JCCLS standardization and traceability activities.

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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
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

<table>
<thead>
<tr>
<th>Item</th>
<th>Origin</th>
<th>method</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST</td>
<td>Recombinant (Human liver gene)</td>
<td>JSCC SOP method</td>
</tr>
<tr>
<td>ALT</td>
<td>Recombinant (Human liver gene)</td>
<td>JSCC SOP method</td>
</tr>
<tr>
<td>CK</td>
<td>Recombinant (Human skeletal muscle gene)</td>
<td>JSCC SOP method</td>
</tr>
<tr>
<td>ALP</td>
<td>Recombinant (Human liver gene)</td>
<td>JSCC SOP method</td>
</tr>
<tr>
<td>LD</td>
<td>Human erythrocyte</td>
<td>JSCC SOP method</td>
</tr>
<tr>
<td>Gamma-GT</td>
<td>Recombinant (Human liver gene)</td>
<td>JSCC SOP method</td>
</tr>
<tr>
<td>AMY</td>
<td>Recombinant (Human pancreas gene &amp; Human saliva)</td>
<td>JSCC SOP method (IFCC SOP method)</td>
</tr>
</tbody>
</table>

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

- JSCC recommended method
- JSCC consensus method
- Enzyme reference material (JC-ERM)
- JSCC routine method (JSCC transferable method)
- Working Enzyme reference material

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

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

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Turning points

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

Ref: 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 material
- Development of working reference material
- Development of recommended method

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 local area.
- Daily survey among these reference laboratories, using a common pooled serum.
- Monthly survey among all other laboratories with one of the reference laboratories, using the same pooled serum.
- Standardization within 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 (1500 beds) are the reference laboratories in Fukuoka.
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 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.

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

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.
JCCLS ongoing project on nationwide standardization
Organized by JCCLS and JAMT.

a patch (=a prefecture)

Regional Standardization

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.

⑤ Nationwide standardization among individual Ref. Labs, using internet systems.
Establishment of the Nationwide Network System by JCCLS and JAMT.

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

CV% (inter-institution among 90 labs)

< 3%: TP, Urea, UA, LD, γ-GT,
    Glu, Na, K, Cl, RBC
3- 5%: Alb, Crea, AST, ALT, ALP,
    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),

Results

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)
  - Improvement in commutability
  - Improvement in precision

- Development of Clinical testing results database

- Harmonization of Laboratory measurements nationwide (Working Group 2)
  - Practice of scientific based medicine
  - Accurate diagnostics • medical treatment in consideration for individual variance
  - Practice of trustable medicine
  - Cut in overlapped clinical testing.

- Database project for diagnoses (Working Group 3)
  - 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...

JCCLS ongoing project

- 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
Thank you for your attention!