Materials
3. External Quality Assessment

Activities in JCCLS

1. Recommendation of Measurement Methods

(by Japan Society of Clinical Chemistry)

- Ion Selective Electrode Measurement methods for Electrolytes; Na, K, Cl
- Measurement Methods for Enzymes;
  AST, ALT, CK, LD, γ -GT, ALP, AMY, ChE
- Enzymatic Measurement Methods;
  Glucose, Creatinine, Uric Acid, Total Cholesterol
  Triglycerides (Total Glycerides measurement)
- Measurement Method for Hemoglobin A1c
- Tonometry-based Measurement Methods for Blood Gases; pH, *p*CO2, *p*O2

Activities in JCCLS

2. Development of Multi-Analytes Reference Materials for Catalytic Concentration of Enzymes in Serum

(Japan Society of Clinical Chemistry)

All analytes are in one bottle

- AST (holo type in cytosol)
- ALT (holo type in cytosol)
- ***CK***
- ***LD***
- ***γ-GT***
- ***ALP***
- AMY

(Freeze dried)

They are produced from *recombinants* of human enzymes, except LD.

(Underlined Items have been already listed in α-lists.)

Activities in JCCLS

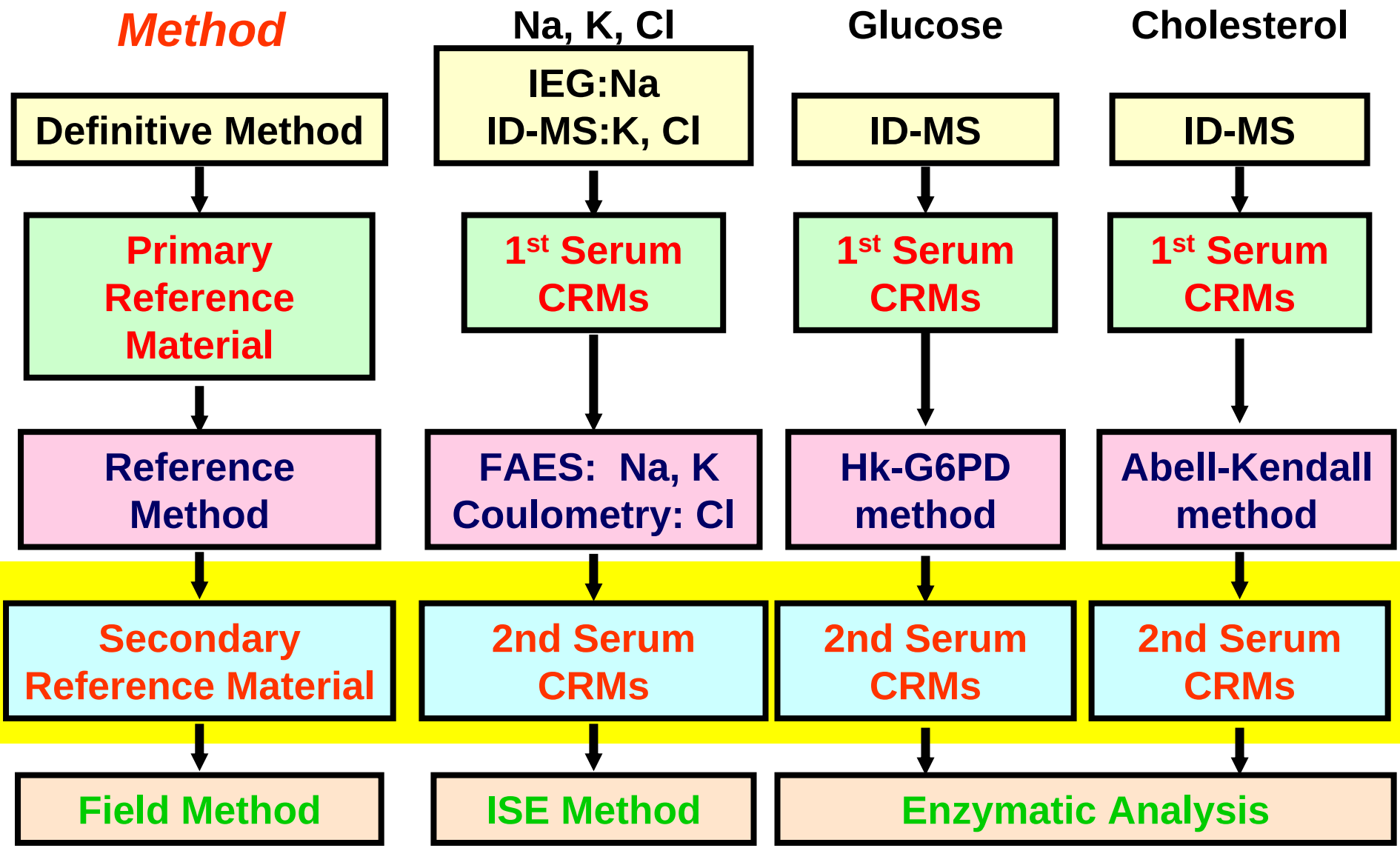
3. Development of Matrix Reference Materials

(by Japan Society of Clinical Chemistry)

- **Electrolytes:** ***Na, K and Cl for ISEs***
  Total Calcium & Total Magnesium
- **Lipid:** ***Total cholesterol for enzymatic analysis***
  HDL-Cholesterol for enzymatic analysis
  Triglycerides for enzymatic analysis
- **Glucose**
- ***HemoglobinA1c***
- **Creatinine**
- **Uric Acid**
- **Urea Nitrogen**
- **Blood Gases (pH, pCO_2, pO_2)**

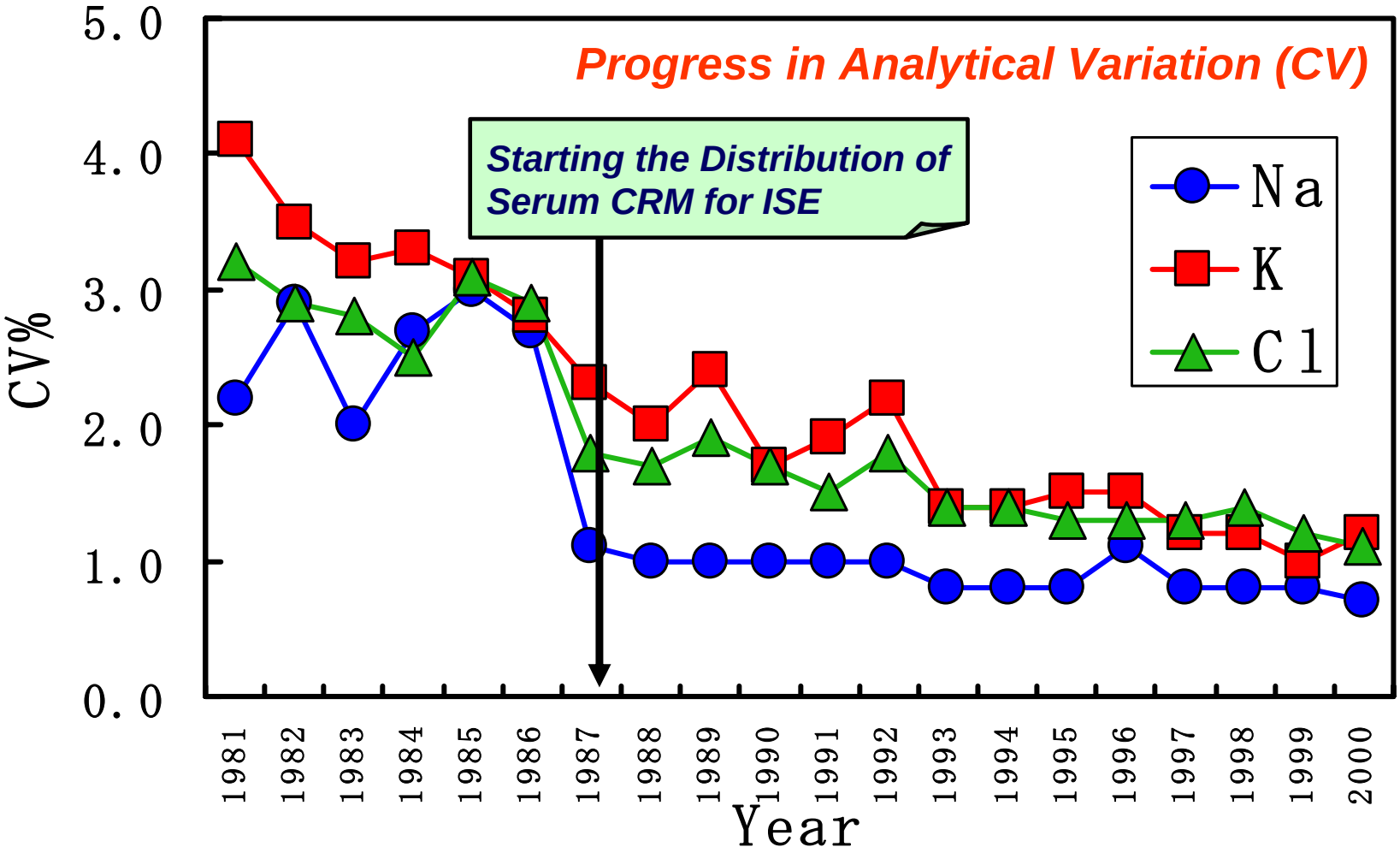
(Underlined Items have been already listed in α-lists.)

Traceability System of Matrix CRMs

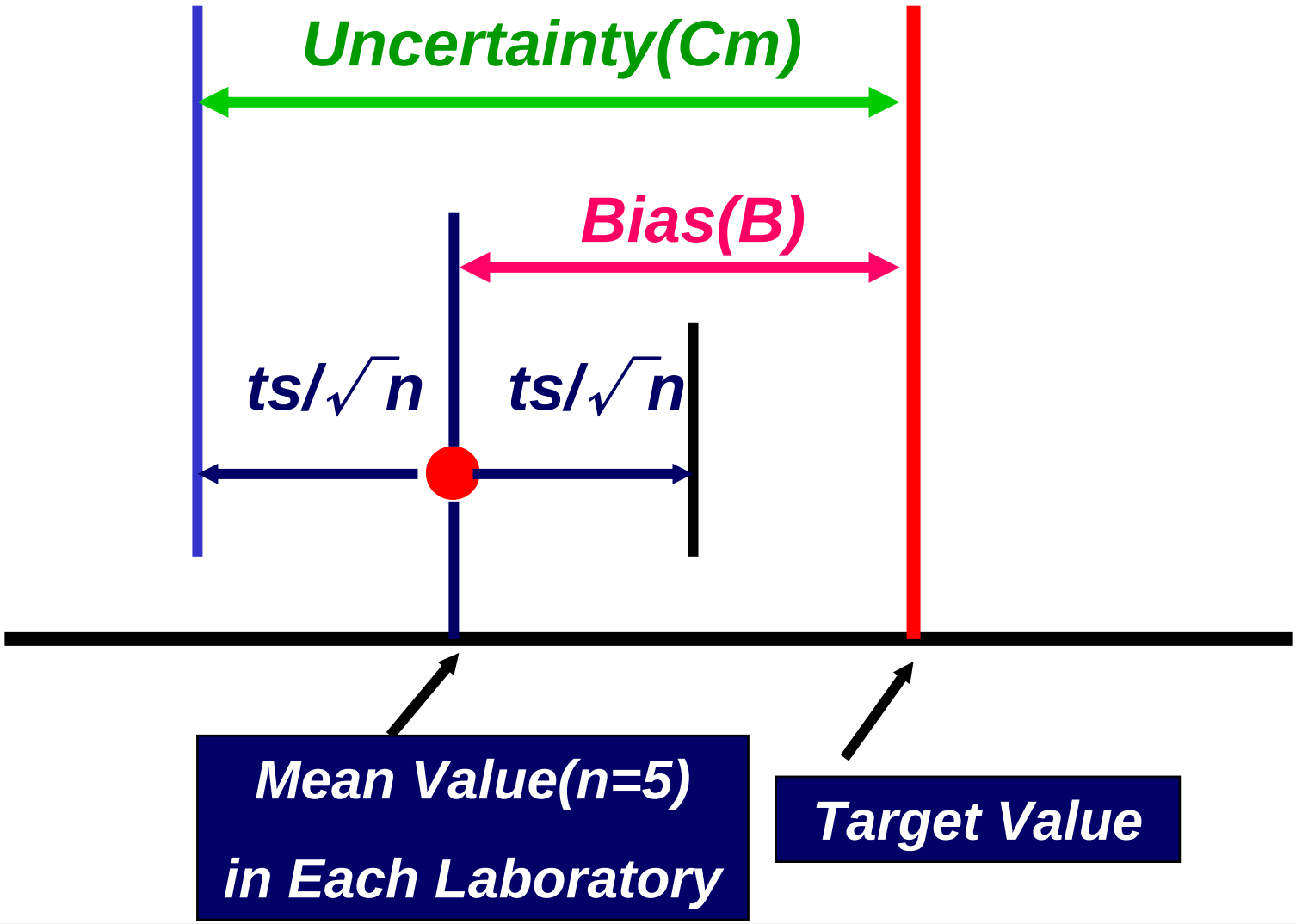


4. External Quality Control of Na, K and Cl Measurement by ISE Method

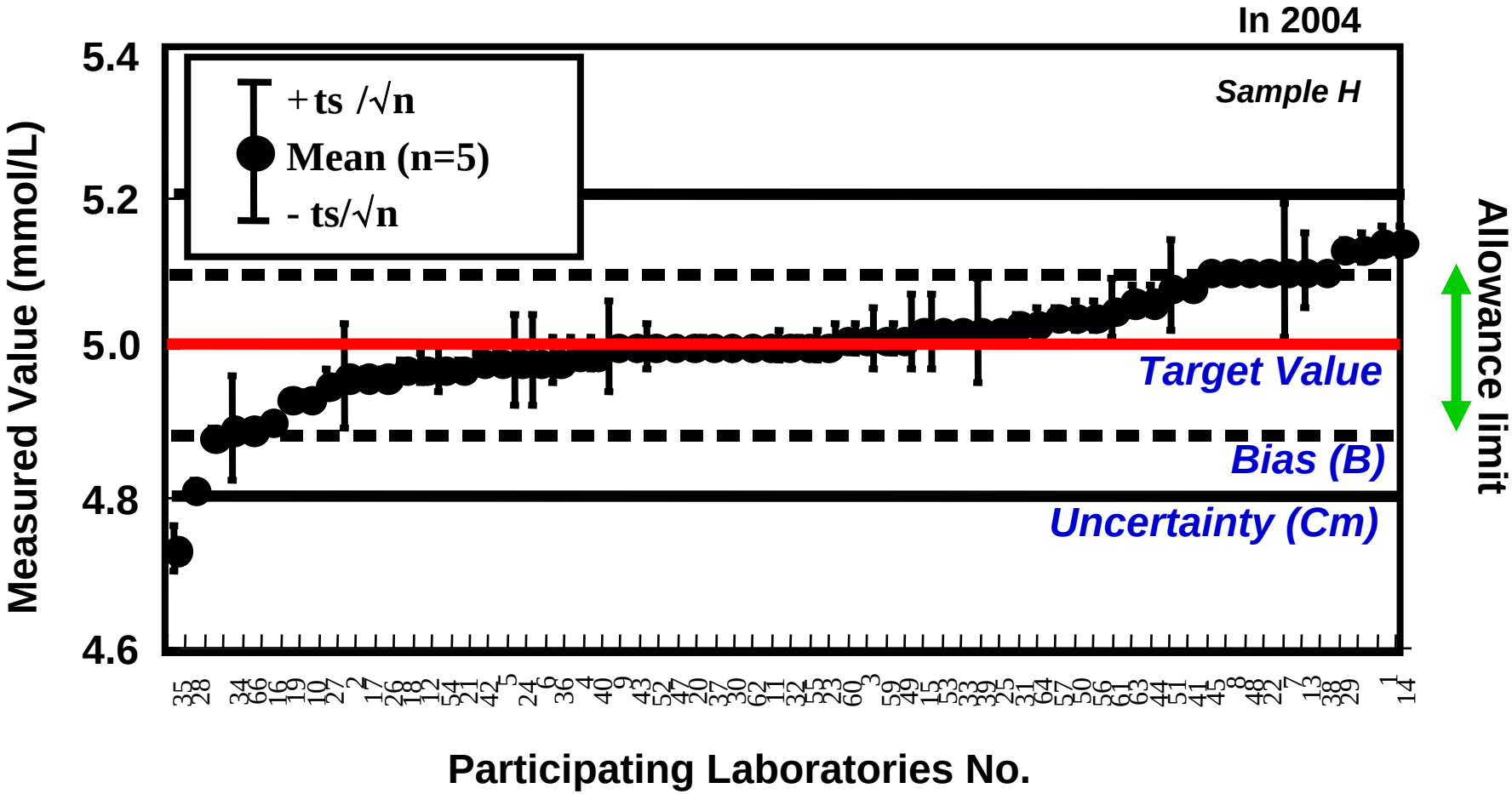
(EQA by Japan Medical Association)



Trueness Evaluation Using Uncertainty of Measured Value in Proficiency Testing



K Measurement by ISE Method



Target Value : 4.96±0.01 mmol/L
Allowable Limit: ±0.1 mmol/L including *B*
: ±0.2 mmol/L including *Cm*

JOINT COMMITTEE for TRACEABILITY in LABORATORY MEDICINE (JCTLM)

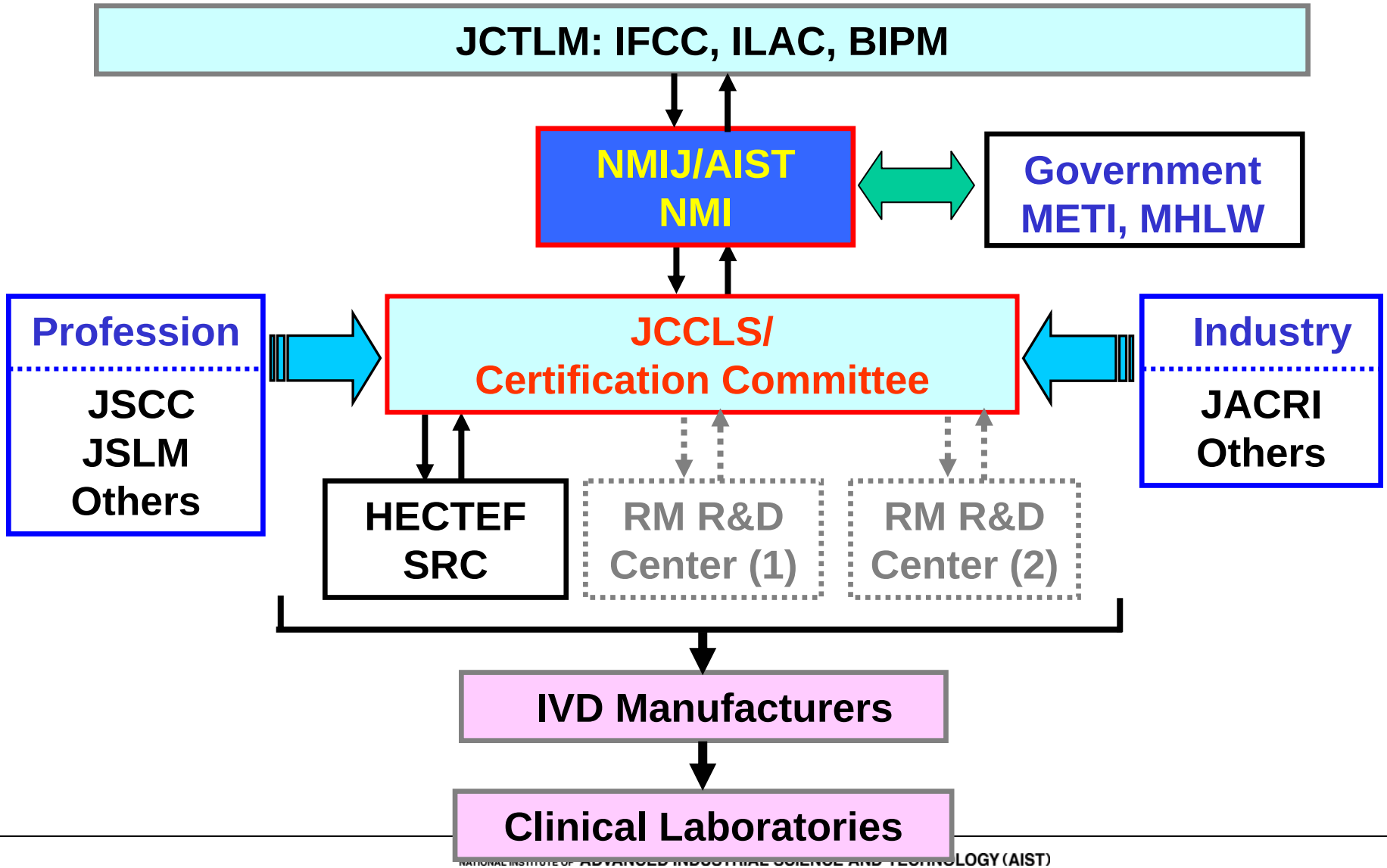
Established in Sevres on 12 June 2002

Declaration of co-operati

A framework for ional recognition of available higher-ord aterials, measurement procedures and reference measurement laboratories

New System of Developing and Providing Reference Materials in Japan

(under Construction)



Collaboration System for Standardization of Clinical Chemical in Japan

- Japan Commission of Clinical Laboratory Standards -

1. Clinical Chemistry Organization

- JSCC (Clinical Chemistry)
- JSLM (Laboratory Medicine)
- JAMT (Medical Technologists)
- JRCLA (Registered Clinical Laboratory)

2. Metrology Organization

NMIJ/AIST

3. IVD Industry Organization

- JACRI
- JAIMA

4. Accreditation Organization

- JAB
- NITE

5. Authorities

- METI
- MHLW

JCTLM (International) and Domestic Standardization

Structure of Clinical Chemistry Standardization

Clinical Chemistry Organization
JSCC
JSLM
JAMT
JRCLA

NMIJ/AIST

JACRI

Authorities
METI
MHLW

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Collaboration

JCCLS

WG1: Reference Materials/ Reference Measurement Procedures

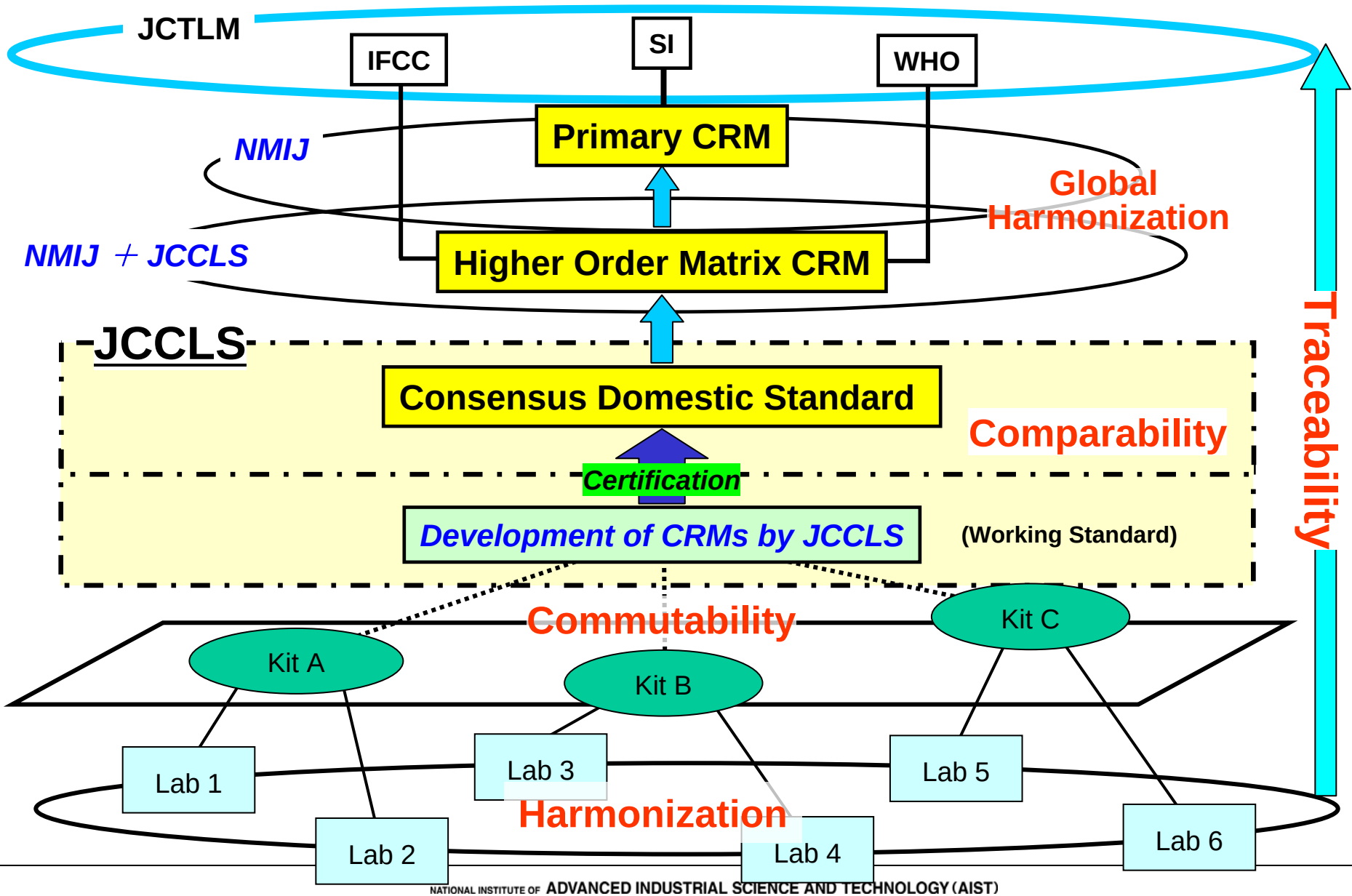
- National Standards
- Higher Order Reference Materials
- Matrix Reference Materials for Working Standards
- Reference Methods and Recommended Methods
- Standardization of Routine Methods
- ≪Fund from NEDO≫

WG2: Harmonization for Measurement Values

- Standardization of Protocol for Internal Quality Control in a Lab.
- External Quality Control in each Area or Group
- Nationwide Standardization – Patchwork Standardization (Nationwide External Quality Control)

≪ Fund from METI ≫

Structure and Strategy of WG 1



Development Program of Clinical CRMs in Japan

NMIJ: ***Pure Material Type of CRMS***

SI Traceable CRMs

JCCLS: ***Higher Order Matrix CRMs***

Metabolite and Substrates
Blood Gases
Electrolytes
Hormones
Lipids
Proteins/Enzymes

JACRI: ***Feasibility Study on Standardization of Clinical Chemical Reagents***

Standardization of Working Standard Level of Calibrators

1. Development Program of Clinical CRMs by NMIJ

- Development of SI Traceable CRMs -

Metabolites

- Cholesterol
- Creatinine
- Uric Acid
- Urea
- Triglycerides

Hormones

- Progesterone
- Estradiol
- Teststerone
- Cortisol

BIPM & NMIJ Joint Research

Proteins

- Albumin (ALB)
- C-reactive protein
- PSA
- Insuline
- C-peptide(CPR)

NMIJ CRM 6001-a Cholesterol

Pure Cholesterol
Purity：99.9±0.1%

Certification Method:
Freezing-point depression method

Certified on March 2005

2. Development Program of Clinical RMs by JCCLS

Metabolite and Substrates

- Glucose
- Creatinine
- Uric acid
- Urea
- Hemoblobin A1C
- Glycoalbumin

Blood Gases

- Blood gases

Electrolytes

- Ionized calcium
- Total calcium
- Total magnesium

Hormones

- Cortisol
- Insulin
- C-peptide (CPR)

Lipids

- HDL-cholesterol
- LDL-cholesterol

Proteins/Enzymes

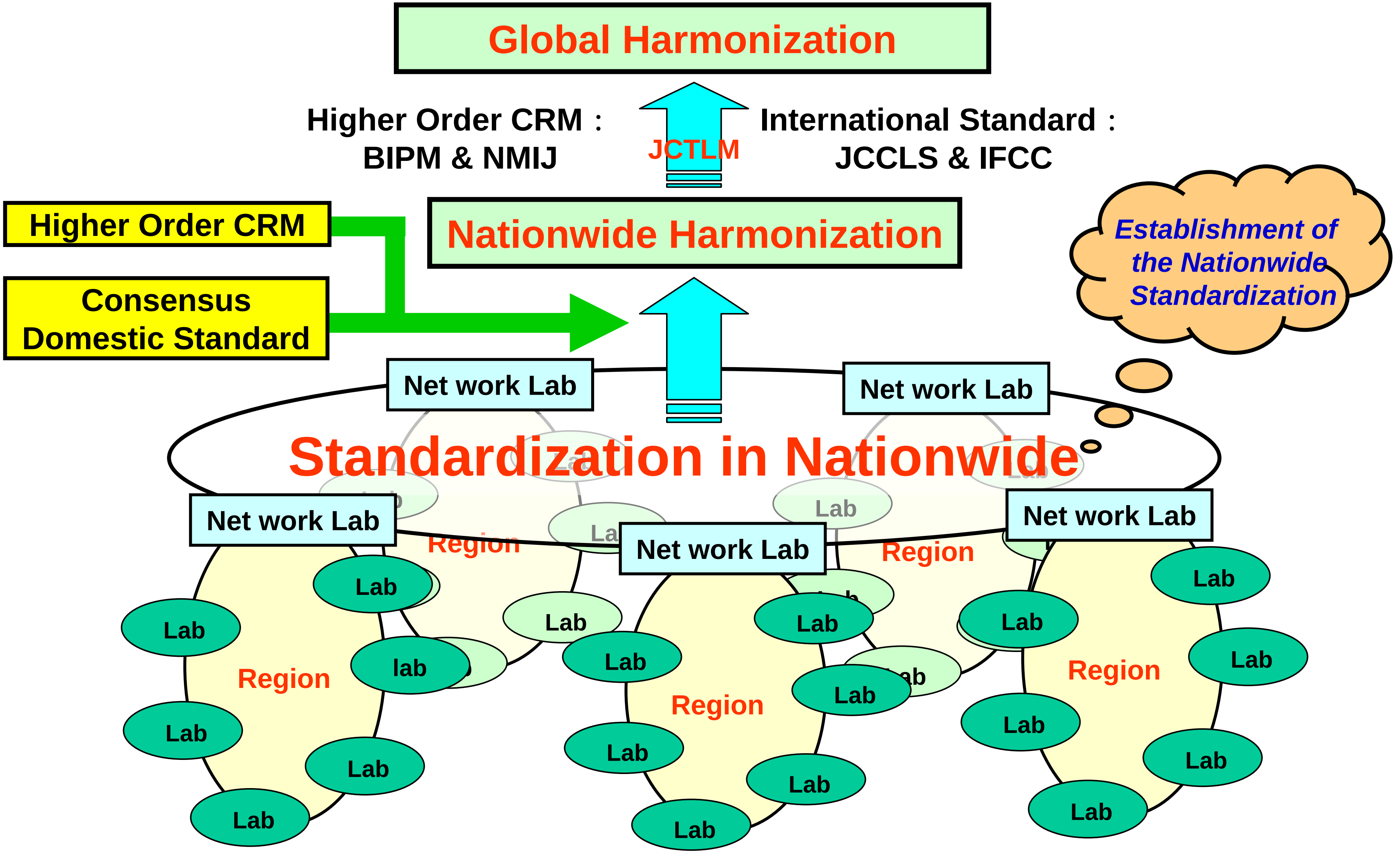
- Secondary CRM of Albumin
- Serum albumin
- Urine albumin
- Pancreatic amylase
- Serum CRM for CRP
- Cholineesterase
- Lipase

3. Feasibility Study of Standardization of Clinical Reagents by JACRI

Urine sodium (Na)
Urine potassium （K）
Urine chloride （Cl）
Urine magnesium （Mg）
Urine calcium （Ca）
Urine urea nitrogen （UN）
Urine uric acid （UA）
Urine creatinine （Cre）
Urine amylase （ AMY ）
Urine glucose （GLU）
Urine inorganic phosphorus （IP)
Serum iorganic phosphorus （IP)
Serum prostate specific antigen
Serum antinuclear antigen
Serum lithium (Li)

Digoxin
Theophylline
β 2－microglobulin
Estradiol
Progesterone
Testosterone
Thyroid stimulating hormone
Thyroxine
β-human choriogonadotropin
Fibrinogen degradation products (FDP)
D-dimer
Carcinoembryonic antigen （CEA)
Alpha-feto protein （AFP)
Carbohydrate antigen 125 （CA125)
Ferritin

GW2: Patchwork Standardization for Nationwide



Clin. Chem. Lab. Med. 39(3), 256-262 (2001)

Feasibility Study of Patchwork Standardization
- *Intra-* and *Inter-*Laboratory Variation -

Participants; 40 Labs.

Testing Items

1. Biochemical Analytes : 26
2. CBC (Blood Counts and Hemoglobin) : 5

Assay Procedure

1. Intra-laboratory variation
   (1) Single assay : Biochemical analytes
   Assay is performed at morning and evening.
   (2) Double assay : CBC
   Assay is performed at morning.
2. Inter-laboratory variation
   Comparison of mean values

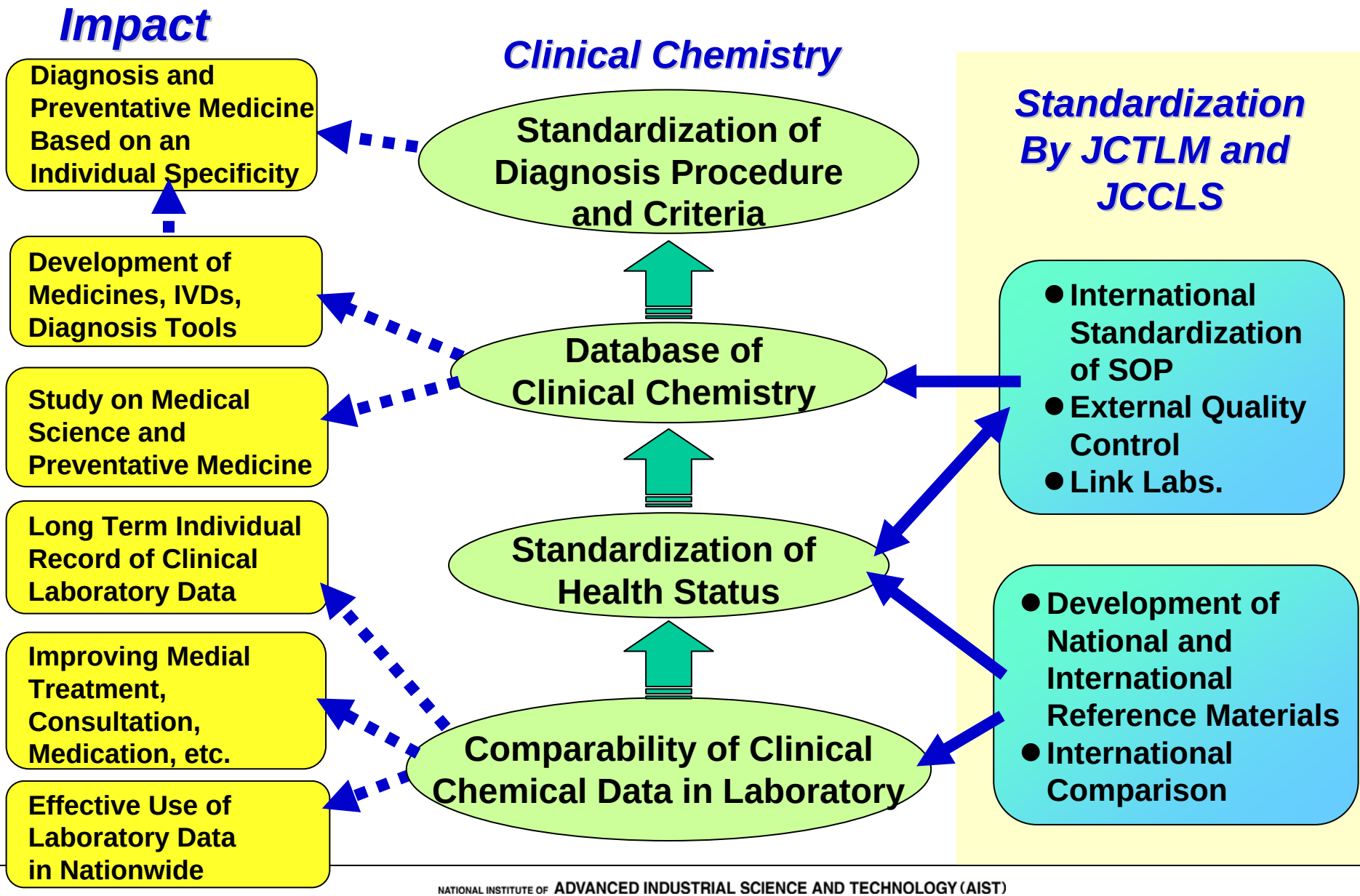
*Intra-*laboratory Variation on Biochemical Analytes

Analytes		Abnormal Pooled Serum	Normal Pooled Serum	Data Trol	Aalto
Total Bilirubin	mg/dL	5.43	0.69	0.75	3.37
	CV(%)	0.61～3.41	0～7.15	0～5.75	0.79～2.38
Glucose	mg/dL	353.7	94.7	90.9	275.8
	CV(%)	0.21～2.85	0.34～1.73	0.39～1.42	0.42～1.21
Urea Nitrogen	mg/dL	65.9	13.9	15.6	54.2
	CV(%)	0.44～3.16	0.81～3.03	1.01～3.01	0.60～2.13
Creatinine	mg/dL	6.74	0.76	1.11	4.78
	CV(%)	0.46～3.35	1.32～5.04	0～2.32	0.38～2.53

*Inter-*laboratory variation on Biochemical Analytes

Analyte		Abnormal Pooled Serum	Normal Pooled Serum	Data Trol	Aalto
Total Bilirubin	SD(mg/dL)	0.16	0.05	0.04	0.14
	CV(%)	2.87	7.33	5.27	4.14
Glucose	SD(mg/dL)	5.12	1.06	1.19	3.11
	CV(%)	1.45	1.12	1.30	1.13
Urea Nitogen	SD(mg/dL)	1.73	0.51	0.37	1.88
	CV(%)	2.62	3.68	2.38	3.47
Creatinine	SD(mg/dL)	0.13	0.04	0.04	0.09
	CV(%)	1.93	4.77	3.32	1.90

Medical and Economic Impact of JCTLM



Thank you for your Attention!!