Standardization Activities at the National Center for Clinical Laboratories

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About the Center

- An institution and agency of the Ministry of Health
- Mission: to improve the quality of clinical laboratory testing through evaluation, investigation and management
- Organization: EQA Offices and Laboratories specialized in clinical biochemistry, hematology, immunology, microbiology and molecular biology

Scientific activities

- National EQA for clinical laboratories
- Researches and investigations on quality issues
- Reference system development and implementation

Collaborations

- Professional organizations
- Local Centers for Clinical laboratories
- University and institute laboratories
- Metrological institutes
- Clinical laboratories
- Manufacturers

2003-07 National EQA, selected analytes

- All method interlaboratory CV
- Participants ~900, mostly Tier III hospital laboratories

	2003	2004	2005	2006
Cholesterol	4.4	4.7	4.6	4.2
Triglycerides	11.3	11.1	17.5	11.4
HDLC	18.7	16.8	14.6	14.3
LDLC	15.1	13.6	13.7	12.9
ALT	11.3	9.7	9.9	7.9
AST	10.7	9.4	10.1	8.2
Sodium	2.4	2.3	2.5	2.2
Chloride	3.7	3.3	3.9	3.2
Glucose	4.5	4.8	4.3	4.4
Creatinine	10.8	13.8	13.6	7.0
Uric acid	6.3	6.1	5.6	5.2
Urea	5.3	5.9	4.7	4.5

Beijing 2006 fresh serum HDL-C survey

- Fresh serum pool distributed
- Repeated measurements

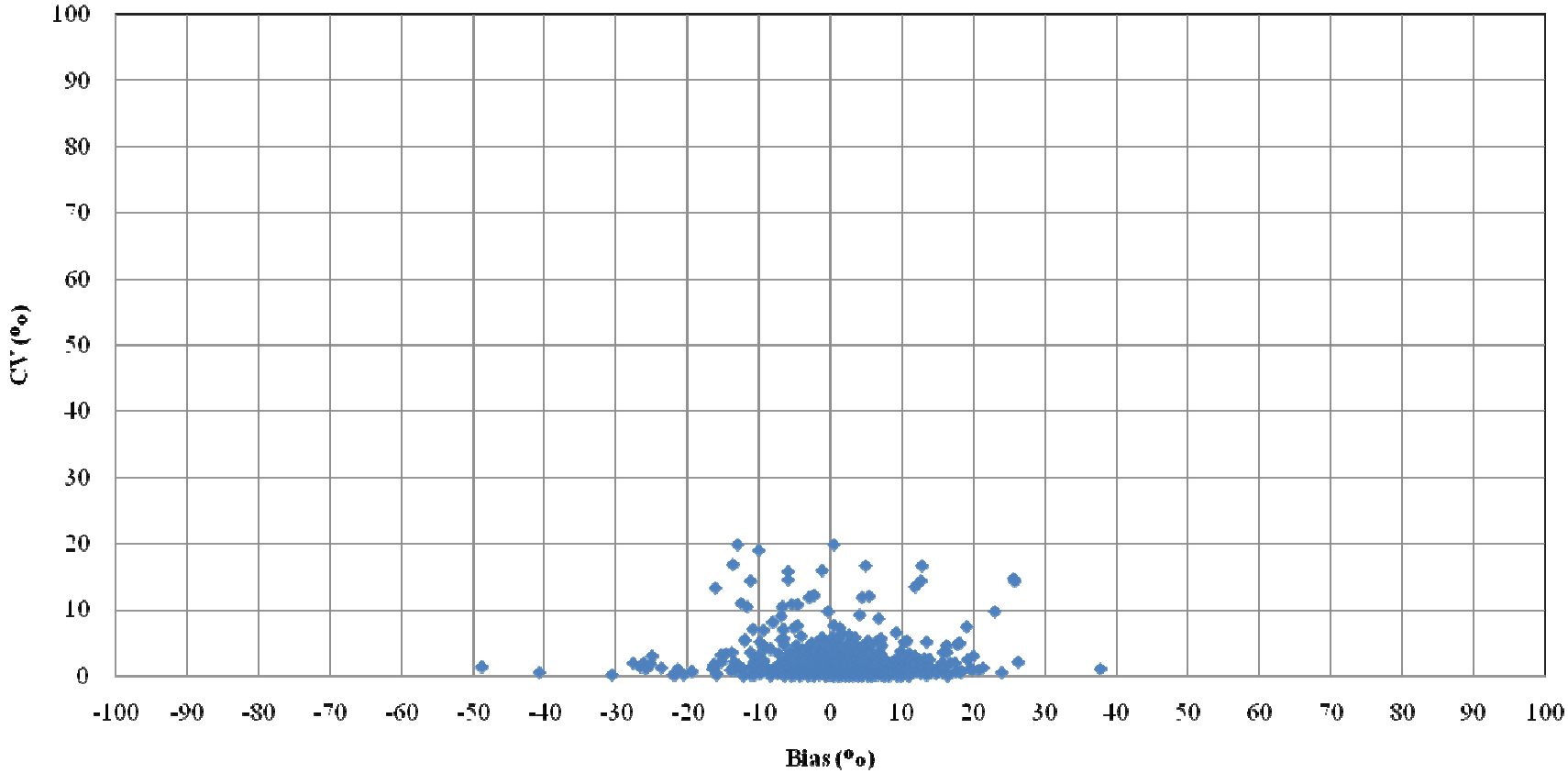
	Mean	Bias
Lab 1	1.53	24%
Lab 2	1.22	-1%
Lab 3	1.23	0%
Lab 4	1.53	24%
Lab 5	1.58	28%
Lab 6	1.05	-15%
Lab 7	1.22	-1%
Median	1.23	
Average	1.34	
CV	15%	

Lipid and lipoprotein performance in a clinical study, 1997-2000

- CHD secondary prevention study
- 65 participating laboratories nationwide
- 1997-2000, 8 surveys
- Frozen serum, 3 levels
- Measured by each lab 3 times in triplicate
- ~1500 measurement events, CV and Biases calculated

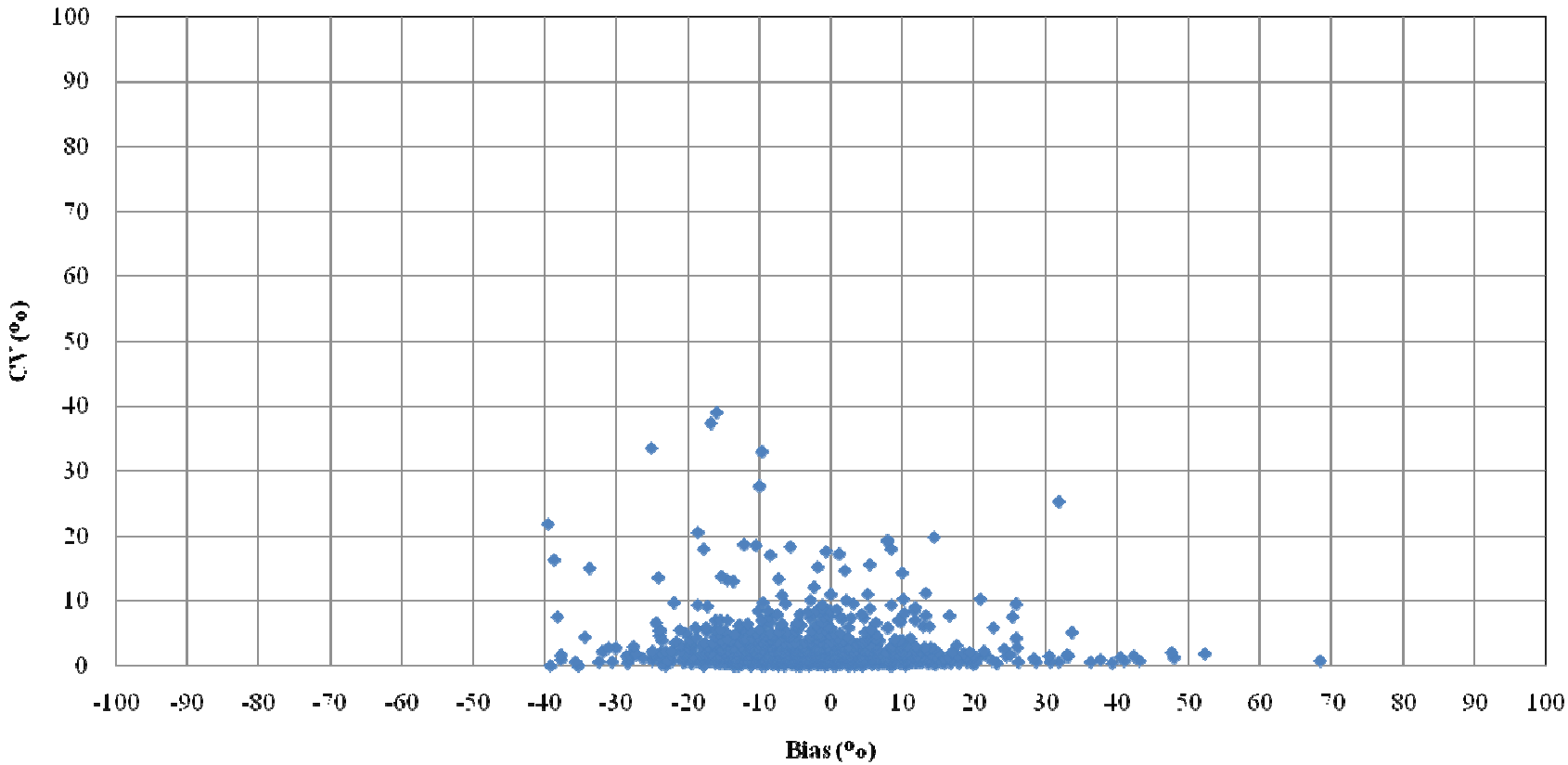
Lipid and lipoprotein performance in a clinical study, 1997-2000

Total cholesterol, ~50% Bias<3%



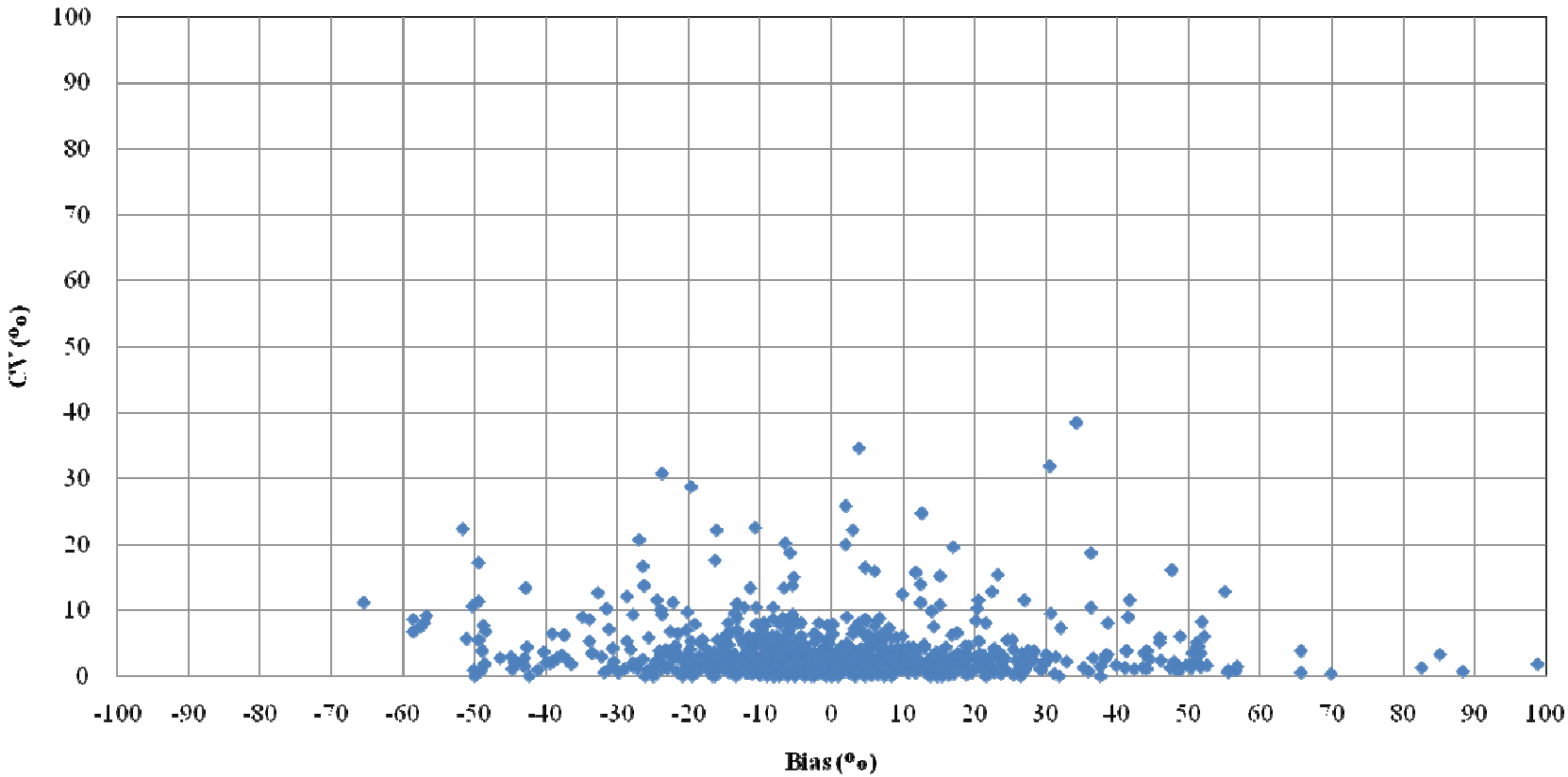
Lipid and lipoprotein performance in a clinical study, 1997-2000

Triglycerides, ~40% Bias<5%



Lipid and lipoprotein performance in a clinical study, 1997-2000

HDL cholesterol, ~25% Bias<5%



Situations and issues

- Diverse analytical systems
  - number of manufacturers
  - method combinations and modifications
  - national EQA 2007, chemistry :
    - ~1000 participants
    - ~130 instrument models
    - >90 reagent and calibrator manufacturers
    - hundreds of systems
- EQA difficult
  - peer group impossible or difficult for some analytes
  - pass one, fail another

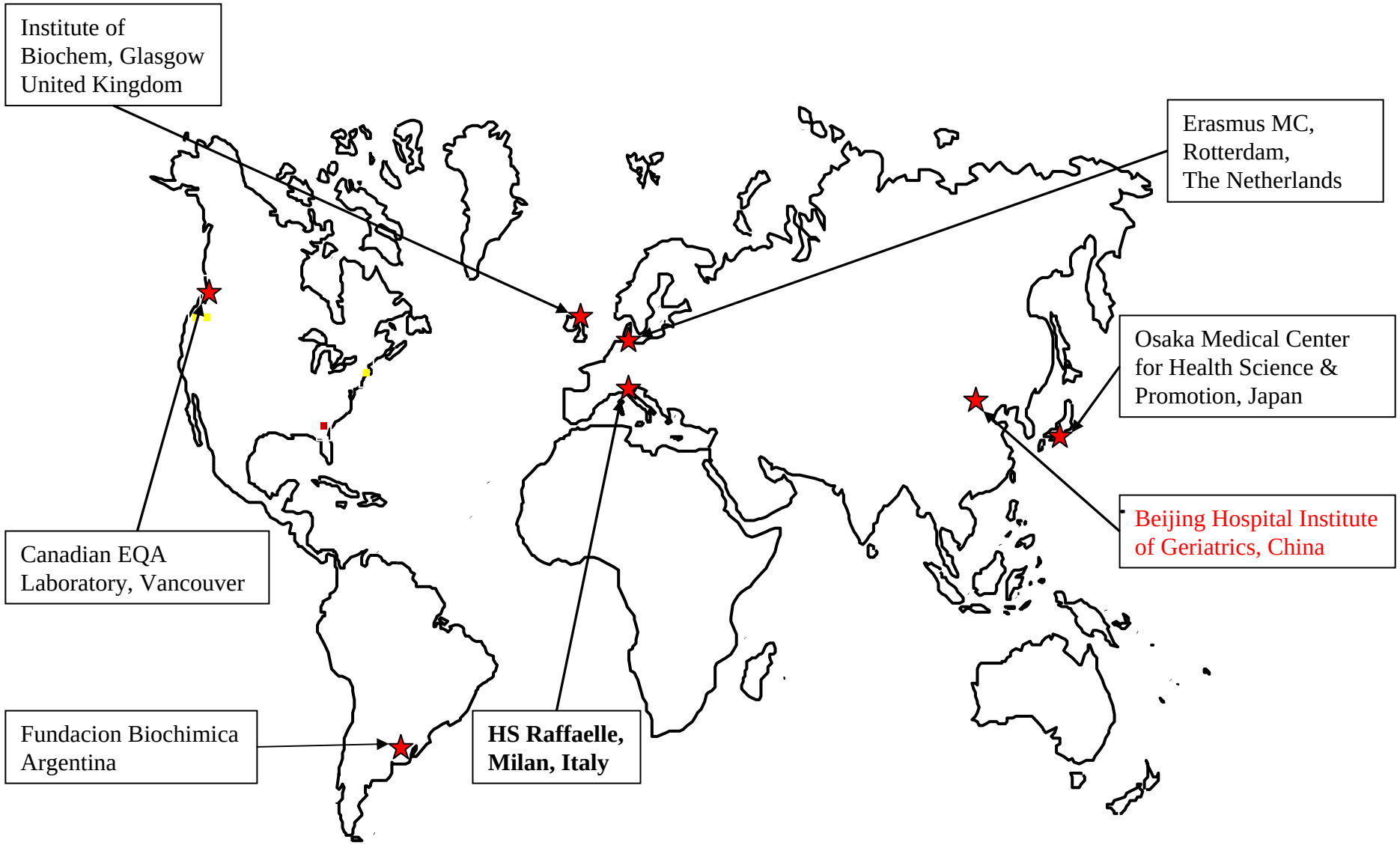
The Roles of reference systems

- EQA organizers
  - target value assignment
  - property investigations of the materials
- Manufacturers
  - calibration
  - evaluation or verification
- Clinical laboratories
  - verification of the trueness

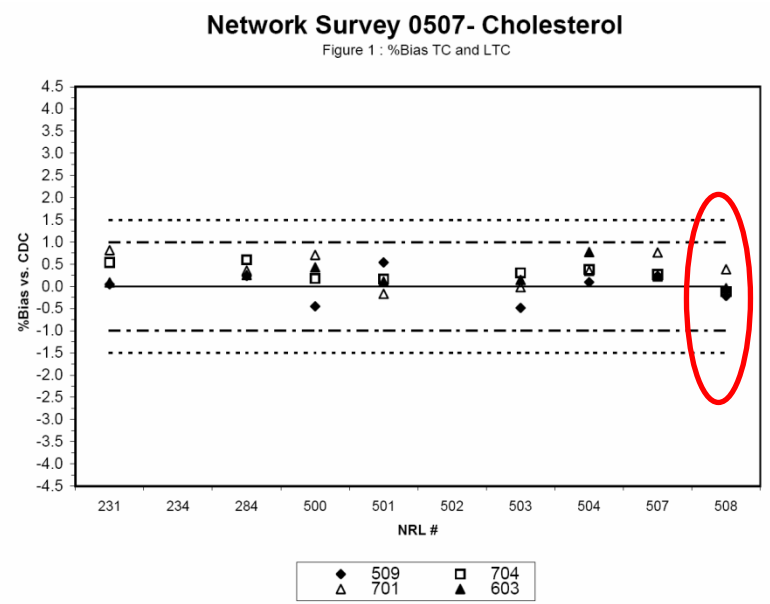
Reference system activities: lipids and lipoproteins

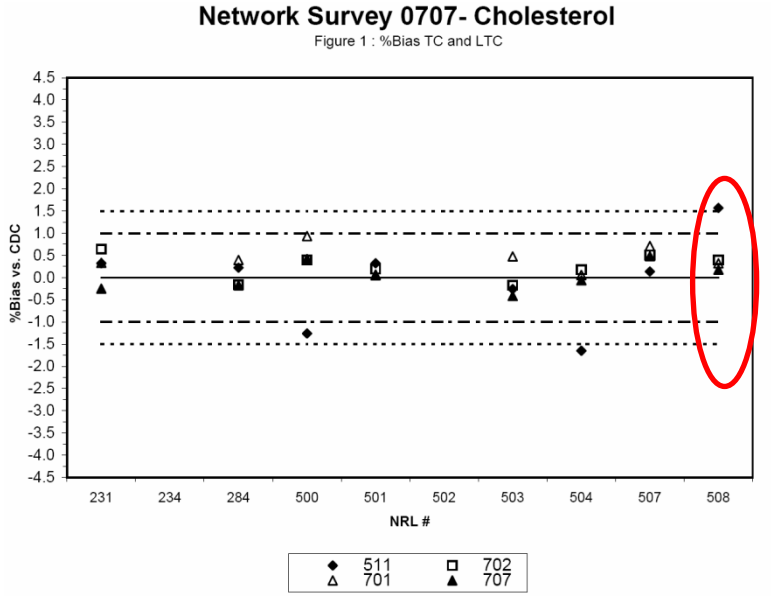
- Started in the early 80s by Dr. Jianzhai Li
- Candidate reference methods for cholesterol and triglyrides by HPLC
- IFCC apo AI and B calibrations
- CDC Abell-Kendall cholesterol and DCM HDL
- CDC CRMLN member since 2003
- National CRMs (GBWs) for cholesterol and triglycerides (pure substances and serum matrix)
- The CDC CRMLN cholesterol and HDL certifications
- Researches on UC/HPLC lipoprotein cholesterol and ID/MS cholesterol and triglycerides
- Beijing Hospital Institute of Geriatrics in collaboration with NIM

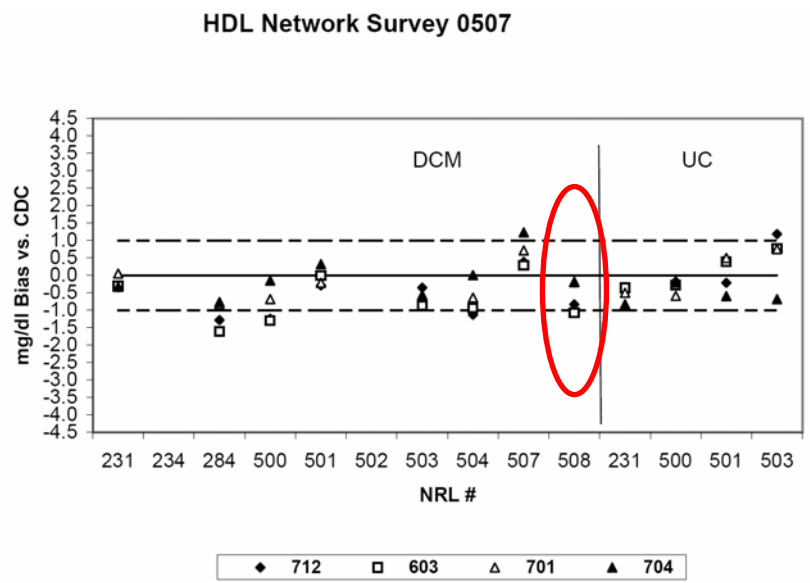
CRMLN International Members

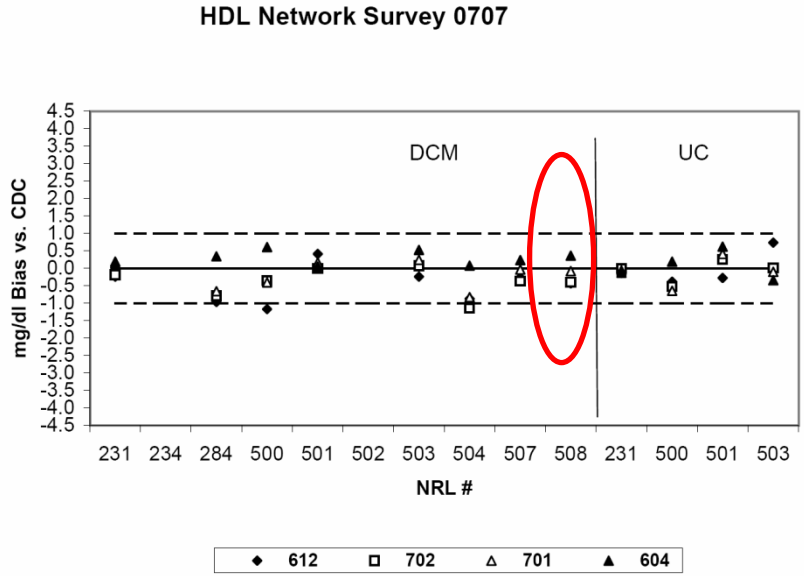


CDC CRMLN bimonthly survey



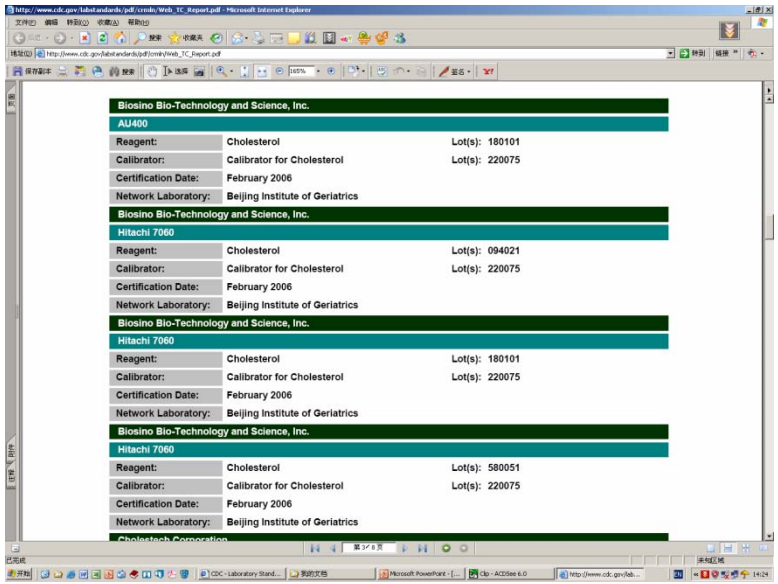






The cholesterol A-K reference method and HDL DCM activities

- 16 Chol systems of 3 manufacturers certified
- Certification of 2 HDL systems ongoing
- EQAS targeting
- Method evaluations

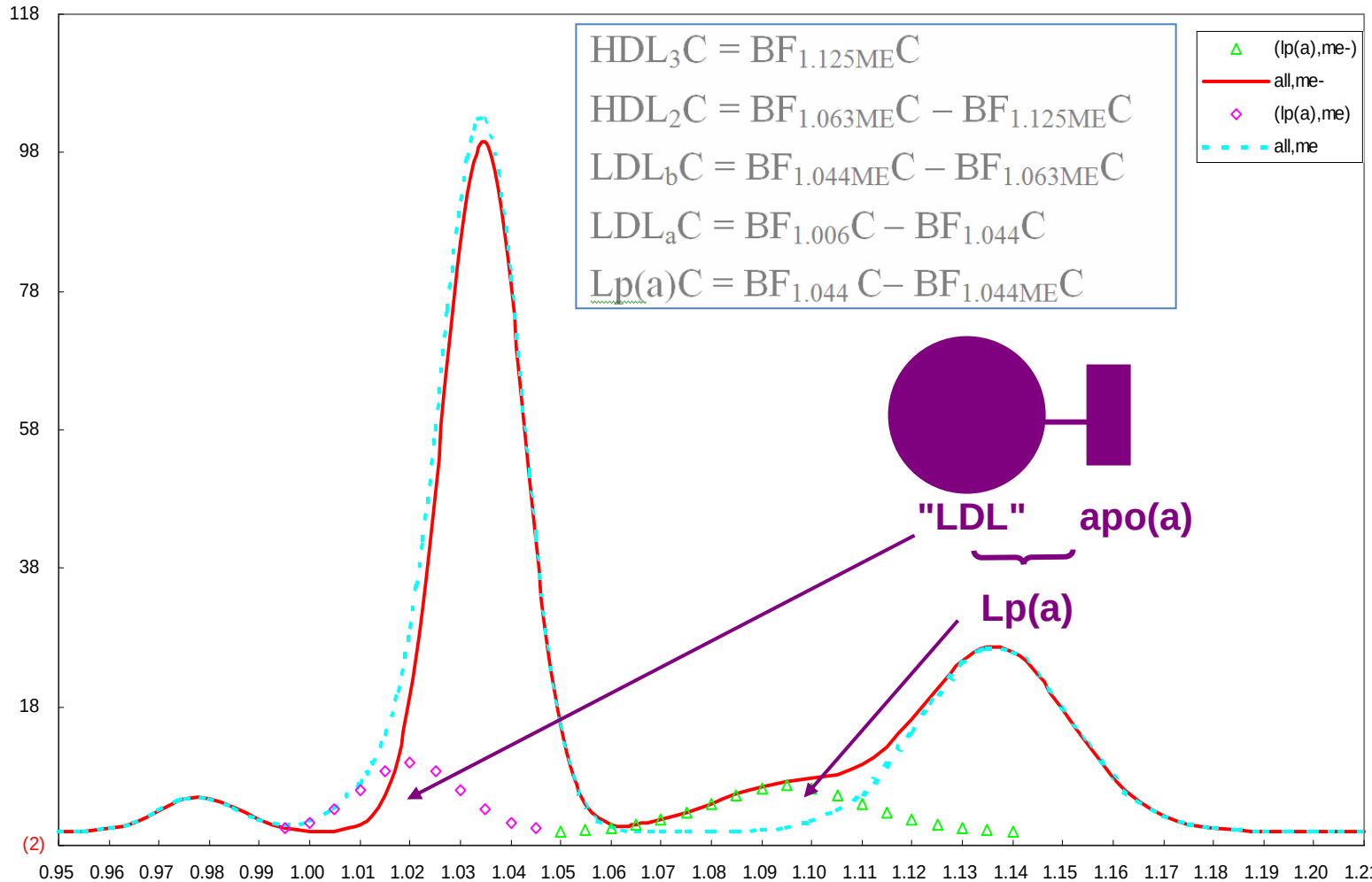


Biosino Bio-Technology and Science, Inc.		
AU400		
Reagent:	Cholesterol	Lot(s): 180101
Calibrator:	Calibrator for Cholesterol	Lot(s): 220075
Certification Date:	February 2006	
Network Laboratory:	Beijing Institute of Geriatrics	
Biosino Bio-Technology and Science, Inc.		
Hitachi 7060		
Reagent:	Cholesterol	Lot(s): 094021
Calibrator:	Calibrator for Cholesterol	Lot(s): 220075
Certification Date:	February 2006	
Network Laboratory:	Beijing Institute of Geriatrics	
Biosino Bio-Technology and Science, Inc.		
Hitachi 7060		
Reagent:	Cholesterol	Lot(s): 180101
Calibrator:	Calibrator for Cholesterol	Lot(s): 220075
Certification Date:	February 2006	
Network Laboratory:	Beijing Institute of Geriatrics	
Biosino Bio-Technology and Science, Inc.		
Hitachi 7060		
Reagent:	Cholesterol	Lot(s): 580051
Calibrator:	Calibrator for Cholesterol	Lot(s): 220075
Certification Date:	February 2006	
Network Laboratory:	Beijing Institute of Geriatrics	

- Standardization of lipid and lipoprotein measurements in clinical, epidemiological studies

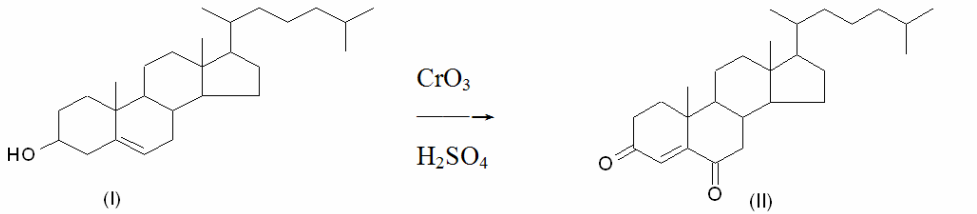
UC/HPLC HDL, LDL, Lp(a) and subclass cholesterol

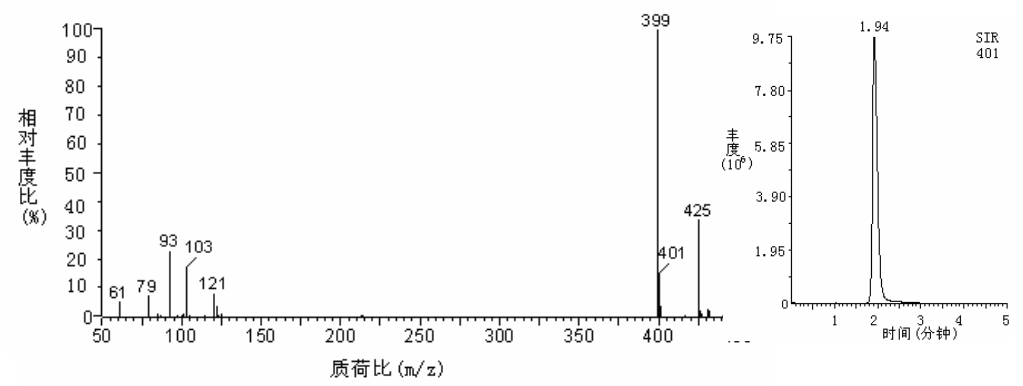
- Sample volume 0.1 ml (vs. 5 ml in the traditional betaquantification)
- HDL separation by UC [Lp(a) breakdown by mercaptoethanol] (vs. precipitation)
- Type 25 rotor (100 1-ml tubes)
- Lp(a) and subclass cholesterol possible



ID/LC/MS/MS Serum total cholesterol

- 3,4-$^{13}C_2$ cholesterol as internal standard
- Oxidized to 4-en-3,6-dione
- Positive ion APCI
- SIR and MRM detections
- Total CV <1%
- NIST SRM analysis





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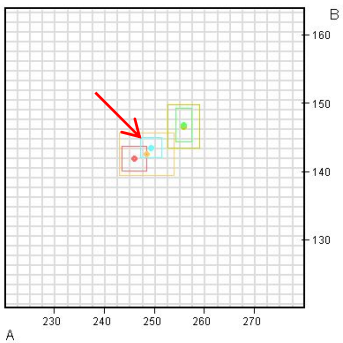
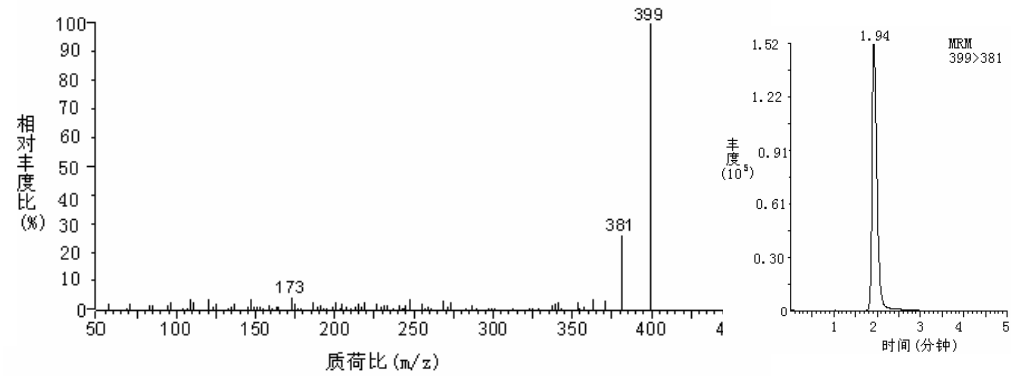
Total cholesterol [mg/dl]

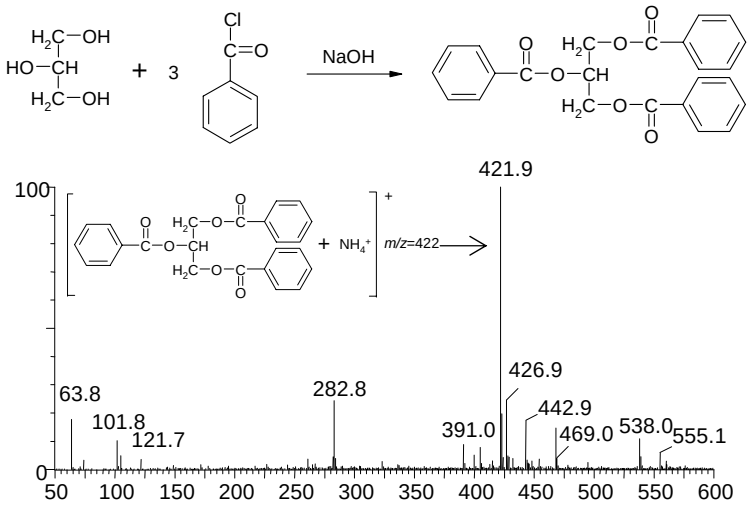


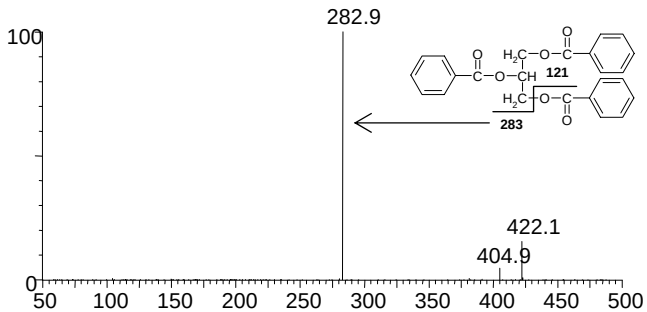
Lab	A	e.u.	B	e.u.	method
01	245,945	2,471	141,891	1,776	ID-MS
05	248,45	5,47	142,53	3,14	ID-MS
12	255,9	3,23	146,6	3,18	spectrometry (Abell-Kendall)
16	255,8	1,6	146,8	2,5	spectrometry (Abell-Kendall)
18	249,3	2,1	143,5	1,5	ID-MS

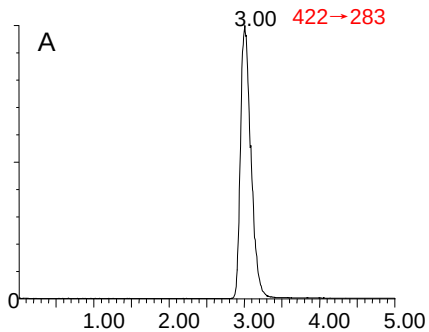


ID/LC/MS/MS Serum total glycerides

- 1,2,3-$^{13}C_3$ glycerol as internal standard
- Extracted by benzoylation
- Positive ion ESI
- MRM detection
- Total CV ~1%
- NIST SRM analysis







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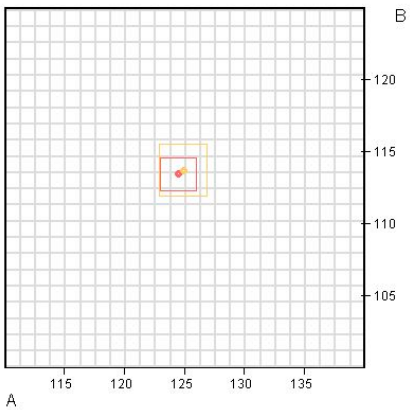
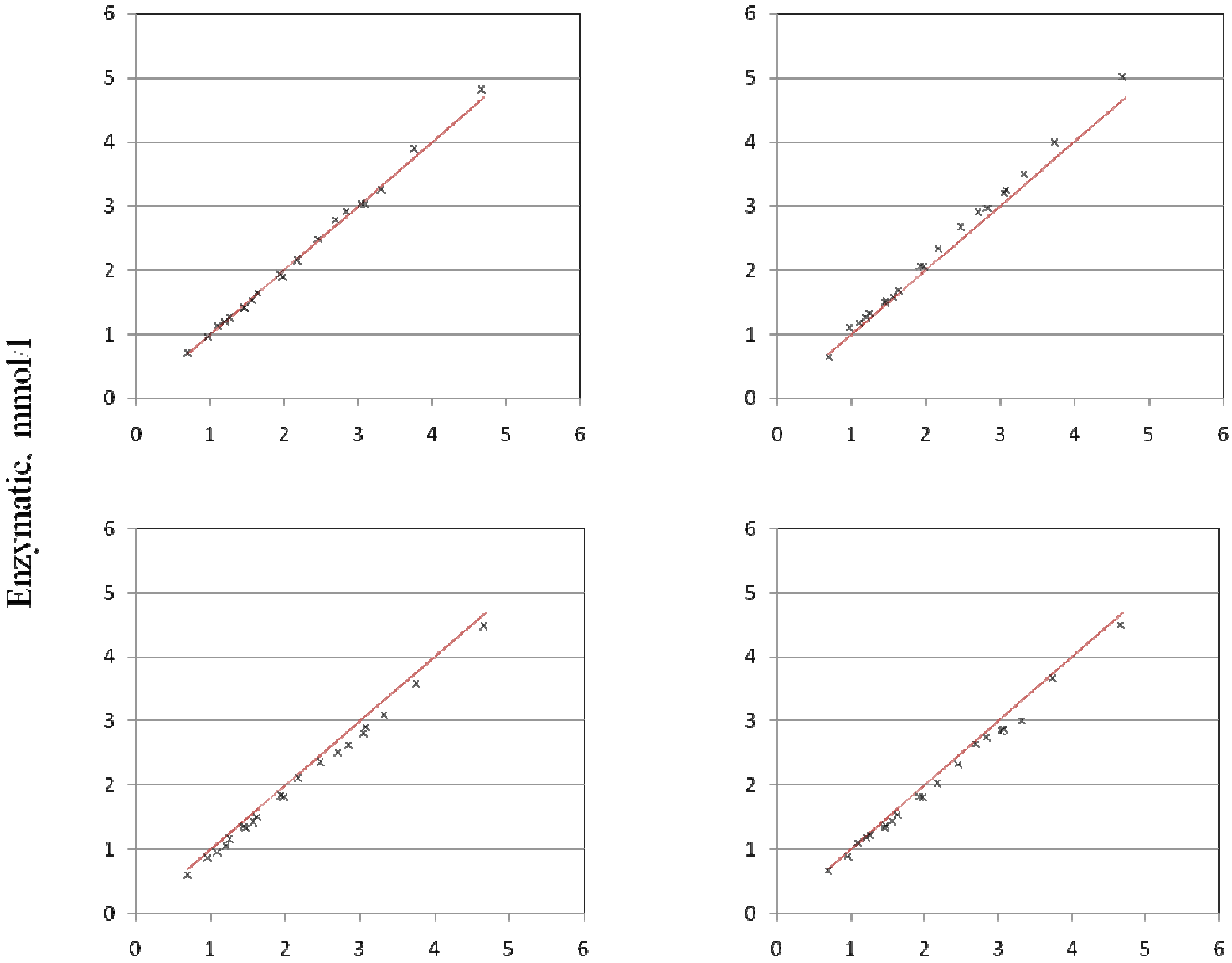
Total glycerol [mg/dl]

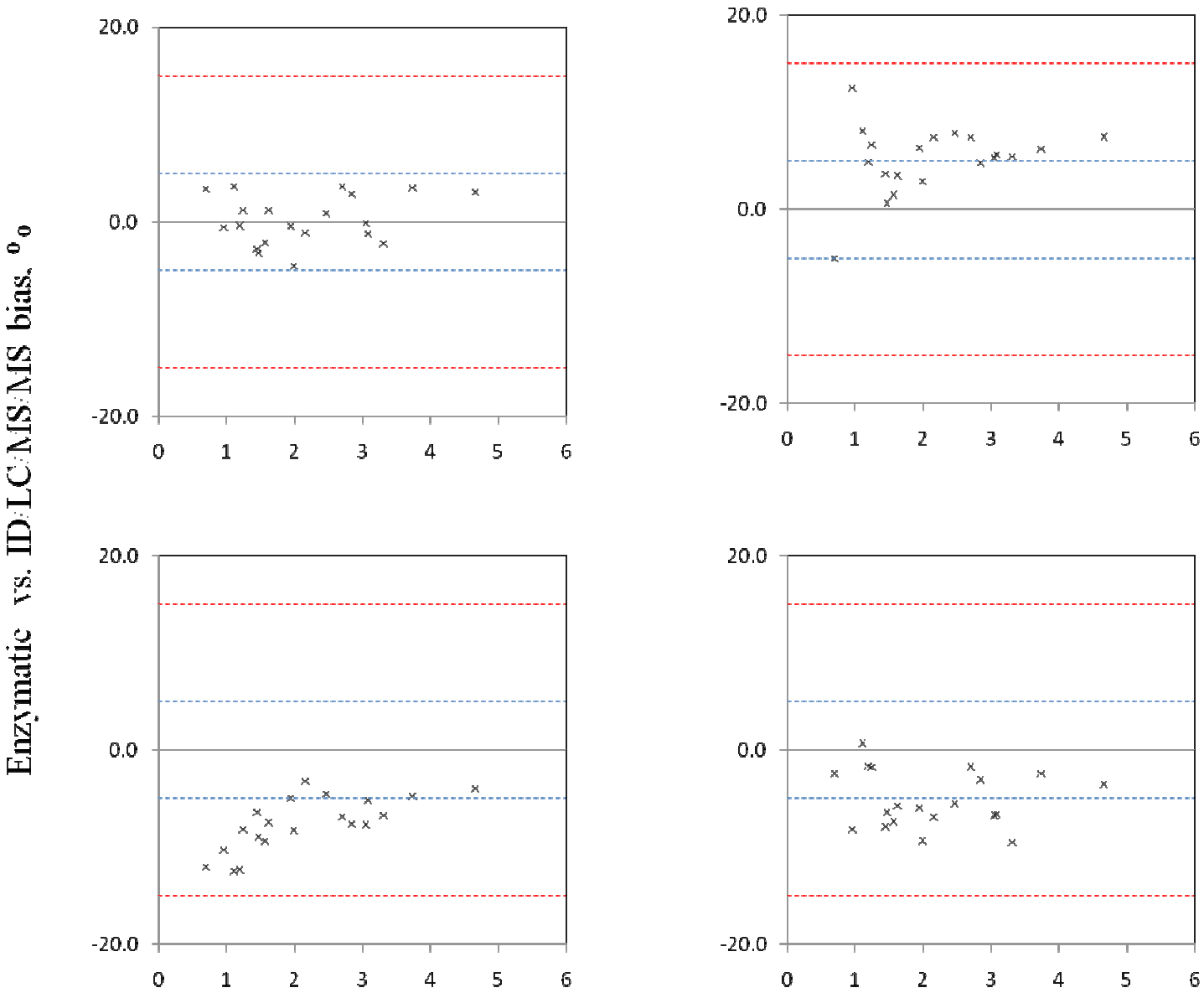


Lab	A	e.u.	B	e.u.	method
01	124,513	1,504	113,451	1,150	ID-MS
18	124,9	2,0	113,7	1,8	ID-MS

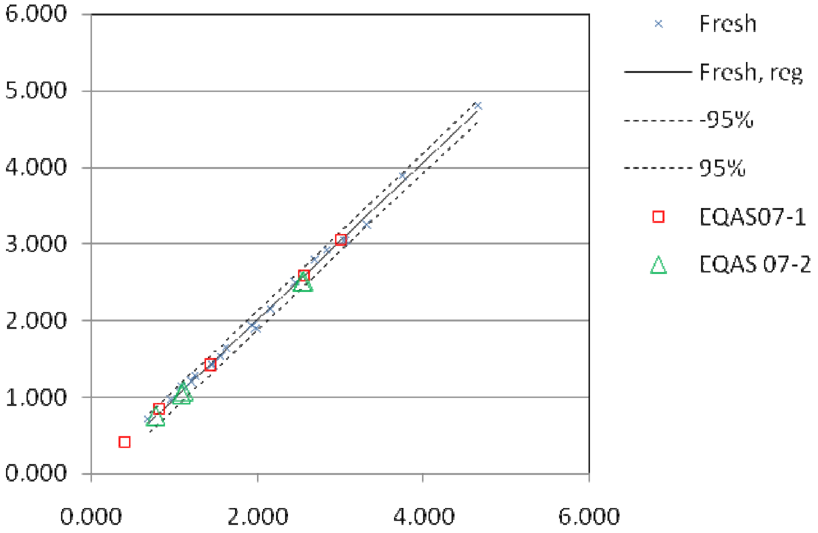
Triglycerides: enzymatic vs. ID-LC/MS/MS, correlation

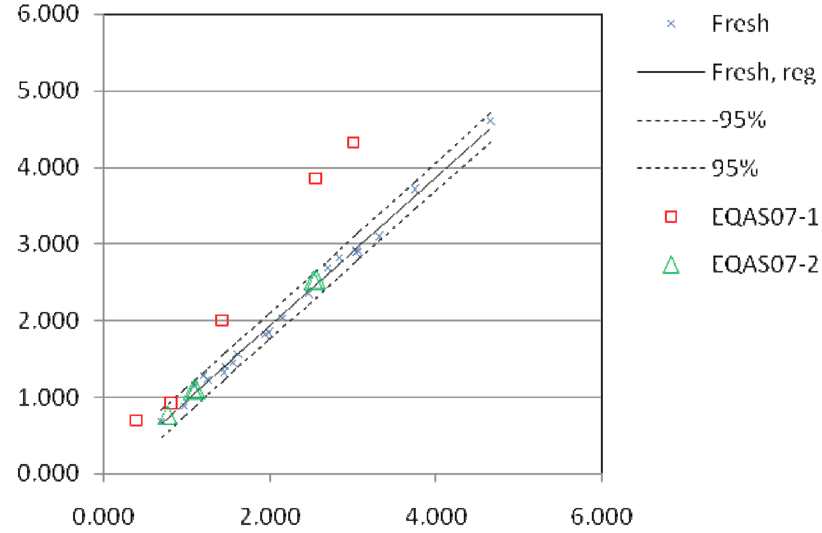


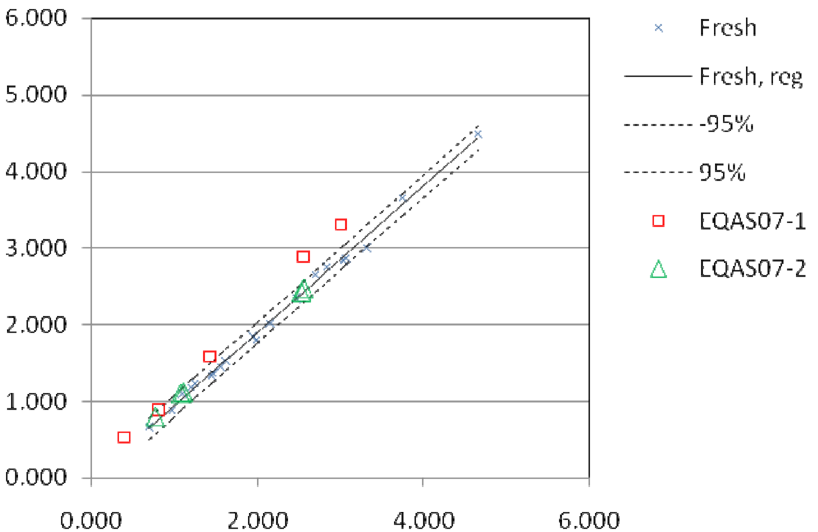
Triglycerides: enzymatic vs. ID/LC/MS/MS, bias

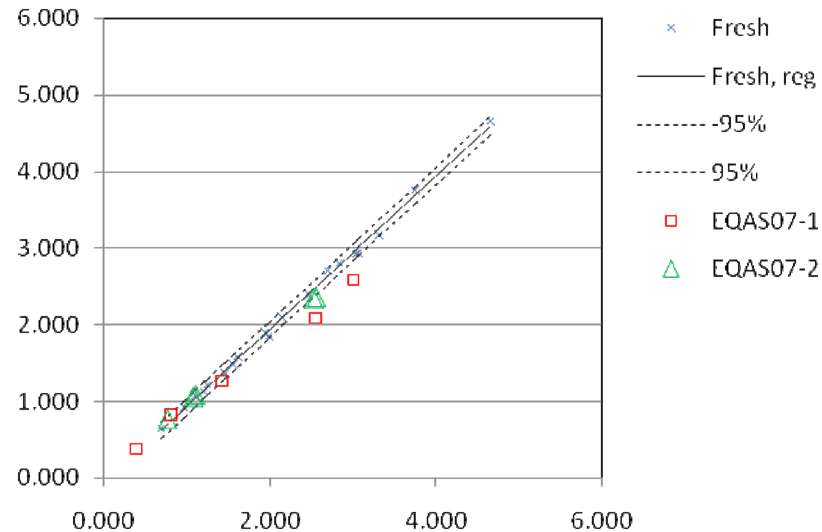


Triglycerides: commutability, 2007 EQA materials









Reference system activities: enzymes

- Transfer of IFCC reference procedures since 2003
- Preliminary laboratory network by CCCLS, Dr. Zhenhua Yang

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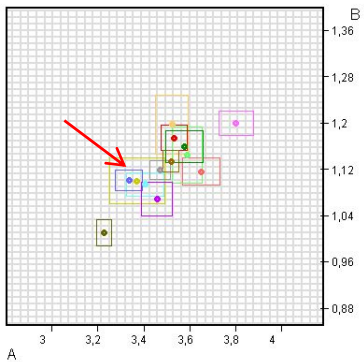
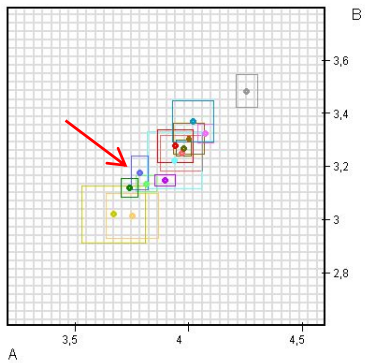
ALT [ukat/l]



Lab	A	e.u.	B	e.u.	method
03	3,648	0,080	1,115	0,023	kinetic spectrophotometry (IFCC)
06	3,522	0,070	1,197	0,050	kinetic spectrophotometry (IFCC)
12	3,37	0,12	1,1	0,039	kinetic spectrophotometry (IFCC)
16	3,587	0,065	1,143	0,048	kinetic spectrophotometry (IFCC)
18	3,406	0,080	1,093	0,020	kinetic spectrophotometry (IFCC)
23	3,336	0,059	1,101	0,018	kinetic spectrophotometry (IFCC)
41	3,799	0,074	1,200	0,021	kinetic spectrophotometry (IFCC)
46	3,471	0,045	1,119	0,016	kinetic spectrophotometry (IFCC)
47	3,457	0,068	1,069	0,029	kinetic spectrophotometry (IFCC)
48	3,531	0,058	1,174	0,022	kinetic spectrophotometry (IFCC)
49	3,518	0,035	1,134	0,018	kinetic spectrophotometry (IFCC)
51	3,228	0,033	1,010	0,023	kinetic spectrophotometry (IFCC)
54	3,577	0,082	1,159	0,027	kinetic spectrophotometry (IFCC)

RELA 2006

AST [ukat/l]



Lab	A	e.u.	B	e.u.	method
03	3,969	0,091	3,249	0,068	kinetic spectrophotometry (IFCC)
06	3,754	0,115	3,014	0,084	kinetic spectrophotometry (IFCC)
12	3,67	0,14	3,02	0,108	kinetic spectrophotometry (IFCC)
13	3,814	0,046	3,134	0,030	kinetic spectrophotometry (IFCC)
16	3,937	0,118	3,223	0,108	kinetic spectrophotometry (IFCC)
18	3,785	0,036	3,174	0,064	kinetic spectrophotometry (IFCC)
38	4,074	0,035	3,323	0,035	kinetic spectrophotometry (IFCC)
41	4,256	0,046	3,483	0,062	kinetic spectrophotometry (IFCC)
46	3,896	0,046	3,146	0,021	kinetic spectrophotometry (IFCC)
47	3,941	0,078	3,277	0,061	kinetic spectrophotometry (IFCC)
48	4,002	0,067	3,304	0,059	kinetic spectrophotometry (IFCC)
49	3,98	0,032	3,268	0,03	kinetic spectrophotometry (IFCC)
51	3,740	0,038	3,117	0,035	kinetic spectrophotometry (IFCC)
54	4,02	0,092	3,37	0,079	kinetic spectrophotometry (IFCC)

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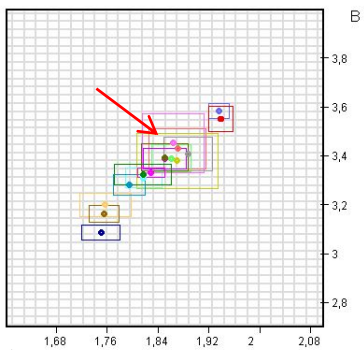
GGT [ukat/l]



Lab	A	e.u.	B	e.u.	method
03	1,870	0,044	3,430	0,082	kinetic spectrophotometry (IFCC)
06	1,756	0,040	3,199	0,046	kinetic spectrophotometry (IFCC)
12	1,87	0,064	3,38	0,113	kinetic spectrophotometry (IFCC)
13	1,860	0,030	3,390	0,056	kinetic spectrophotometry (IFCC)
16	1,816	0,028	3,309	0,040	kinetic spectrophotometry (IFCC)
17	1,935	0,016	3,583	0,031	spectrophotometry (JSCC)
18	1,863	0,048	3,451	0,120	kinetic spectrophotometry (IFCC)
27	1,887	0,037	3,406	0,068	Kinetic spectrophotometry (IFCC)
38	1,850	0,034	3,388	0,040	kinetic spectrophotometry (IFCC)
41	1,938	0,018	3,551	0,049	kinetic spectrophotometry (IFCC)
46	1,755	0,023	3,163	0,036	kinetic spectrophotometry (IFCC)
47	1,85	0,037	3,394	0,055	kinetic spectrophotometry (IFCC)
48	1,816	0,045	3,322	0,042	kinetic spectrophotometry (IFCC)
49	1,794	0,025	3,281	0,041	kinetic spectrophotometry (IFCC)
51	1,750	0,030	3,086	0,030	kinetic spectrophotometry (IFCC)
55	1,829	0,021	3,331	0,019	kinetic spectrophotometry (IFCC)

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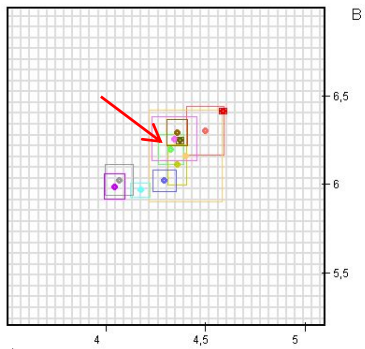
LDH [ukat/l]



Lab	A	e.u.	B	e.u.	method
03	4,498	0,094	6,300	0,138	kinetic spectrophotometry (IFCC)
13	4,398	0,184	6,158	0,258	kinetic spectrophotometry (IFCC)
16	4,358	0,046	6,110	0,113	kinetic spectrophotometry (IFCC)
18	4,326	0,064	6,195	0,084	kinetic spectrophotometry (IFCC)
41	4,173	0,048	5,966	0,038	kinetic spectrophotometry (IFCC)
46	4,293	0,058	6,02	0,06	kinetic spectrophotometry (IFCC)
47	4,344	0,113	6,256	0,124	kinetic spectrophotometry (IFCC)
48	4,066	0,071	6,022	0,087	kinetic spectrophotometry (IFCC)
49	4,042	0,053	5,985	0,072	kinetic spectrophotometry (IFCC)
51	4,589	0,018	6,412	0,018	kinetic spectrophotometry (IFCC)
54	4,358	0,052	6,292	0,073	kinetic spectrophotometry (IFCC)
55	4,373	0,019	6,247	0,019	kinetic spectrophotometry (IFCC)

Reference system activities: hematology and infectious disease

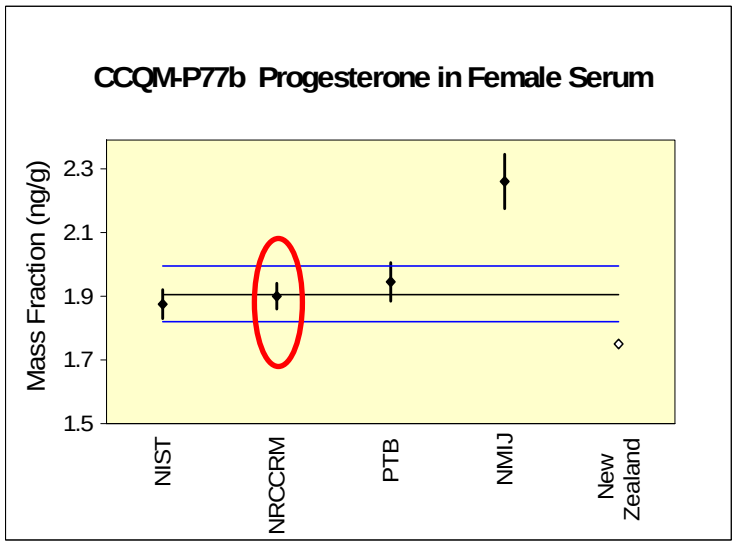
- Hematology
  - ICSH reference procedures for blood cells established
  - platelet and hemoglobin procedures and materials ongoing
  - calibration activities in Beijing area
- Infectious disease
  - Hepatitis B and C nucleic acids RMs (GBWs)
  - Antigen or antibody RMs ongoing

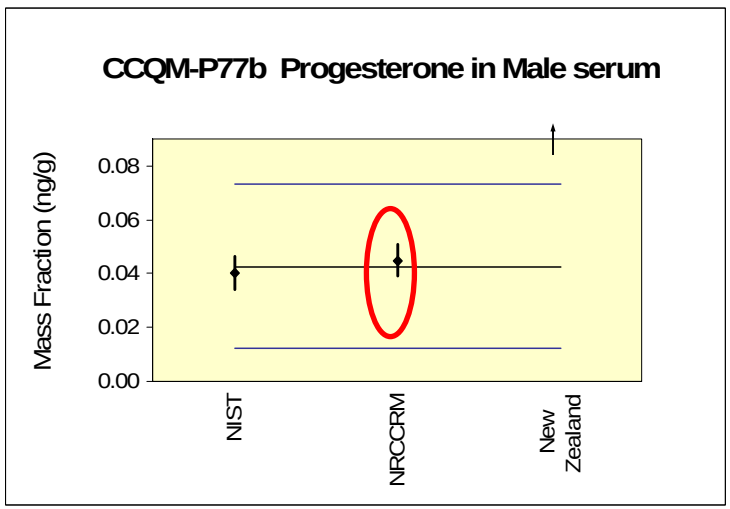
Reference system activities:
metabolites, ions and NP hormones

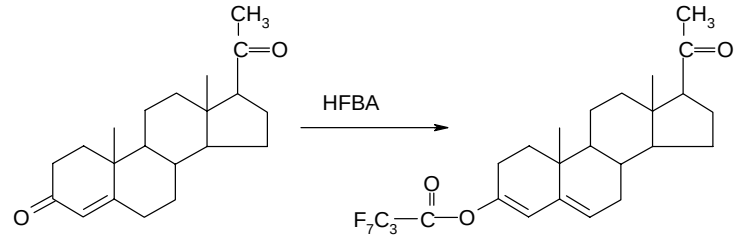
- Multi-organization collaborations
- ID/MS or other reliable principles
- Started and initial progresses made

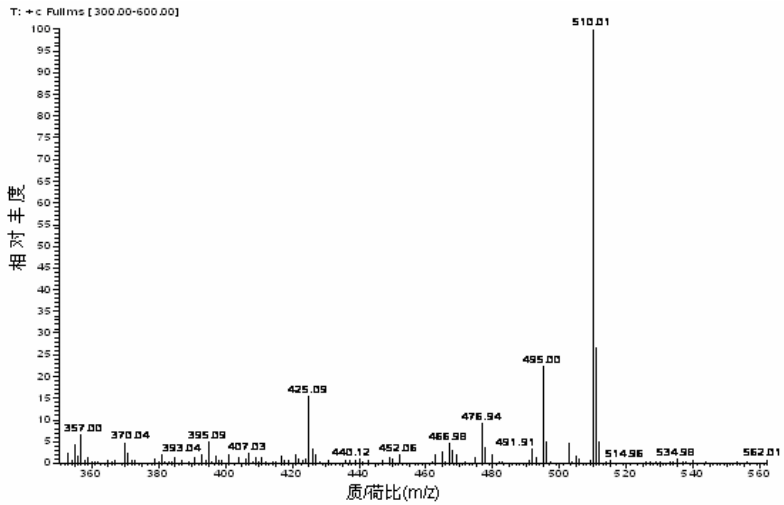
ID/GC/MS Serum progesterone

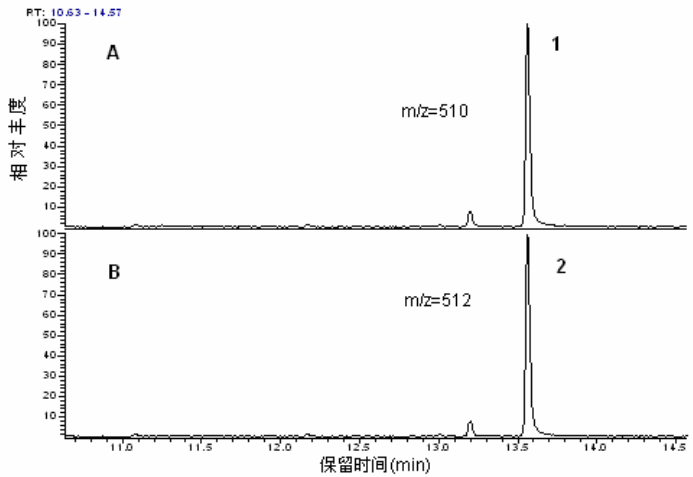
- Method of Thienpont et al (Anal. Chem. 1994)
- Total CV ~2%
- IRMM ERM analysis
- Collaborations with NIM









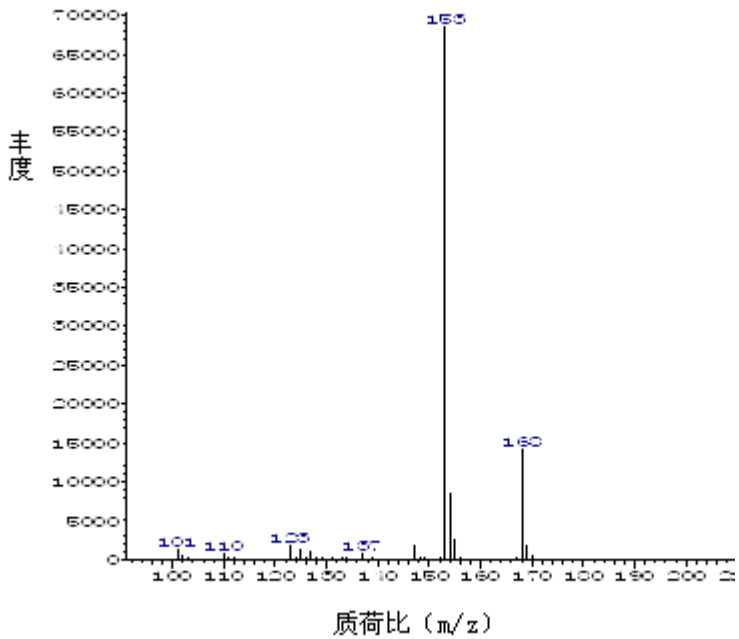


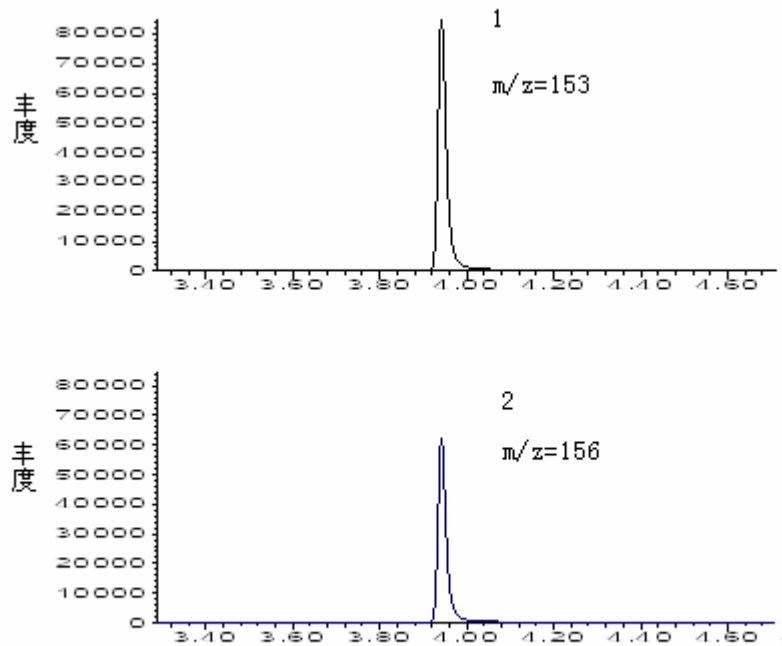
Serum progesterone, EQAS 2006

Sample#	All methods mean	ID/GC/MS
200612	50.00 nmol/L	72.22 nmol/L
200613	36.54 nmol/L	48.71 nmol/L

ID/GC/MS serum urea

- Method of Kessler and Siekmann (Clin Chem 1999)
- Total CV <1%
- NIST SRM analysis





ICP/MS serum sodium

- Aluminum as internal standard
- Serum digested with nitric acid
- Total CV ~ 0.2%
- NIST SRM analysis
- Collaborations with the Army's General Hospital and Laboratory Center

National research programs supporting reference systems

- National Key Technologies R&D Program
  (Project #2007BAI05B09)

  - Reference or comparison measurement procedures for important metabolites/substrates, electrolytes and metal ions, enzymes, non-peptide hormones, CVD risk factors, hematology and infectious disease tests

- National High-tech R&D Program (the 863 Program)
  (Project #2006AA020909)

  - Reference materials for important chemistry, infectious disease and hematology and genetic tests

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