

JCCLS standardization and traceability activities.

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Standardization in Japan

Phase of harmonization and standardization:

- Development of external quality control system and validation.

- For density items (such as glucose etc.): development of reference materials.

- For enzyme items: development of reference measurement procedures and enzyme reference material (ERM).

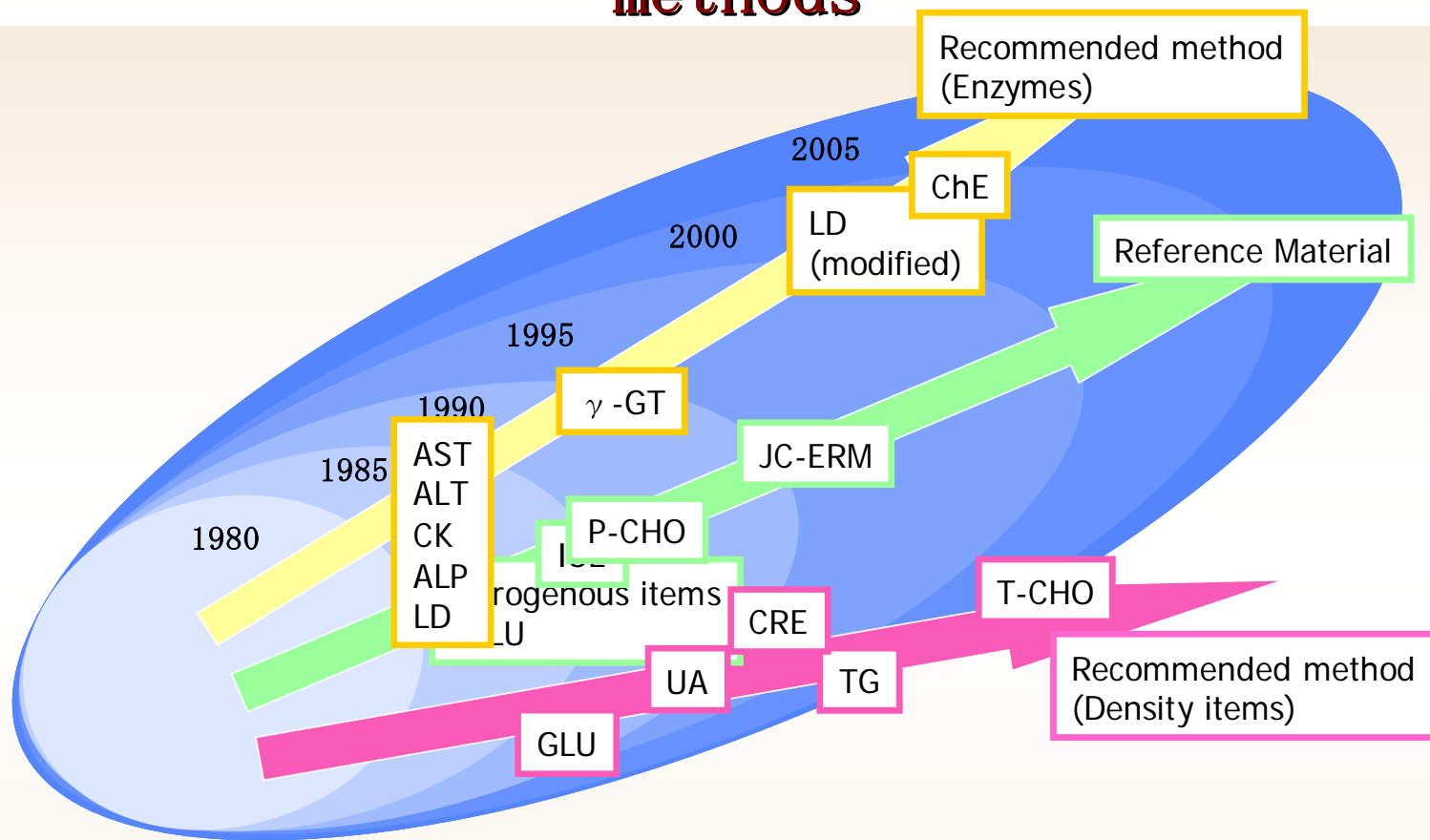


External quality control programs in Japan

- Nationwide
 - Japan Medical Association
 - Japan Association of Medical Technologists
 - CAP (College of American Pathologists)
- Regional
 - Association of Medical Technologists in each prefecture
 - Medical facilities Group
 - Reagent Manufacturers



Progress in development of JSCC recommended methods



Since 1980's, collaborative activity between Japan Society of Clinical Chemistry (JSCC) and Japan Association of Clinical Reagents Industries (JACRI) have been providing recommended methods and reference materials.



Standardization in Japan

As for the standardization of enzyme items,

- Enactment of the recommended method: based on the IFCC methods which were already existing.
- By examining better reaction conditions for enzymes: the reactivity of isozymes for AST, ALT, LD, & CK. (JSCC-improved methods)



Enzyme Reference Material (JC-ERM) established by JSCC (since 1998)

Matrix ; blood plasma (bovine serum albumin)

Composition of JC-ERM

Item	Origin	method
AST	Recombinant (Human liver gene)	JSCC SOP method
ALT	Recombinant (Human liver gene)	JSCC SOP method
CK	Recombinant (Human skeletal muscle gene)	JSCC SOP method
ALP	Recombinant (Human liver gene)	JSCC SOP method
LD	Human erythrocyte	JSCC SOP method
Gamma-GT	Recombinant (Human liver gene)	JSCC SOP method
AMY	Recombinant (Human pancreas gene & Human saliva)	JSCC SOP method (IFCC SOPmethod)

We defined the following things as REM.

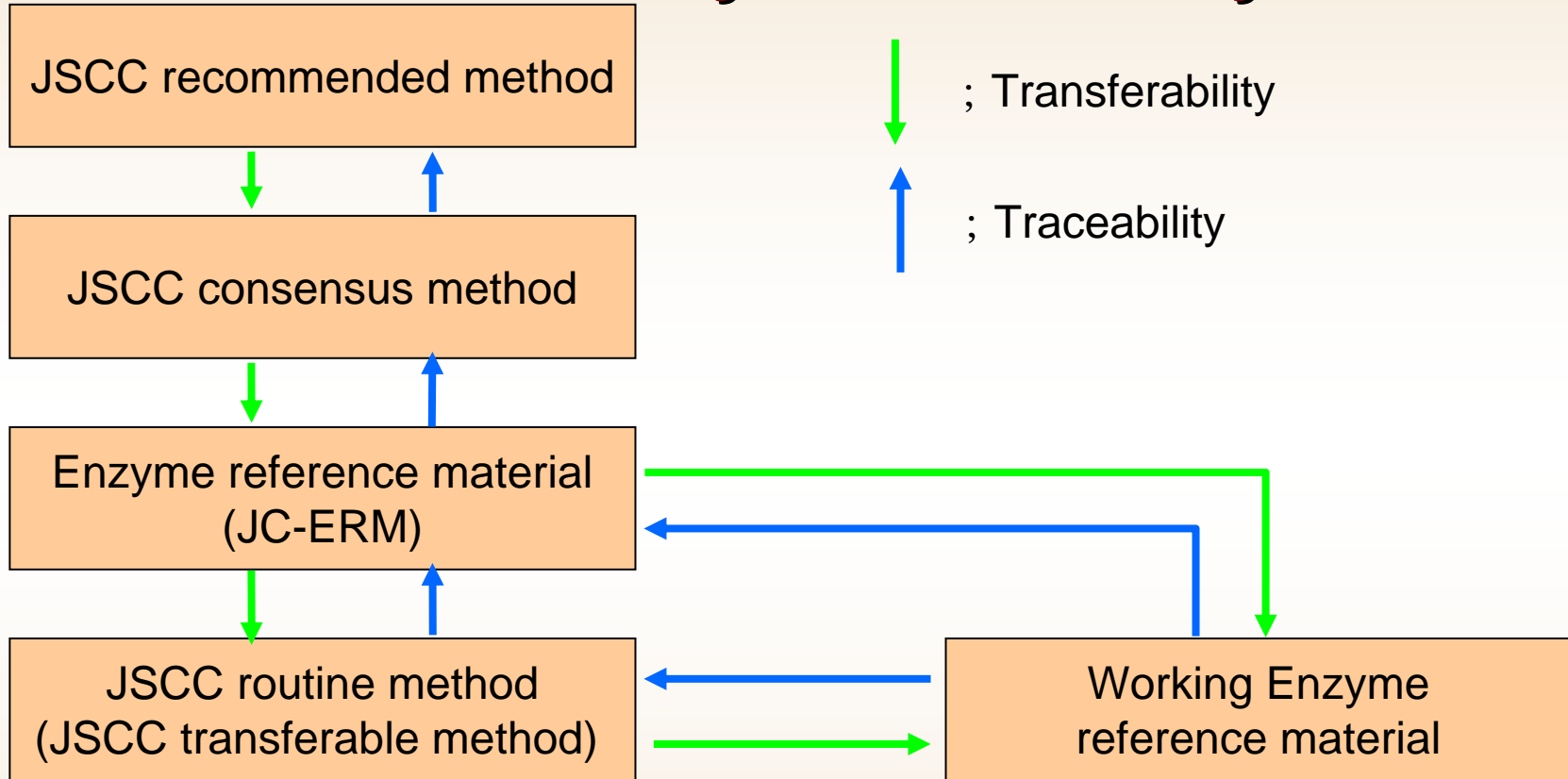
- 1) The enzyme used by JC-ERM should be human origin type.
- 2) The physical character of JC-ERM should be equivalent to human sera.

We confirmed that JC-ERM is a good enzyme reference materials for all commercial assay kits.



Transferability and Traceability

in Measurement system for enzyme items

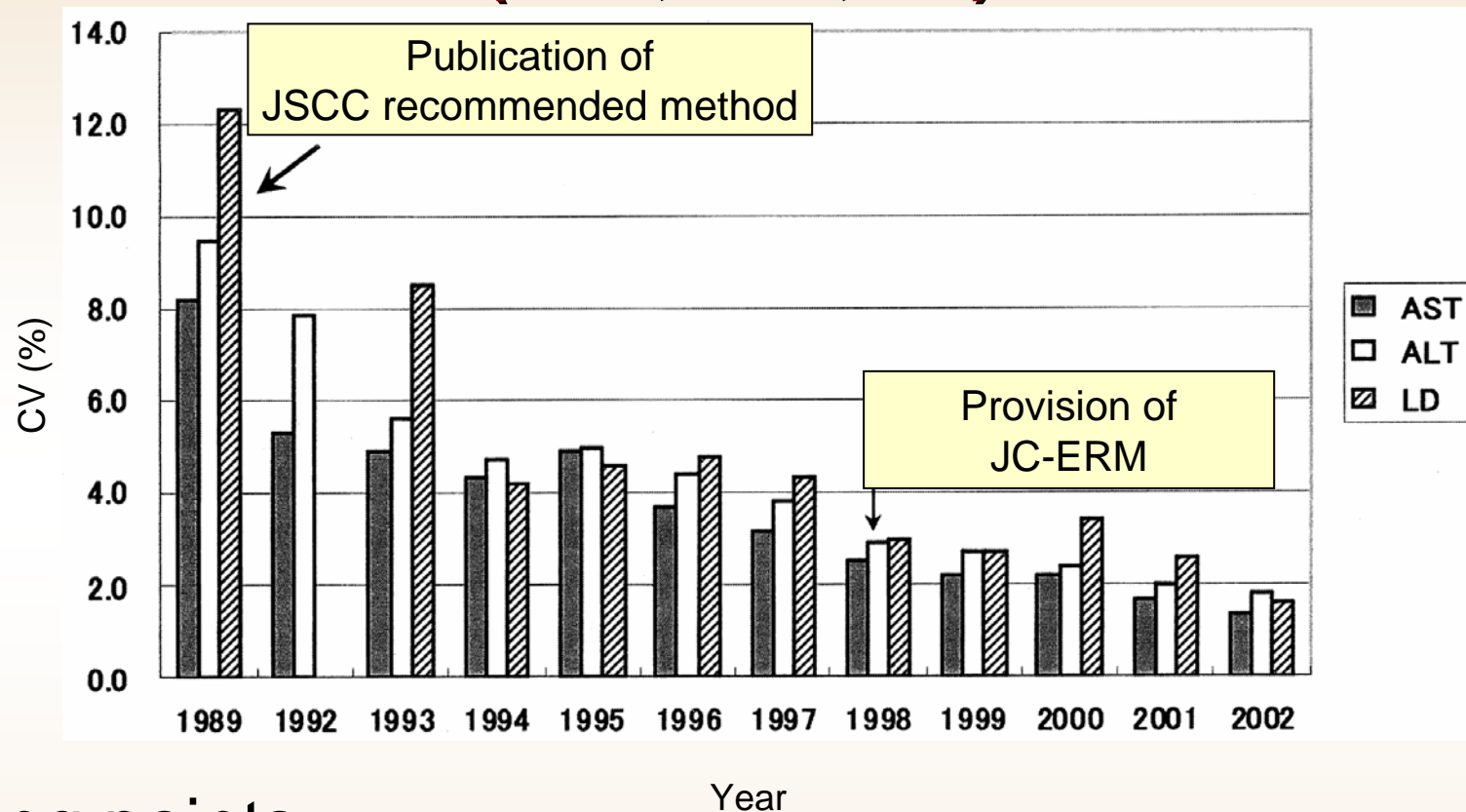


The measurement system for enzymes in Japan have been established transferability and traceability from the JSCC-recommended methods to routine methods.

Re f; Japanese journal of clinical chemistry 25:135-148 1996.



Improvement of inter-laboratories variance (CV%) (AST, ALT, LD)



Turning points

- Publication of recommended method; JSCC recommended method
- Provision of reference material; JC-ERM

Re f; JMA Survey report 2002



**In 2003,
JCCLS**

(Japanese Committee for Clinical Laboratory Standards)

**set up
a new committee
for standardization of laboratory
medicine.**



Structure of JCCLS committee on Standardization in Laboratory medicine (since 2003)

JCCLS committee on standardization
in Laboratory medicine

Development of
Reference Material/
Recommended method
(Working Group 1)

- Development of Primary reference materials .
- Development of working reference materials .
- Development of recommended methods .

Harmonization of laboratory
Measurements nationwide
(Working Group 2)

- Maintenance of SOP for clinical laboratory (Internal-QC).
- Harmonization in regional medical institution group.
- Harmonization in nationwide.

Database project
for diagnoses
(Working Group 3)

- Setup database for diagnosis.
- Standardization of a guideline and a diagnostic criteria.
- Standardization of Clinical-Pass and a medical treatment criteria.



Development of Reference Material/ Recommended method (Working Group 1)

C-reactive protein (CRP),
Albumin,
Cortisol,
Glucose,
Creatinine,
Cholinesterase,
Glycoalbumin,
Hb A1c,
Calcium,
Magnesium,
HDL-C,
LDL-C, etc.



Harmonization of laboratory measurements nationwide (Working Group 2)

Phase I

- Select regional reference laboratories in a patch area.
- Daily survey among these reference laboratories, using a common pooled serum.
- Monthly survey among all laboratories with one of the reference laboratories using the same pooled serum.
- Standardization of a regional unit (a patch).

Phase II

- Standardization among regional reference laboratories nationwide.

We named this strategy as "Patchwork Standardization Program"



A trial in the Fukuoka Prefecture, as a model area

- Fukuoka is located in the northern part of Kyushu, the leading city of western Japan.
- Fukuoka has flourished since ca. 200 years ago as the gate of Chinese and Korean culture to Japan.
- Population of Fukuoka is ca. 5 million.
- Fukuoka prefecture has been selected as the first patch for the standardization of laboratory medicine in Japan.

Establishment of the Association of Five Hospitals as reference laboratories.

- Fukuoka has 4 University Hospitals.
- The 4 university hospitals and Iizuka Hospital (1500beds) are the reference laboratories in Fukuoka.



Scope of the standardization project: focusing points

We focused on

- the education of physicians, medical technologists, and staff of medical institutions, and the publication of manuals on how to standardize laboratory data,
- the determination of target values for accuracy control samples at three levels of concentration (low, normal and high abnormal), for daily, monthly and yearly control surveys,
- monitoring of the measurement accuracy through analysis of data obtained from outpatients in the Kyushu University Hospital,
- monitoring and analyses of the standardization project during monthly meetings with representative members of the Association of Five Hospitals.
- Reference materials used were commercial reference materials based on NIST906 (NIST), CRM470 (IFCC) and ERM (JCCLS).



Standardization of Laboratory Data and Establishment of Reference Intervals in the Fukuoka Prefecture: A Japanese Perspective

Summary

- Standardization of 22 clinical chemistry analytes and serum protein constituents (IgG, A, M, C3, C4) in Fukuoka.
- Reference intervals were established for all these items.
- Regional collaboration based on international guidelines led to a significant improvement in inter-laboratory comparability.
- Standardization extended to 97% of the institutions in Fukuoka Prefecture.

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The association of five hospitals
(reference laboratories in Fukuoka)

- ① Kyushu University Hospital
- ② Kurume University Hospital
- ③ Fukuoka University Hospital
- ④ University Hospital of Occupational and Environmental Health
- ⑤ Iizuka Hospital



CV (coefficient of variation) of RLs (daily survey) and regional laboratories (monthly survey)

Tab. 2 Comparison of the coefficient of variation and allowable error limit in the major six institutions of the Association of Five Hospitals (daily survey) and 58 regional institutions (monthly survey).

Analytes	Units	Target values	Allowable bias		Daily	Monthly
			0.25B _A % (0.3758B _A)	CV(%)	CV(%)	
TP	g/l	74	1.06(1.59)		0.74	1.76* ←
ALB	g/l	41	1.00(1.50)	→	1.09*	3.30** ←
Urea	mmol/l	6.52	5.30		2.53	3.56
CRE	μmol/l	94.6	4.12		3.14	4.09
UA	μmol/l	309.4	7.43		1.02	3.07
TB	μmol/l	10.9	14.70		4.35	9.38
Na	mmol/l	145	0.27(0.41)	→	0.95**	0.97** ←
K	mmol/l	4.8	1.95		1.28	1.26
Cl	mmol/l	108	0.38(0.57)	→	1.59**	1.30** ←
Ca	mmol/l	2.33	0.80(1.19)	→	1.02*	3.32** ←
IP	mmol/l	1.58	3.47		1.40	2.61
TC	mmol/l	5.91	4.34		1.67	2.01
HDL	mmol/l	1.65	5.71		3.59	4.64
TG	mmol/l	0.95	16.28		3.83	3.13
GLU	mmol/l	6.27	2.29		1.64	1.81
AST	U/l	31	7.40		2.12	7.09
ALT	U/l	35	12.56		3.58	7.45
ALP	U/l	379	6.96(10.44)		4.74	20.35* ←
LD	U/l	513	4.06		6.74	–
CK	U/l	182	13.37		2.43	4.91
AMY	U/l	123	6.51 (9.81)		6.36	13.44* ←
γGT	U/l	43	12.85(19.27)		2.14	19.14* ←
IgG	g/l	12.17	3.26		1.76	–
IgA	g/l	2.2	8.45		1.47	–
IgM	g/l	0.54	12.02		5.11	–
C3	g/l	1.11	4.44		2.45	–
C4	g/l	0.2	8.71		4.18	–

Bold: $\leq 0.25 B_A$, $0.25 B_A < * \leq 0.375 B_A$, $** > 0.375 B_A$, (–): not determined

Monthly survey CVs of the representative 58 regional laboratories out of 146 laboratories.

Results

- Among reference laboratories, 23 out of 27 analytes within the allowable bias of 0.25 B_A.
- Among regional laboratories, 13 out of 27 analytes within the allowable bias of 0.25 B_A.
- It was satisfactory at the beginning of our project, though it was not complete.



Our experience in the Fukuoka Prefecture

- In the Fukuoka Prefecture with a population of 5 million, the Prefecture Medical Association, Medical Technologists' Association, and the Association of Five Hospitals have established a project for the standardization of laboratory data.
- As a result, inter-laboratory variation has decreased mainly in clinical chemistry measurements, accomplishing the primary aim of the project.
- In the future, we will continue our efforts to increase the number of measured analytes and expand the area for this standardization project.
- We have integrated the internet system into the standardization project for the real time monitoring.

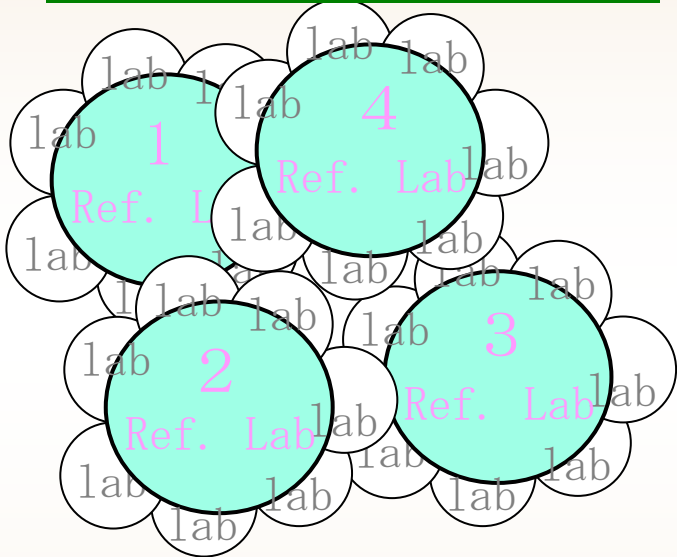


Patchwork Standardization for Nationwide (cartoon)

JCCLS ongoing project on nationwide standardization

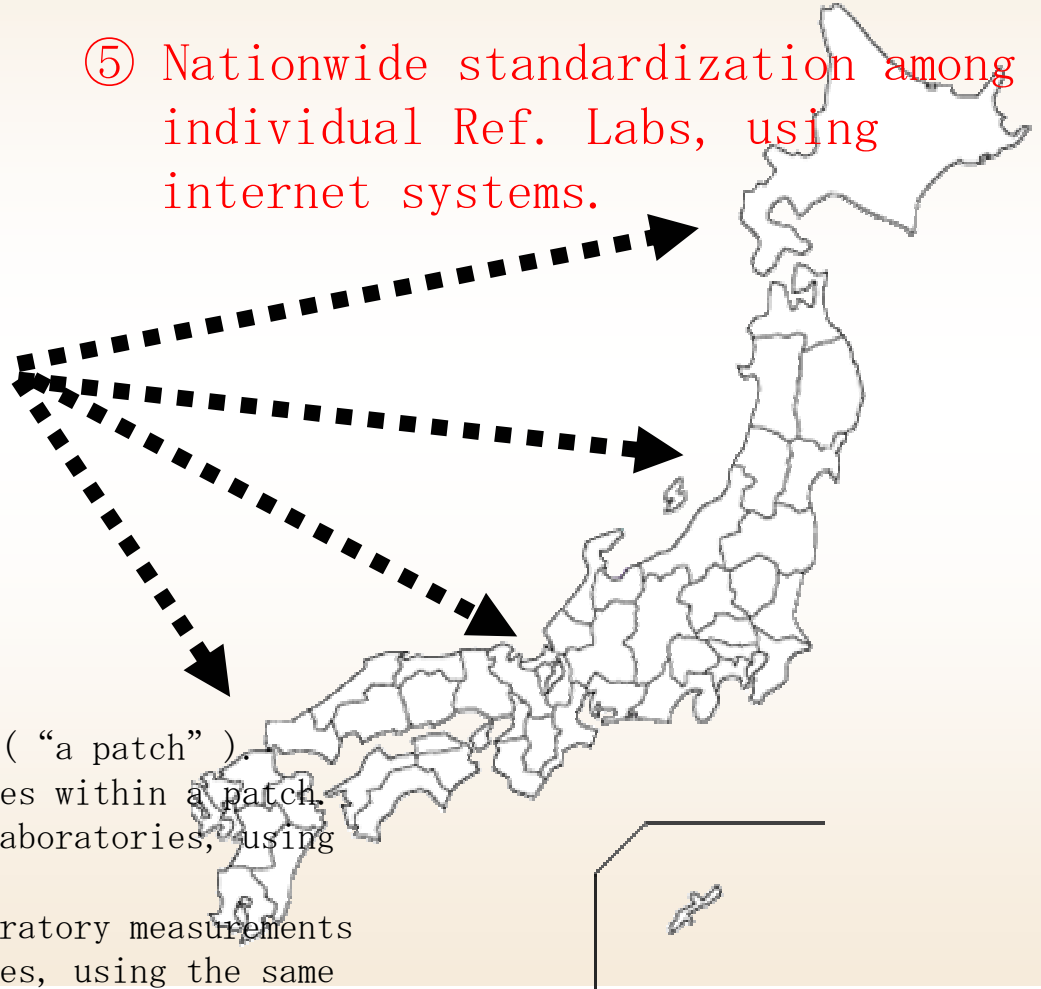
Organized by JCCLS and JAMT.

a patch (=a prefecture)



Regional Standardization

⑤ Nationwide standardization among individual Ref. Labs, using internet systems.



- ① Standardization within a prefecture (“a patch”)
- ② Select regional reference laboratories within a patch.
- ③ Daily survey among these reference laboratories, using common pooled sera.
- ④ Other laboratories adjust their laboratory measurements with one of the reference laboratories, using the same pooled sera.



JCCLS (Working Group 2) 2005~

Establishment of the Nationwide Network System by JCCLS and JAMT.

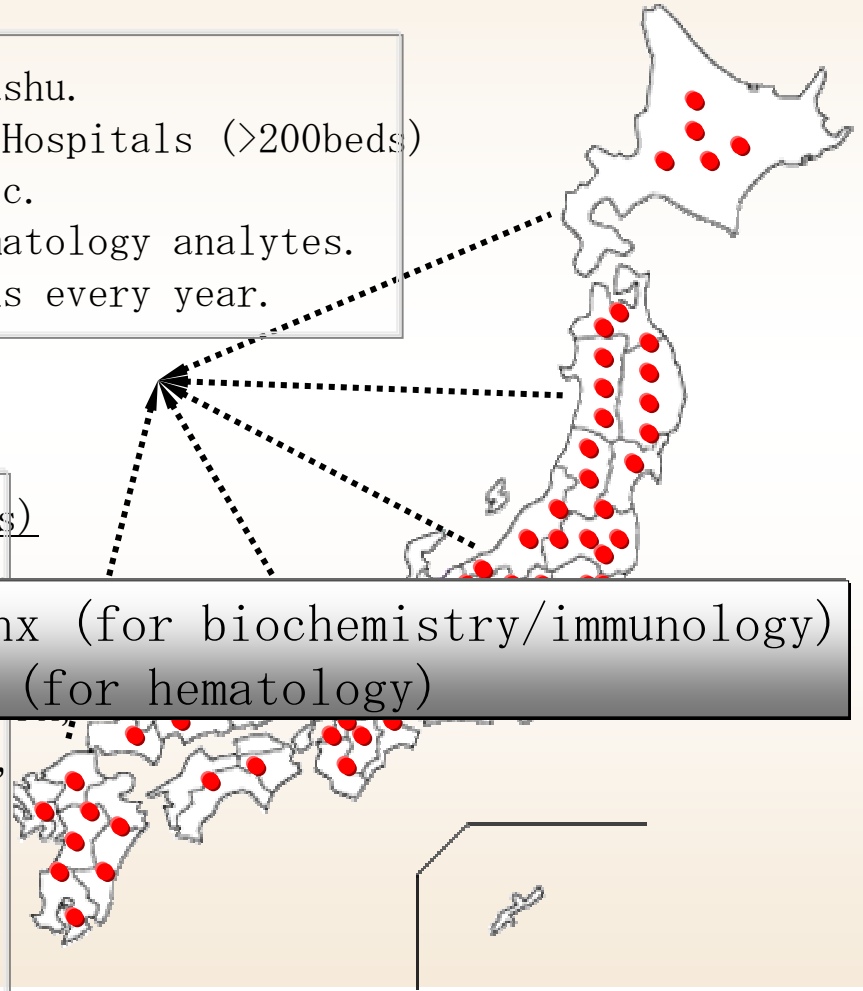
- (1) 90 laboratories from Hokkaido to Kyushu.
- (2) 34 University Hospitals, 37 General Hospitals (>200beds)
4 General Hospitals (<200beds) etc.
- (3) 27 biochemistry/immunology and 5 hematology analytes.
- (4) Real-time monitoring during 10 months every year.

Results

CV% (inter-institution among 90 labs)

- < 3%: TP, Urea, UA, LD, γ -Glu, Na, K, Cl, RBC
- 3- 5%: Alb, Crea, AST, ALT, A, CRP(normal), HDL-C(normal),
- 5-10%: T-Bil, D-Bil(normal), Ca, Fe, LDL-C(high abnormal), PLT,
- 10-15%: AMY, CRP(low abnormal), HDL-C(low abnormal),
- 15%< : CHE, LDL-C(low abnormal),

QCLinx (for biochemistry/immunology)
SNCS (for hematology)



Patchwork standardization project

- Relatively easy and quite effective quality control system.
- Using internet systems, we could control clinical laboratory measurements regionally as well as nationwide.
- This internet standardization system is applicable to the inter-nations quality control of laboratory testing.



Development of reliable IVD systems

Development of Reference Material/Recommended method (**Working Group 1**)

Harmonization of Laboratory measurements nationwide (**Working Group 2**)

Database project for diagnoses (**Working Group 3**)

- Improvement in commutability
- Improvement in precision

Development of Clinical testing results database

- Practice of scientific based medicine
- Accurate diagnostics · medical treatment in consideration for individual variance
- Practice of trustable medicine
- Cut in overlapped clinical testing.

- Monitoring of individual clinical testing data
- Acceleration for practice of diagnostics and preventive medicine
- Development of reliable diagnostic systems
- Development of medicine, medical device etc...

- Expansion of IVD systems market
- Development of health care systems
- Producing health care market and preventive medicine
- Development of advanced medical treatment
- Medical bill cut

JCCLS ongoing project



Thank you for your attention !

