Standardization Activities of the Centers for Disease Control & Prevention

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- Laboratory improvement programs and activities at CDC.
- Cholesterol Reference Method Laboratory Network's Quality Management System
- Accreditation of reference method laboratory networks

Laboratory improvement programs and activities at CDC

CDC Activities

- Improving quality of clinical laboratory measurements
  - Cardiovascular disease
  - Diabetes
  - Kidney disease
  - Osteoporosis

Cardiovascular Disease

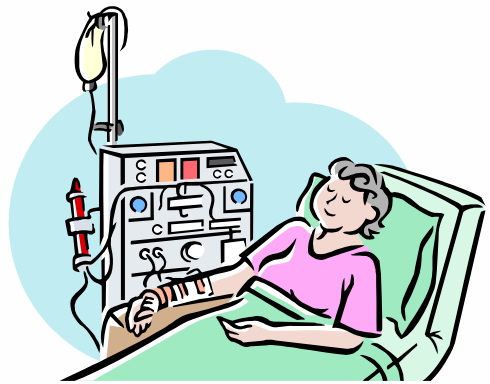
- Lipid Standardization Program
  - TC, HDLC, TG
- Cholesterol Reference Method Laboratory Network
  - TC, HDLC, LDLC
- IFCC
  - Apo-A1, Apo B
- LDL subclasses

Diabetes

- IFCC HbA1c Network
- NGSP Steering Committee
  - Funding for administrative core
- Glucose Monitor Variability Project
- Autoantibody Standardization Program
- ADA Insulin Standardization Program

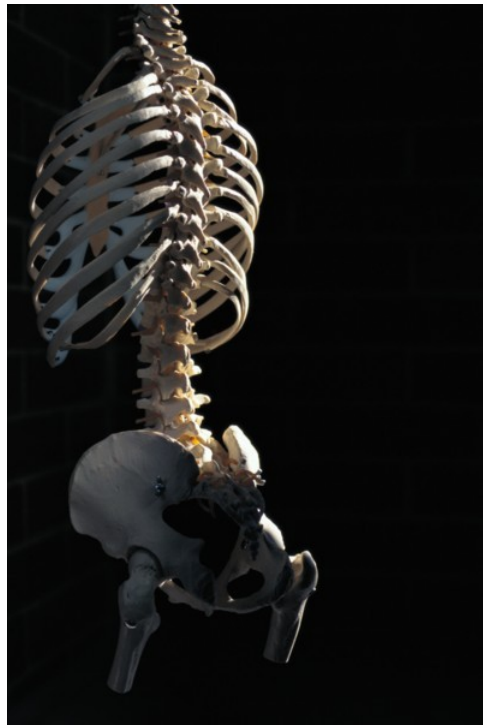
Kidney Disease

- National Kidney Disease Education Program
  - Collaborated with CAP for state-of-the-art study of serum creatinine measurement
  - NKDEP Lab Working Group
    - Recommendations for improving and standardizing creatinine measurement for use in estimating GFR (scheduled for publication in Jan 2006).
  - IFCC WG to improve estimation and use of GFR



Osteoporosis

- Bone marker standardization
  - Developed a reference system for standardization of pyridinoline and deoxypyridinoline
    - Primary reference materials
    - Primary reference method
    - Secondary reference materials
  - Transferred knowledge and experience to IFCC and CLSI.



Cholesterol Reference Method Laboratory Network's Quality Management System

Cholesterol Reference Method Laboratory Network (CRMLN)

- Program to improve laboratory performance
- Focus on manufacturers of diagnostic assays
- Goals of CRMLN
  - assist manufacturers to minimize calibration bias compared to CDC reference methods
  - provide traceability of clinical laboratory measurements
  - transfer improved performance to clinical laboratories

ISO 15195
Management System Requirements

Requirement	CRMLN
Organization & Management	COI policy CRMLN coordinator
Quality Management System	Manual of Operations
Personnel	Can be documented
Documentation & Records	Paper and electronic
Contracting	NA?

ISO 15195
Quality Management System

This requirement has 24 elements, most of which can be easily incorporated into an updated Manual of Operations for the CRMLN

- Quality policy
- Org. chart & description
- Description of premises
- Safety requirements
- Reference materials
- Equipment description, maintenance, & validation
- Measurands
- RMPs used
- Internal and external QC assessments
- CoI policies
- Internal audit and review
- Document control and maintenance
- Regulatory requirements
- Signatories for certificates

ISO 15195
Quality Management System

- Some other issues will take some work and development of policies
  - Error feedback, corrective action, and reporting
  - Deviations from approved procedures
  - Complaints and resulting actions
  - Confidentiality and proprietary rights of customers
  - Accreditation status and accrediting body.

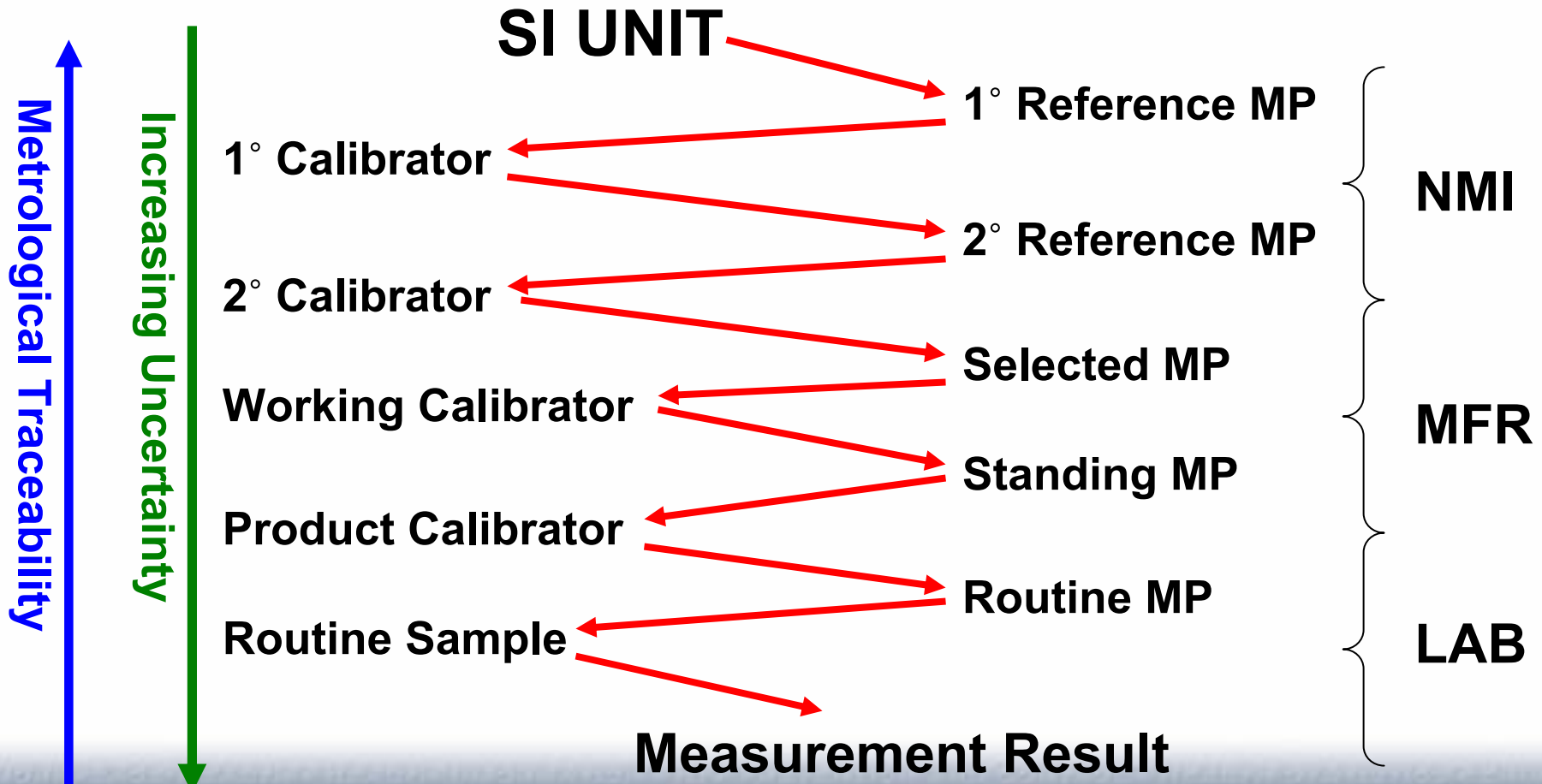
ISO 15195
Technical Requirements

Requirement	CRMLN
Premises and environmental	Documentation needed
Sample handling	Fully described in customer protocols
Equipment	Fully described in RMP
Reference Materials	SRM 911b, CDC reference materials prepared by CLSI C37-A

ISO 15195
Technical Requirements

Requirement	CRMLN
RMPs	Fully described and documented
Traceability/Uncertainty	Completed for CDC. Needs to be completed for CRMLN labs
Quality Assurance	Fully described and documented
Reporting	Certificate partially meets requirements

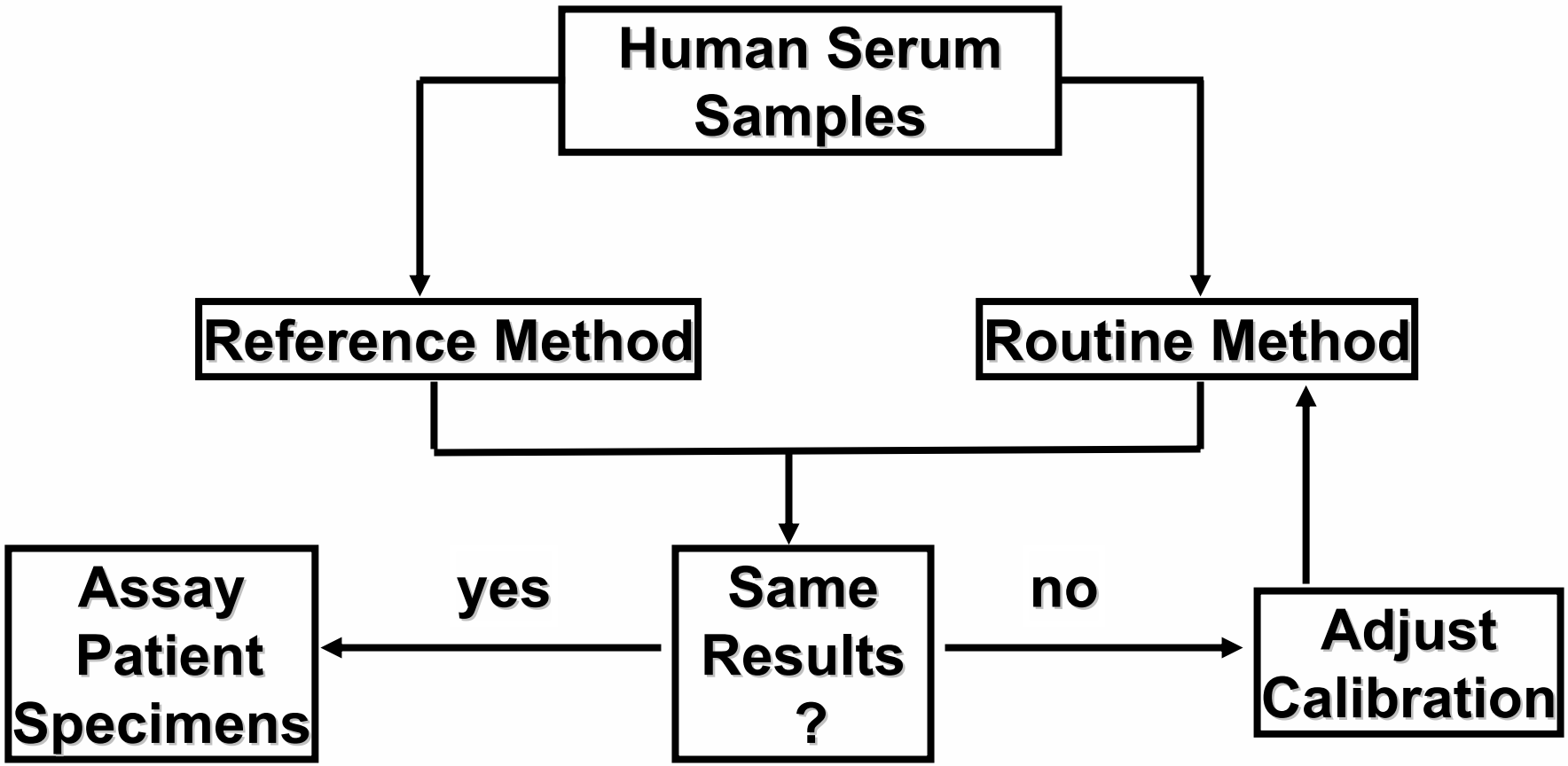
Traceability Chain



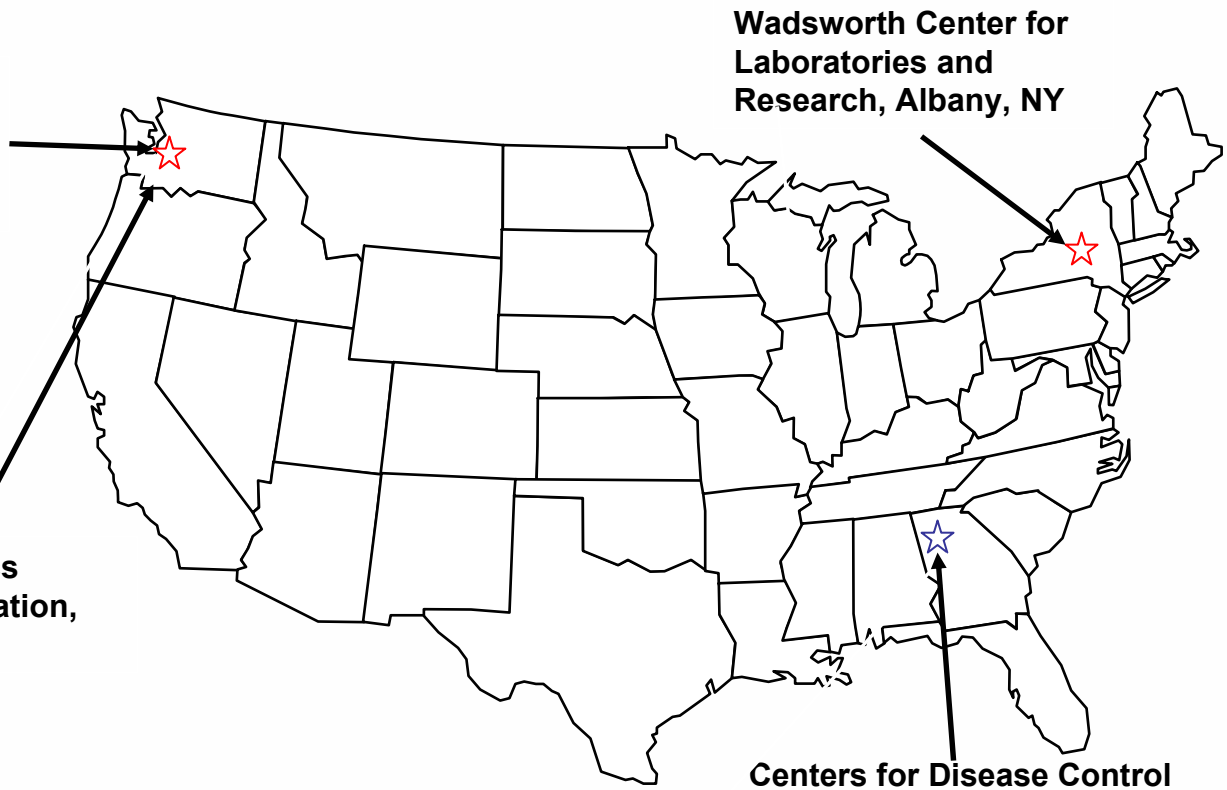
CRMLN Traceability

Responsible Party	Service/Activity	Method/Material
BIPM	SI units Key Comparisons	NMI Interlab Comparisons
NIST	Primary RMPs Primary RM Secondary RM	Gravimetry → SRM 911b IDMS → SRM 1951a, 1951b
CDC	Secondary RMP	SRM 911b → Abell-Kendall
CDC	Comparison to IDMS	AK → SRM 1951
CDC	Secondary RM	AK → CLSI C37-A materials
CRMLN	Secondary RMP	SRM 911b → Abell-Kendall
Manufacturer	Comparison to AK	Routine MP Fresh serum samples Product Calibrator
Clinical laboratory	Patient Sample Analysis	Product Calibrator Routine MP Patient Samples

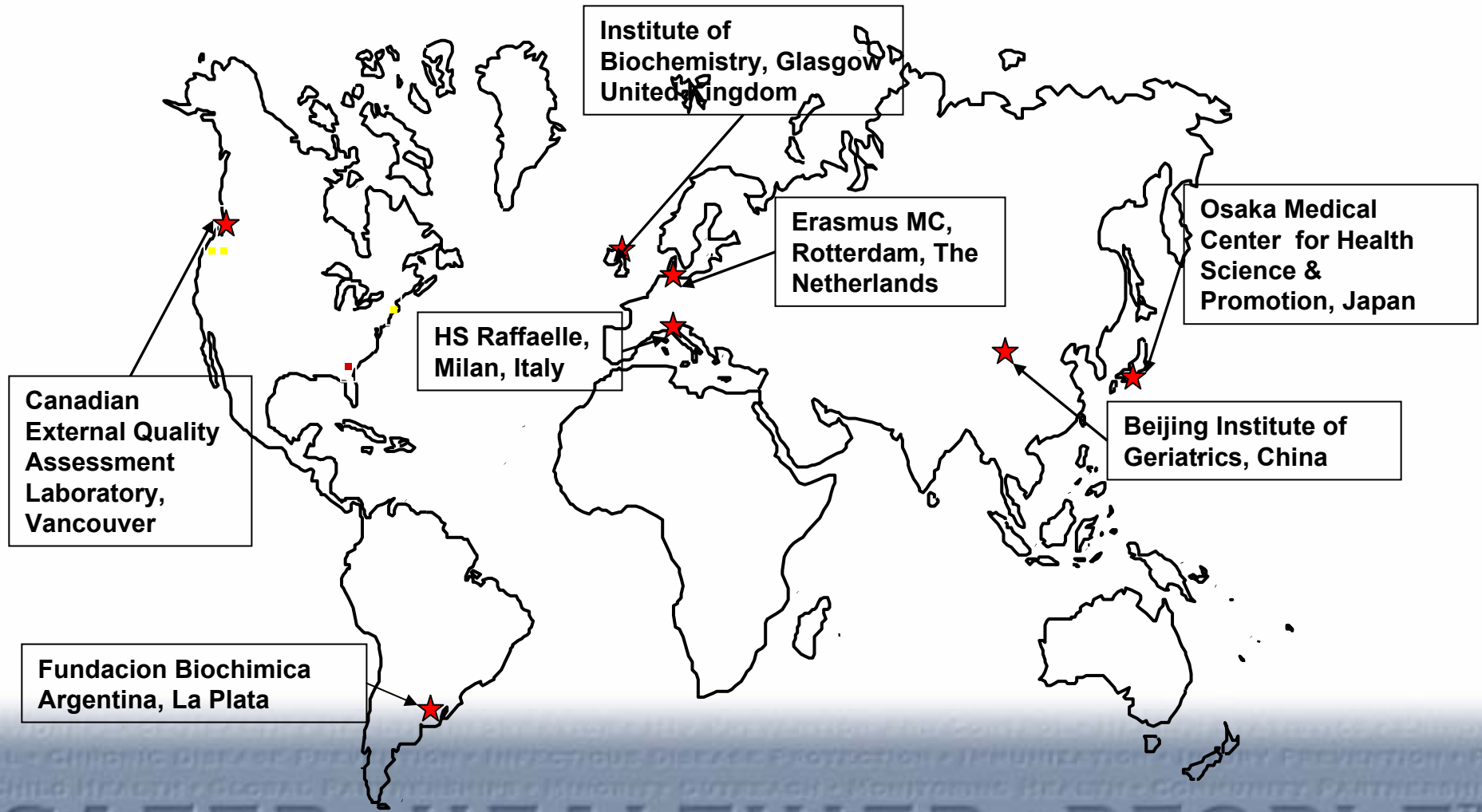
CDC Approach to Traceability



CRMLN
US Members



CRMLN
International Members



Quality Management

- Manual of Operations
- Establish performance criteria
- Method audits
  - identify critical aspect in each procedural step
- Training: on-site at CDC

Quality Management

- Quality Assurance
  - common QC materials and procedures
  - common calibrators
  - blind external performance audits (bimonthly)
- Communication
  - conference calls
  - face-to-face meetings
  - virtual communication

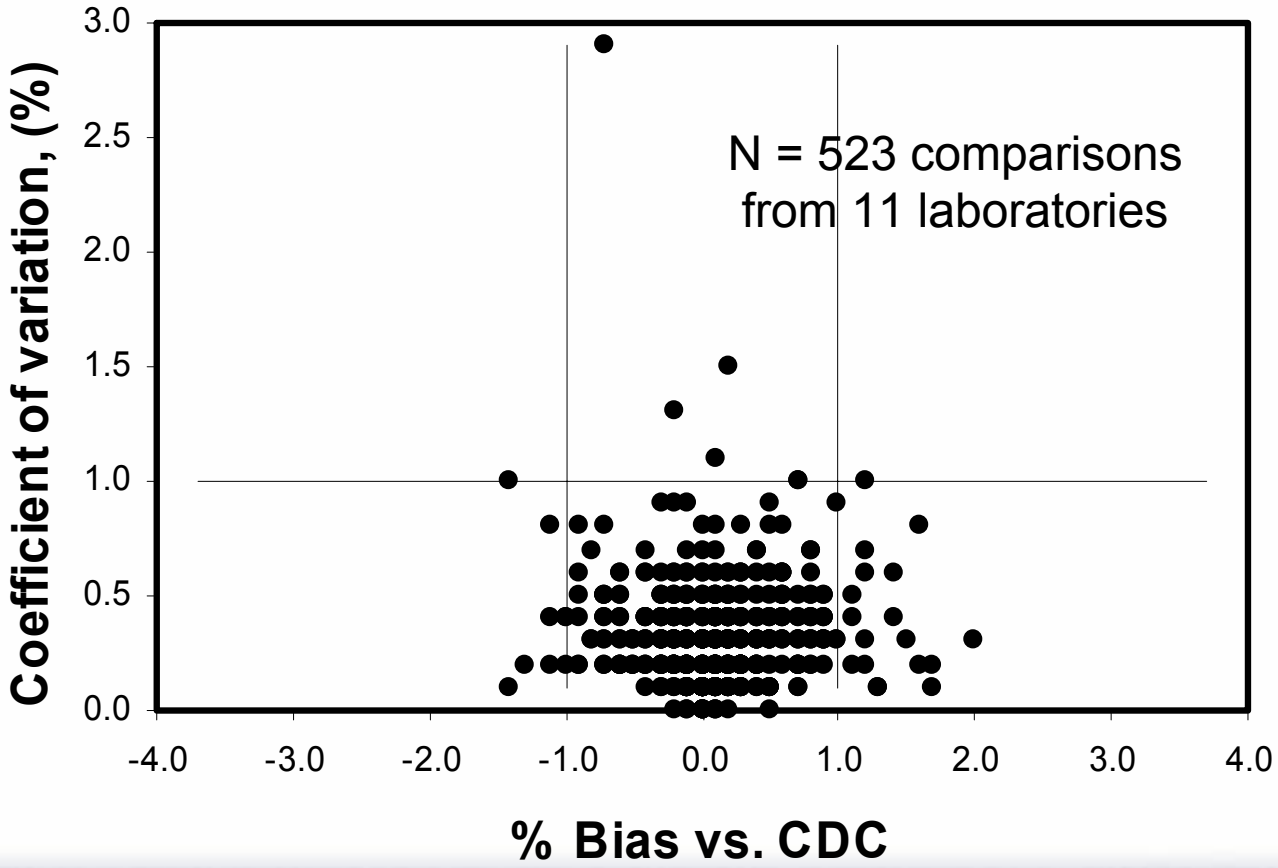
Methods and Performance Criteria

Analyte	Method	Bias vs CDC	Imprecision
TC	Abell-Kendall (AK)	≤ 1%	CV ≤ 1%
HDLC	50K dextran-sulfate with AK or Ultracentrifugation with AK	≤ 1 mg/dL	SD ≤ 1 mg/dL
LDLC	Betaquantification with AK	≤ 2%	CV ≤ 1.5%

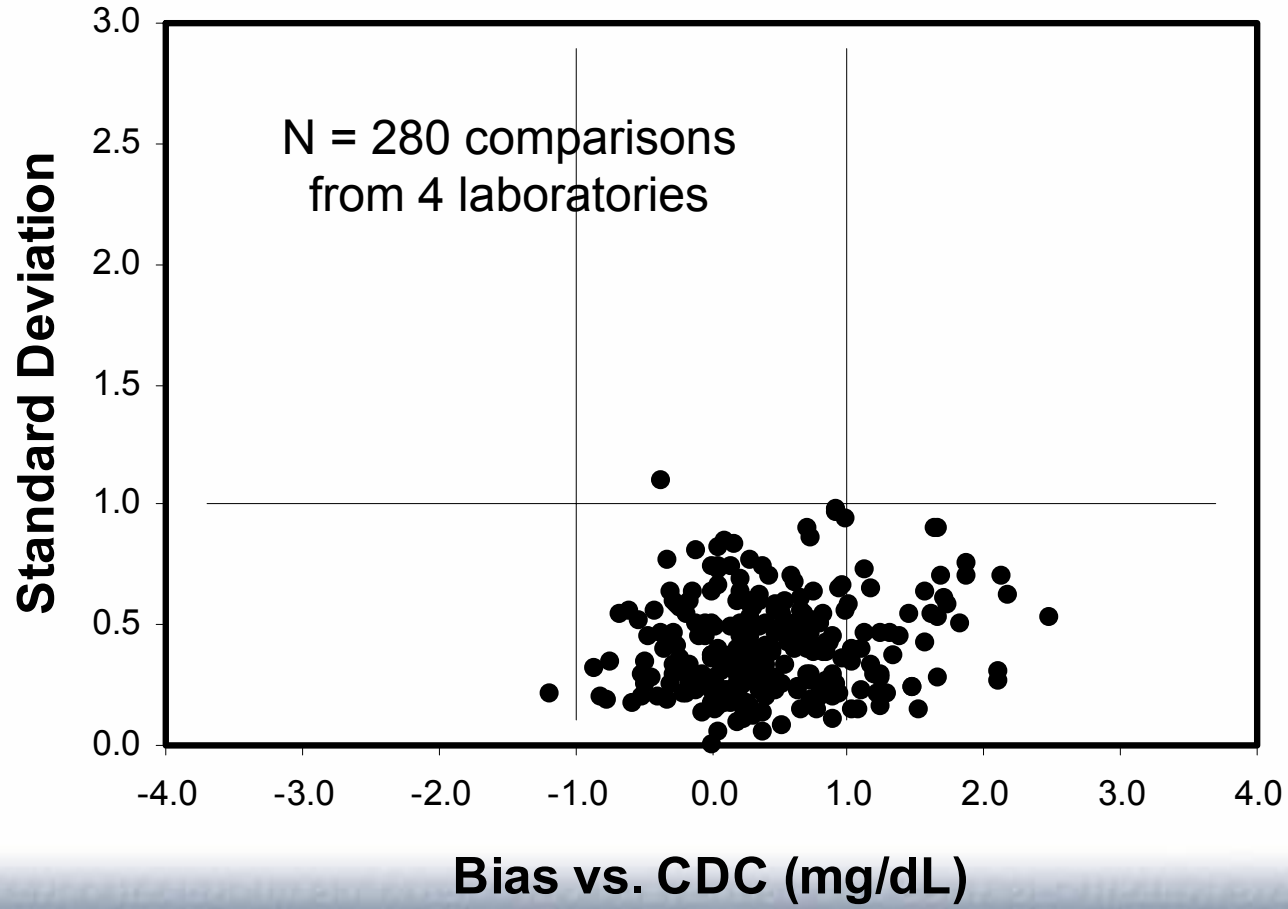
Performance Survey

- Total Cholesterol
  - 3 unknown pools (low, medium, high)
  - Each pool analyzed in duplicate in 2 runs
- HDL-C DCM and UC
  - 4 unknown pools (levels 1-4)
  - Each pool analyzed in duplicate in 4 runs
- LDL-C
  - 4 unknown pools (levels 1-4)
  - Each pool analyzed in quadruplicate in 4 runs

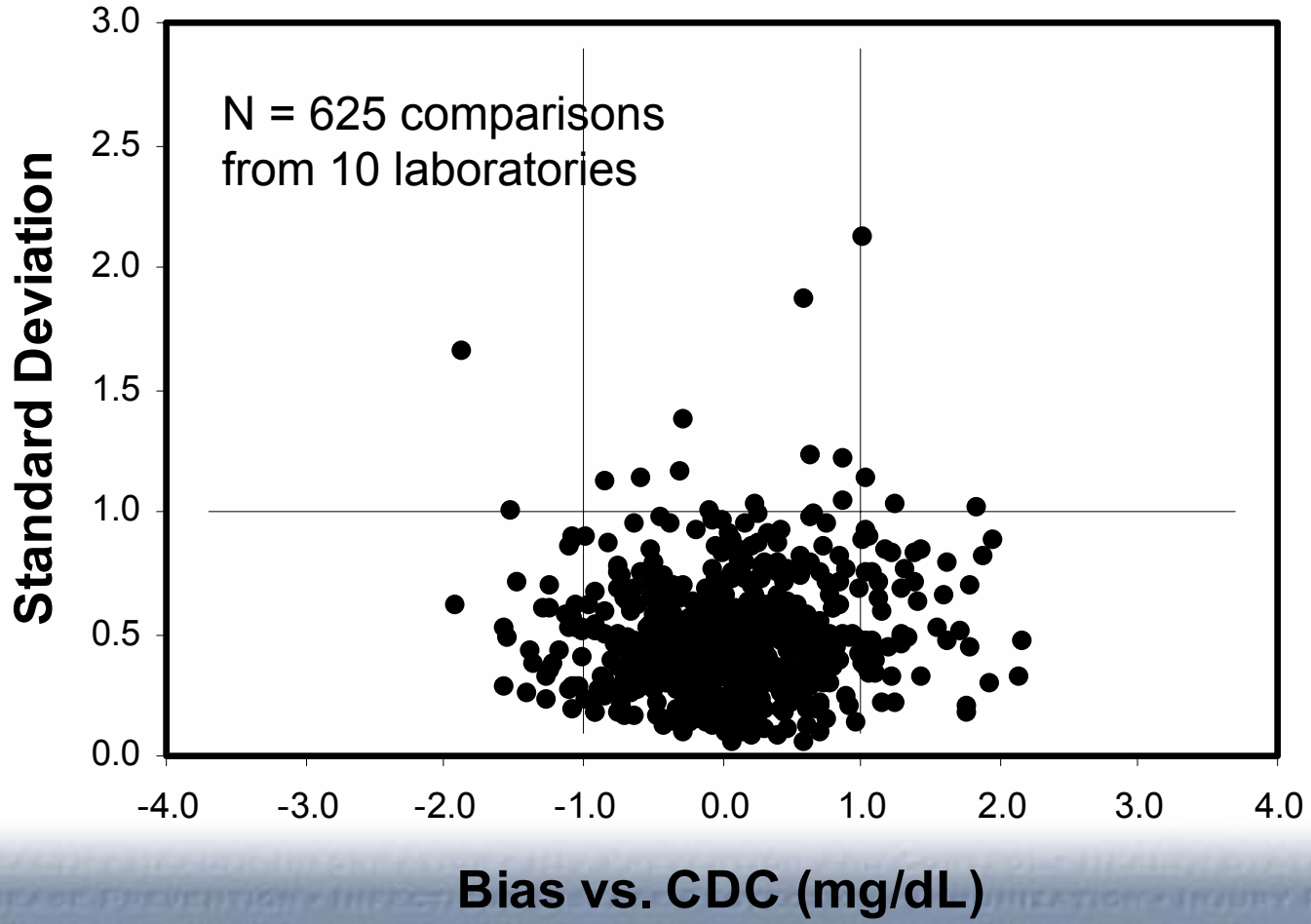
CRMLN Total Cholesterol CV vs. Bias for 2001-2003



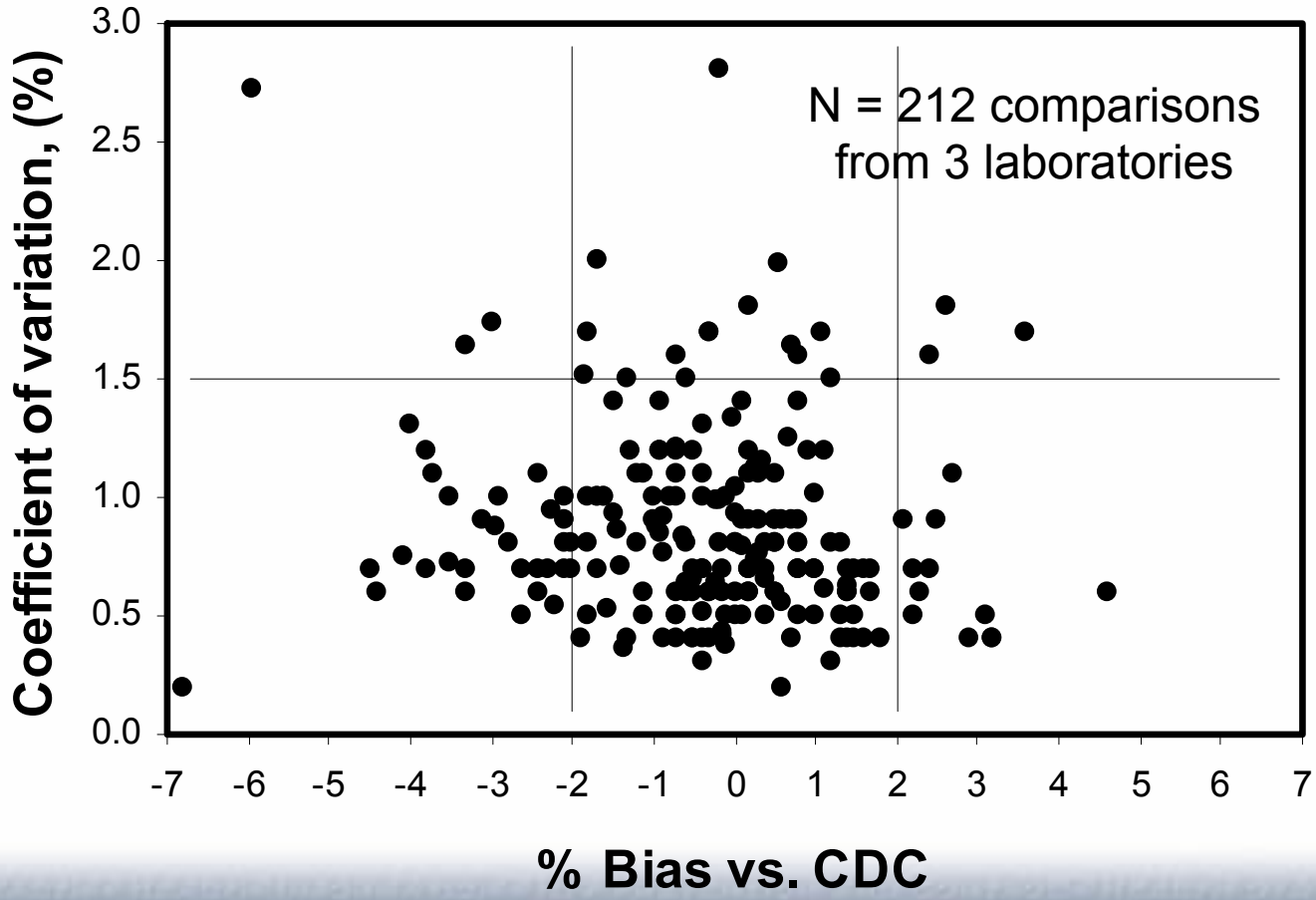
CRMLN HDLC-UC SD vs. Bias for 2001-2003



CRMLN HDLC-DCM SD vs. Bias for 2001-2003



CRMLN LDL-C CV vs. Bias for 2001-2003



Manufacturer Certification

- Fresh sample comparison
  - Manufacturer is responsible for sample collection.
  - Fresh samples analyzed by test method.
  - Frozen samples (≤ –70ºC) analyzed by reference method (except for LDLC).
- Sample collection: CLSI H3-A4.
- Precision testing, e.g. CLSI EP5-A.
- CLSI EP-9A

Criteria

- Based on NCEP guidelines
  - Average absolute bias
  - Bias at medical decision points
  - Imprecision
- Correlation coefficient ≥ 0.975
- No between-method outliers (one sample may be omitted).
- ≤ 1 within-method outlier allowed.

CHOLESTEROL REFERENCE METHOD LABORATORY NETWORK

Certificate of Traceability

This certifies that

Manufacturer Name
City, State (or Country)

has documented traceability to the **National Reference System for Cholesterol** by performing a direct comparison with the cholesterol reference method using fresh human specimens which cover the National Cholesterol Education Program medical decision points. This analytical system is representative of the manufacturer's product and has demonstrated the ability to meet the NCEP's performance criteria for accuracy and precision. The comparison shows that the performance of this analytical system is as follows:

Among-run %CV	Average %Bias	Total Error
0.6%	0.6%	1.8%

The comparison was performed with

CRMLN Laboratory Name
City, State (or Country)

The system evaluated was:

Instrument:
Model XYZ

Calibrator:
Total Cholesterol Calibrator
Lot#: 111ABC
Set point: 177 mg/dL

Cholesterol reagent:
Total Cholesterol Reagent
Lot #'s: R1: 000RAB; R2: 000RLA

Matrix:
Venous Serum

Date of evaluation: March 25, 2004

Date of expiration: March 25, 2006

CRMLN Laboratory Director _____

http://www.cdc.gov/labstandards/crmln.htm

Accreditation of reference method laboratory networks

Accreditation of Networks

- Recommendation: JCTLM Executive consider a model for accreditation of a network of reference laboratories by an ILAC signatory with the central laboratory responsible for:
  - an overarching management system and documentation for the network, and
  - monitoring and documenting compliance of network laboratories with that system.

Accreditation of Networks

- ISO requirements must be met within the network.
- CRMLN, IFCC HbA1c, NGSP have quality systems already in place and have demonstrated that they can maintain quality and performance over time.
- If an individual lab within the network wants accreditation for a measurand outside the purview of the network, then that lab can get accredited separately.
- Resourceful, economical.

Thank you!