

## NIM China biennial activity report

All JCTLM Members are invited to attend the Members' and Stakeholders' Meeting, which is held once every two years, and submit a report of their activities in support of traceability in laboratory medicine over the preceding period.

For that purpose this template document provides guidance to JCTLM Members for drafting their biennial activity report. Organizations are invited to provide the information below for submission to the Executive Committee.

<p><b>Organization Name: National Institute of Metrology, China</b></p> <p><b>JCTLM Member status: National and Regional Member</b></p> <p><b>Author(s):</b> Hongmei Li, Dewei Song, Xianzhang Huang, Yi Ju, Min Shen, Xiaojian Wang, Tao Yang, Baorong Chen, Yan Shao, Yingguo Wang, Jianxin Wang, Peng Xiao</p> <p><b>Author(s) email(s):</b> lihm@nim.ac.cn</p> <p><b>Period covered: 2020 – 2021</b></p>
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### 1. Major achievement(s) in support of standardization in laboratory medicine

(Please describe what activities your organization has undertaken related to the implementation of reference measurement systems in laboratory medicine during the last two years, including but not limited to information on: the production of certified reference materials; the development of reference measurement methods; or the establishment of calibration (reference) measurement services. Outline the measurement area(s)/measurands covered, and provide a listing of the relevant technical/scientific publications.)

#### 1.1 Purity certified reference materials

Description	Code	Researcher
Beta-2 Microglobulin Solution Reference Material	GBW09869	NIM
Cystatin C Solution Reference Material	GBW09870	NIM

#### 1.2 Matrix certified reference materials

Type	Description	Code	Researcher
Hormones	uE3 in Frozen Human Serum	GBW(E)091048-091052	c
	Aldosterone in human plasma (level 1)	GBW(E)091171	a & d
	Aldosterone in human plasma (level 2)	GBW(E)091172	a & d
Amino acids and Proteins	Total Protein in Frozen Human Serum	GBW(E) 091041	c
	Homocysteine and testosterone in frozen human serum	Ongoing	e
	Homocysteine in Frozen Human Serum (Four levels)	GBW09861-4	a
	C-Reactive Protein in Frozen Human Serum (Four levels)	GBW09865-8	a
	C-peptide in Frozen Human Serum (Three levels)	GBW09871-3	a
	Cystatin C in Frozen Human Serum (Four levels)	GBW(E) 091173-6	a & d

	Multi-biomarkers in frozen human serum	GBW(E) 091040	c
Metabolites and substrates	Urea, Creatinine in Frozen Human Serum	GBW(E) 091044	a & c
	Uric Acid in Frozen Human Serum	GBW(E) 091045	c
	Urea, uric acid and total protein in compound frozen human serum	Ongoing	e
Electrolyte in serum	Lithium, sodium, potassium, magnesium, calcium and chlorine in compound frozen human serum	Ongoing	e
Enzymes	Catalytic Activity Concentration of $\gamma$ -Glutamyltransferase and Alkaline Phosphatase in Frozen Human Serum	GBW(E) 091042	c
	Catalytic Activity Concentration of Alpha-Amylase in Frozen Human Serum	GBW(E) 091046	c
	Catalytic Activity Concentration of Creatine Kinase in Frozen Human Serum	GBW(E) 091047	c
	Glucose in Frozen Human Serum	GBW(E) 091043	c
Medicine & Drugs	Cyclosporin A, Sirolimus, Tacrolimus and Everolimus in compound frozen human serum	Ongoing	e

a, National Institute of Metrology

b, Maccura Biotechnology Co., Ltd.

c, The Second Affiliated Hospital of Guangzhou University of Chinese Medicine

d, Beijing Aerospace General Hospital

e, Medicalsystem Biotechnology Co., Ltd

### 1.3 Reference measurement methods (Ongoing and completed)

Stakeholder	Analyte	Approach	Matrix
Maccura Biotechnology Co., Ltd.	Alanine Aminotransferase	spectrophotometry	Serum
	Aspartate Aminotransferase	spectrophotometry	Serum
	$\gamma$ -Glutamyltransferase	spectrophotometry	Serum
	Lactate Dehydrogenase	spectrophotometry	Serum
	Creatine Kinase	spectrophotometry	Serum
	$\alpha$ -Amylase	spectrophotometry	Serum
	alkaline phosphatase	spectrophotometry	Serum
	Glucose	spectrophotometry	Calibration solution, Serum
	Urea	spectrophotometry	Calibration solution, Serum
	Total Bilirubin	spectrophotometry	Calibration solution, Serum
	Total Protein	spectrophotometry	Serum
	Uric acid	ID-LC-MS/MS	Calibration solution, Serum
	Creatinine	ID-LC-MS/MS	Calibration solution, Serum
	Total Thyroxine	ID-LC-MS/MS	Calibration solution, Serum
	Testosterone	ID-LC-MS/MS	Calibration solution, Serum
	Progesterone	ID-LC-MS/MS	Calibration solution, Serum
	Estradiol	ID-LC-MS/MS	Calibration solution, Serum
Cortisol	ID-LC-MS/MS	Calibration solution, Serum	
Total triiodothyronine	ID-LC-MS/MS	Calibration solution, Serum	

	Estriol	ID-LC-MS/MS	Calibration solution, Serum
	Aldosterone	ID-LC-MS/MS	Calibration solution, Serum
	17-hydroxyprogesterone	ID-LC-MS/MS	Calibration solution, Serum
	Digitoxin	ID-LC-MS/MS	Calibration solution, Serum
	Digoxin	ID-LC-MS/MS	Calibration solution, Serum
	Theophylline	ID-LC-MS/MS	Calibration solution, Serum
	Homocysteine	ID-LC-MS/MS	Calibration solution, Serum
	Total cholesterol	ID-LC-MS/MS	Calibration solution, Serum
	Total glycerides	ID-LC-MS/MS	Calibration solution, Serum
	25-Hydroxyvitamin D3	ID-LC-MS/MS	Calibration solution, Serum
	HbA1c	LC-MS/MS	Whole blood
	Leucocytes	Counting	Whole blood
	Erythrocytes	Counting	Whole blood
	Haemoglobinometry	spectrophotometry	Whole blood
	Hematocrit	microhematocrit	Whole blood
	Platelet	Counting	Whole blood
	Reticulocyte	Counting	Whole blood
	Calcium	ID-ICP MS	Serum
	Magnesium	ID-ICP MS	Serum
	Potassium	ID-ICP MS	Serum
	Sodium	ID-ICP MS	Serum
	Lithium	ID-ICP MS	Serum
	Chloride	Ion chromatography	Serum
The Second Affiliated Hospital of Guangzhou University of Chinese Medicine	Estriol	ID-LC/MS/MS	Serum
	Estradiol	ID-LC/MS/MS	Serum
	Urea	ID-LC/MS/MS	Serum
	Albumin	ID-LC/MS/MS	Serum
	Cys C	ID-LC/MS/MS	Serum
	HbA1c	ID-LC/MS/MS	Serum
	Aldosterone	ID-LC/MS/MS	Serum
Progesterone	ID-LC/MS/MS	Serum	
Shanghai Center for Clinical Laboratory	Apolipoproteins	ID-LC/MS/MS	Serum
	Cystatin C	ID-LC/MS/MS	Serum
Medicalsystem Biotechnology Co., Ltd	Sodium	Ion Chromatography	Serum
	Potassium	Ion Chromatography	Serum
	Magnesium	Ion Chromatography	Serum
	Calcium	Ion Chromatography	Serum
	Chloride	Ion Chromatography	Serum
	Lithium	Ion Chromatography	Serum
	25-OH-vitamin D	ID-LC-MS/MS	Serum
	Estriol	ID-LC-MS/MS	Serum
	Estradiol-17 $\beta$	ID-LC-MS/MS	Serum
	Testosterone	ID-LC-MS/MS	Serum
	Aldosterone	ID-LC-MS/MS	Serum
	Progesterone	ID-LC-MS/MS	Serum
	Cortisol	ID-LC-MS/MS	Serum
	17-OH-progesterone	ID-LC-MS/MS	Serum
TT3	ID-LC-MS/MS	Serum	

Total thyroxine	ID-LC-MS/MS	Serum
Carbamazepine	LC-MS/MS	Serum
Cyclosporin A	ID-LC-MS/MS	Whole blood
Sirolimus	ID-LC-MS/MS	Whole blood
Tacrolimus	ID-LC-MS/MS	Whole blood
Everolimus	ID-LC-MS/MS	Whole blood
Vancomycin	LC-MS/MS	Serum
Lamotrigine	ID-LC-MS/MS	Serum
Phenobarbital	ID-LC-MS/MS	Serum
Phenytoin	ID-LC-MS/MS	Serum
Theophylline	ID-MS/MS	Serum
Digitoxin	ID-LC-MS/MS	Serum
ALT	IFCC reference measurement procedure (37 °C)	Serum
AST	IFCC reference measurement procedure (37 °C)	Serum
LDH	IFCC reference measurement procedure (37 °C)	Serum
CK	IFCC reference measurement procedure (37 °C)	Serum
GGT	IFCC reference measurement procedure (37 °C)	Serum
AMY	IFCC reference measurement procedure (37 °C)	Serum
ALP	IFCC reference measurement procedure (37 °C)	Serum
Homocysteine	ID-LC-MS/MS	Serum
Total bilirubine	Spectrophotometry	Serum
Glucose	Spectrophotometry	Serum
Urea	Spectrophotometry	Serum
Uric acid	Spectrophotometry	Serum
Creatinine	Spectrophotometry	Serum
Total Cholesterol	HPLC	Serum
Total protein	Spectrophotometry	Serum
Red blood cell counting		Blood
White blood cell counting		Blood
Hemoglobin		Blood
Hematocrit		Blood
Platelet		Blood
Vitamin A	ID-LC-MS/MS	Serum
Vitamin E	ID-LC-MS/MS	Serum
Vitamin K1	ID-LC-MS/MS	Serum
Olanzapine	ID-LC-MS/MS	Serum
Clozapine	ID-LC-MS/MS	Serum
N-desmethylozapine	ID-LC-MS/MS	Serum
Quetiapine	ID-LC-MS/MS	Serum
Risperidone	ID-LC-MS/MS	Serum
Aripiprazole	ID-LC-MS/MS	Serum
Ziprasidone	ID-LC-MS/MS	Serum
Chlorpromazine	ID-LC-MS/MS	Serum
Haloperidol	ID-LC-MS/MS	Serum
Prochlorperazine	ID-LC-MS/MS	Serum

	FLUPHENAZINE	ID-LC-MS/MS	Serum
	Amisulpride	ID-LC-MS/MS	Serum
	Sulpiride	ID-LC-MS/MS	Serum
	Thioridazine	ID-LC-MS/MS	Serum
	Chlorprothixene	ID-LC-MS/MS	Serum
	SERTINDOLE	ID-LC-MS/MS	Serum
Shenzhen Mindray Bio-Medical Electronics CO., Ltd, China	ALT	Spectrophotometry	Serum
	ALP	Spectrophotometry	Serum
	$\alpha$ -Amylase	Spectrophotometry	Serum
	Aldosterone	ID-LC-MS/MS	Serum, Urine
	Bilirubine	Spectrophotometry	Serum
	Creatinine	ID-LC-MS/MS	Serum
	Cortisol	ID-LC-MS/MS	Serum
	CK	Spectrophotometry	Serum
	Estradiol-17 $\beta$	ID-LC-MS/MS	Serum
	Estriol	ID-LC-MS/MS	Serum
	Homocysteine	ID-LC-MS/MS	Serum
	Glucose	Spectrophotometry	Serum
	GGT	Spectrophotometry	Serum
	LDH	Spectrophotometry	Serum
	Progesterone	ID-LC-MS/MS	Serum
	Protein	Spectrophotometry	Serum
	Thyroxine	ID-LC-MS/MS	Serum
	Tri-iodthronine	ID-LC-MS/MS	Serum
	rT3	ID-LC-MS/MS	Serum
	Testosterone	ID-LC-MS/MS	Serum
	Uric Acid	Spectrophotometry	Serum
		ID-LC-MS/MS	Serum
Urea	Spectrophotometry	Serum	
25-OH Vitamin D3	ID-LC-MS/MS	Serum	
Affiliated Hospital of Nantong University	Retinol binding protein 4	ID-LC-MS/MS	Purity
	Retinol binding protein 4	ID-LC-MS/MS	Serum
BeijingStrong Biotechnologies, Inc. (BSBE)	ALT	Spectrophotometry	Serum
	AST	Spectrophotometry	Serum
	AMY	Spectrophotometry	Serum
	ALP	Spectrophotometry	Serum
	CK	Spectrophotometry	Serum
	LDH	Spectrophotometry	Serum
	GGT	Spectrophotometry	Serum
	TP	Spectrophotometry	Serum
	UREA	Spectrophotometry	Serum
	UA	Spectrophotometry	Serum
	GLU	Spectrophotometry	Serum
	CRE	Spectrophotometry	Serum
	Homocysteine	ID-LC-MS/MS	Serum
	Free estriol	ID-LC-MS/MS	Serum
	Testosterone	ID-LC-MS/MS	Serum
	CRE	ID-LC-MS/MS	Serum

	HbA1C	ID-LC-MS/MS	Serum
	CHO	ID-LC-MS/MS	Serum
	UA	ID-LC-MS/MS	Serum
	25-OH-VD	ID-LC-MS/MS	Serum
	Cortisol	ID-LC-MS/MS	Serum

#### 1.4 Calibration (reference) measurement services

Stakeholder	Analyte	Approach	Clients	Time	Matrix
Maccura Biotechnology Co., Ltd.	25-OH-vitamin D3	ID-LC-MS/MS	Shanghai Center for Clinical Laboratories (SCCL)	2020.04-2020.08	
	Creatinine	ID-LC-MS/MS	National Institutes for Food and Drug Control	2020.11-2021.12	
The Second Affiliated Hospital of Guangzhou University of Chinese Medicine	Liver function, kidney function, blood cells		Guangdong Center for Clinical Laboratory	2020	
	Liver function, kidney function, blood cells		Chongqing Center for Clinical Laboratory	2020	
	Estriol		Beckman Coulter (China)	2020	Serum
	L-Tyrosine		Human Metabolomics Institute, Inc.	2020	
	Taurocholic acid		Human Metabolomics Institute, Inc.	2020	
	blood cell count		URIT Medical Electronic Co., Ltd. and other four companies	2020	Whole blood
	Neutralizing antibody		Mindray		
Beijing Aerospace General Hospital	ALP/CK/GGT/LDH/AMY/T A/TP/GLU	Spectrophotometry	Beijing Chaoyang Hospital	2020.8.21-2021.8.20	Human Serum
Shanghai Center for Clinical Laboratory	25-OH-Vitamin D3 / ALT / ALP / Calcium / Cortisol / Creatinine / GGT / Glucose / HbA1c / Lithium / Potassium / Testosterone / Triiodothyronin / Urea / Uric Acid		Participants who join the Trueness verification programs (TVP)	2020-2021	
	25-OH-Vitamin D2 / Amylase / AST / CK / HCY / LDH / Thyroxin			2021	
	17OH-progesterone / Estradiol-17 $\beta$ / Estriol		NIM	2021	
	Progesterone / Estradiol-17 $\beta$		Guangdong Hospital of Traditional Chinese Medicine	2021	
	Cortisol / Thyroxin / Triiodothyronin		Autobio company	2020	
Medicalsystem Biotechnology Co., Ltd	25-OH-vitamin D	ID-LC-MS/MS	Shanghai Center for Clinical Laboratories (SCCL)	2020.03-2020.12	
	Calcium	Ion Chromatography			
	Lithium	Ion Chromatography			

	25-OH-vitaminD	ID-LC-MS/MS	Shanghai Center for Clinical Laboratories (SCCL)	2020.04-2020.08	
Shenzhen Mindray Bio-Medical Electronics CO., Ltd, China	ALT	spectrophotometry	Guangdong Province Traditional Chinese Medical Hospital	2021.1-2021.06	Frozen human serum
	AST	spectrophotometry	Guangdong Province Traditional Chinese Medical Hospital	2021.1-2021.06	Frozen human serum
	GGT	spectrophotometry	Guangdong Province Traditional Chinese Medical Hospital	2021.1-2021.06	Frozen human serum
	ALP	spectrophotometry	Guangdong Province Traditional Chinese Medical Hospital	2021.1-2021.06	Frozen human serum
	TB	spectrophotometry	Guangdong Province Traditional Chinese Medical Hospital	2021.1-2021.06	Frozen human serum
	UREA	spectrophotometry	Guangdong Province Traditional Chinese Medical Hospital	2021.1-2021.06	Frozen human serum
	GLU	spectrophotometry	Guangdong Province Traditional Chinese Medical Hospital	2021.1-2021.06	Frozen human serum
	TP	spectrophotometry	Guangdong Province Traditional Chinese Medical Hospital	2021.1-2021.06	Frozen human serum
	UA	spectrophotometry	Guangdong Province Traditional Chinese Medical Hospital	2021.1-2021.06	Frozen human serum
Affiliated Hospital of Nantong University	AST		National Center for Clinical Laboratories		
	LDH		National Center for Clinical Laboratories		

### 1.5 Publications

Institution	Authors	Title	Journal/issue/page
National Institute of Metrology, China	Jianyi Liu, Wen Zhu, Haofeng Sun, Dewei Song*, Peng Xiao, Bei Xu, Hongmei Li*	Development of a primary reference material of natural C-reactive protein: verification of its natural pentameric structure and certification by two isotope dilution mass spectrometry	Analytical Methods. 2021 Feb 7;13(5):626-635
	Qinglai Meng, Shichao Liu, Jinhua Meng, Jiao Feng Michael Mecklenburg, Lei Zhu, Lifang Zhou, Leif Bülow Jianyi Liu, Dewei Song*, Changxin Wu, Bin Xie	Rapid personalized AMR diagnostics using two-dimensional antibiotic resistance profiling strategy employing a thermometric NDM-1 biosensor	Biosens Bioelectron. 2021 Dec 1;193:113526.
	Qinglai Meng, Yao Wang, Yali Long, Aiping Yue, Michael Mecklenburg, Shuaiyan Tian, Yujia Fu, Xiangyu Yao, Jianyi Liu, Dewei Song*, Changxin Wu, Bin Xie	Rapid Detection of Multiple Classes of $\beta$ -Lactam Antibiotics in Blood Using an NDM-1 Biosensing Assay	Antibiotics (Basel). 2021 Sep 14;10(9):1110.

	Haofeng Sun, Lingyun Ma, Leyu Wang, Peng Xiao, Hongmei Li, Min Zhou, Dewei Song*	Research advances in hydrogen deuterium exchange mass spectrometry for protein epitope mapping	Anal Bioanal Chem. 2021 Apr;413(9):2345-2359.
	Xinxue Wang, Fangyan Zhang, Hongmei Li, Peng Xiao, Fuhai Su, Bei Xu, Wei Sun, Dewei Song*	Purity determination of synthetic glucagon using a mass balance approach	Scientific Reports. 2020 Mar 10;10(1):4423.
	Jianyi Liu, Jinping Zhang, Meng Bo, Dewei Song*	Research Progress on Traceability of In Vitro Diagnostic Reagents in China	Measurement Technique. 2020 July 8-12
	Peng Xiao*, Fan Zhang, Xinxue Wang, Dewei Song and Hongmei Li*	Analysis of B-type natriuretic peptide impurities using label-free data-independent acquisition mass spectrometry technology	Clin Chem Lab Med 2021; 59(1): 217–226
Maccura Biotechnology Co., Ltd.	TANG Liping, LIU Mingjin, LIU Guancai, YAN Zhonghua, CAI Hua, YANG Tao, SUN Keqi	Application and thinking of laboratory medical reference system in IVD enterprises of China	Laboratory Medicine, March 2021, Vol. 36, No. 3, 250-254
The Second Affiliated Hospital of Guangzhou University of Chinese Medicine	Qiaoxuan Zhang, Liqiao Han, Songbai Zheng, Fen Ouyang, XiaobinWu, Jun Yan, Min Zhan, Peifeng Ke, Junhua Zhuang*, Xianzhang Huang*	An isotope dilution liquid chromatography-tandem mass spectrometry candidate reference measurement procedure for aldosterone measurement in human plasma	Analytical and Bioanalytical Chemistry, 2021, (413) 4471-4481
	Qiaoxuan Zhang#, Zhiliang Cai #, Haibiao Lin, Liqiao Han, Jun Yan, Jianbing Wang, Peifeng Ke, Junhua Zhuang*, Xianzhang Huang*	Expression, purification and identification of isotope-labeled recombinant cystatin C protein in Escheichia coli intended for absolute quantification using isotope dilution mass spectrometry	Protein Expression and Purification, 2021, (178) 105785
	Zhiliang Cai #, Qiaoxuan Zhang#, Ziqiang Xia, Songbai Zheng, Lilan Zeng, Haibiao Lin, Jun Yan, Peifeng Ke, Junhua Zhuang, Xinzhong Wu*, Xianzhang Huang*	Determination of serum 25-hydroxyvitamin D status among population in Southern China by a high accuracy LC-MS/MS method traced to reference measurement procedure	Nutrition & Metabolism, 2020,17(1): 8
	Qiaoxuan Zhang, Zhiliang Cai, Yingyi Liu, Haibiao Lin, Qiqin Wang, Jun Yan, Liqiao Han, Jianbing Wang, Peifeng Ke, Junhua Zhuang*, Xianzhang Huang*	Comparison of bracketing calibration and classical calibration curve quantification methods in establishing a candidate reference measurement procedure for human serum 17 $\beta$ -estradiol by isotope dilution liquid chromatography tandem mass spectrometry	Microchemical Journal, 2020 (152):104270
	Haibiao Lin, Zhiliang Cai, Qiaoxuan Zhang, Weicheng Yang, Jun Yan, Liqiao Han, Fen Ouyang, Jianbing Wang, Zemin Wan, Peifeng Ke, Junhua Zhuang, Xianzhang Huang	Performances Evaluation of Four Systems for Homocysteine Determination by LC-MS/MS Reference Method	Clin. Lab. 2021;67(3):697-706
	Liqiao Han, Stephanie E. Wemm, Lei Shen, David C. Spink, Edelgard Wulfert, Zhimin Tim Cao	Noninvasive detection of human dehydroepiandrosterone, progesterone and testosterone using LC-MS/MS revealed effects of birth control pills/devices and body weight on ovulatory prediction	Journal of Chromatography B. 2021,1174: 122716
	Liqiao Han, Yunxiu Wang, Xiaoting Huang, Jianbing Wang, Qiaoxuan Zhang, Jun Yan, Fen Ouyang, Zhiliang Cai, Xianzhang Huang, and Junhua Zhuang	A method for production of human adenosine deaminase 1 (ADA1) in Pichia pastoris providing needed quality control material for clinical laboratories	Annals of Clinical & Laboratory Science. 2021.11.

	Ahui Wang, Yuzhu Xu, Yangfen Ou, Liqiao Han, Qiaoxuan Zhang, Min Zhan, Hongcan Liu, Peifeng Ke, Jun Yan*, Xianzhang Huang*	A simple and reliable measurement procedure for determination of glycocholic acid in human serum by isotope-dilution liquid chromatography-tandem mass spectrometry	International Journal of Mass Spectrometry, 2021, 464, 116567
	Jun Yan, Yuzhu Xu, Xing Jin, Qiaoxuan Zhang, Feng Ouyang, Liqiao Han, Min Zhan, Xingshu Li, Baoxia Liang*, Xianzhang Huang*	Structure modification and biological evaluation of indole-chalcone derivatives as anti-tumor agents through dual targeting tubulin and TrxR	European Journal of Medicinal Chemistry, 2022, 227, 113897
	Jun Yan, Qizhen Zhuang, Zhenzhen Li, Yujuan Xiong, Min He, Cunmin Kang, Qiaoxuan Zhang, Liqiao Han, Enyu Liang, Hongcan Liu, Peifeng Ke*, Xianzhang Huang*	MIL-1, a novel antitumor agent derived from natural product millepachine, acts as tubulin polymerization inhibitor for the treatment of hepatocellular carcinoma	European Journal of Pharmacology, 2021, 898, 173975
Beijing Aerospace General Hospital	Shao Yan, Liu Shuming, Zhou Xiaofeng, Sun Jing, Yu Hongyuan and Chen Lei	The Performance Verification of a Serum Amyloid A Reagent on Abbott C16000 Automatic Biochemical Analyzer	Labeled immunoassay and clinical medicine 2020,27(11):1990-1994
	Li Min, Sun Jiangman, Yu Hongyuan, Shao Yan	Effects of Different Evaluation Methods on Results of Commutability	Labeled immunoassay and clinical medicine 2021,28(8):1421-1425
Shanghai Center for Clinical Laboratory	Hewei Sun, Qing Li, Yide Lu, Zhonggan Jin and Yi Ju*	A protein standard addition method for absolute quantification of cystatin C in human serum by LC-MS/MS	Clin Chem Lab Med. 2021; 59(11): e426-e427
	Yi Ju, Zhimin Tim Cao*, Qing Li, et al.	Recommendations for proficiency testing criteria for hemoglobin A1c based on the Shanghai Center for Clinical Laboratory's study	Clin Chem Lab Med. 2021; 59(10):1728-1734
	Xiaoyu Fan, Qing Li, Zhonggan Jin, Xiaoxuan Yu, Menglei Ding, Yi Ju*	Establishment and application of a new serum sodium candidate reference method	Clin Chem Acta. 2020; 508:249-253
	OU Yuanzhu, CHEN Baorong*, JU Yi*	Current situation of standardization of clinical chemistry measurement	Laboratory Medicine, 2021,36(3): 240-244
	JU Yi	Research and application of reference measurement system in laboratory medicine	Laboratory Medicine, 2021, 36(3): 237-239
	LI Qing, JU Yi*, TANG Liping, et al.	Application of candidate reference method of apolipoprotein A1 and apolipoprotein B in external quality assessment	Laboratory Medicine, 2021, 36(3): 259-262
	Fan Xiaoyu, Ju Yi*, Li Qing	Establishment of a candidate reference method for serum calcium determination based on inductively coupled plasma mass spectrometry	Chin J Lab Med, 2020,43(1) : 58-62
	JIN Zhonggan, JU Yi*, ZHANG Sujie, et al.	Preliminary study on the application of glucose reference method to determine the target value for EQA samples	Laboratory Medicine, 2020, 35(11): 1190-1193
	ZHANG Sujie, JU Yi, LI Qing, et al	Analysis of serum 25-hydroxyvitamin D levels in healthy subjects	Laboratory Medicine, 2020, 35(10): 1028-1031
Medicalseystem Biotechnology Co., Ltd	Qingqing Pan, Min Shen, Ting Yu, Xiaodong Yang, Quanle Li, Beibei Zhao, Jihua Zou, Man Zhang.	Liquid chromatography as candidate reference method for the determination of vitamins A and E in human serum	Journal of Clinical Laboratory Analysis 2020;00: e23528
	Xiaodong Yang, Min Shen, Qingqing Pan, Minmin Tu, Quanle Li, Beibei Zhao, Danyun Xie, Wei Zhang, Ting Yu, Jihua Zou, Man Zhang	An isotope dilution LC-MS/MS as candidate reference method for the measurement of tacrolimus, sirolimus, everolimus and cyclosporine A in human whole blood	Analytical & Bioanalytical Chemistry,
	Min Shen, Minmin Tu, Wei Zhang, Jihua Zou, Man Zhang, Zheng Cao, Bingde Zou	Ion chromatography as candidate reference method for the determination of chloride in human serum	Journal of Clinical Laboratory Analysis 2020;00:e23296.
	Ting Yu, Min Shen, Shoufang Qu, Nan Sun, Jing Sun, Jie Huang	Development of the national standard material of testosterone in frozen human serum	Laboratory Medicine, Oct 2021, Vol 36, 1081-1083.
	Ting Yu, Min Shen, Shoufang Qu, Jie Huang	Development and performance evaluation of the national standard materials of lithium,	Laboratory Medicine, May 2019, Vol 34, 457-462.

		sodium, potassium, magnesium, calcium and chlorine in compound frozen human serum	
	Ting Yu, Min Shen, Shoufang Qu, Nan Sun, Jie Huang	Development of national standard materials of urea, uric acid and total protein in compound frozen human serum	Laboratory Medicine, August 2018, Vol 33, 755-759.
	Jihua Zou, Quanle Li, Min Shen, Man Zhang, Xiaodong Yang, Minmin Tu, Dongfang Feng, Hongna Sun	Establishment and performance evaluation of candidate reference measurement procedure for serum aldosterone by liquid chromatography-tandem mass spectrometry	Laboratory Medicine, August 2020, Vol. 35, 811-817
Shenzhen Mindray Bio-Medical Electronics CO., Ltd, China		Feasibility of a Mean Platelet Volume Standard: an ICSH inter-laboratory study	

## 1.6 Activities related to IVD traceability of NIM and reference laboratories in recent two years

### (1) Shanghai Center for Clinical Laboratory

Participation of RELA, IFCC HbA1c Network and NCCL study.

a) RELA study: in 2020, 28 measurands got involved in RELA study, including 17OH-Progesterone, 25-OH-Vitamin D3, ALT, Amylase, ALP, AST, Calcium, CK, Cortisol, Creatinine, Digoxin, Estradiol-17 $\beta$ , Estriol, GGT, Glucose, HbA1c, LDH, Lithium, Magnesium, Potassium, Progesterone, Sodium, Testosterone, Thyroxin, Total Cholesterol, Triiodthyronin, Urea and Uric acid. In 2021, the number increased to 29 with addition of Total Hemoglobin. The results are basically satisfactory.

b) IFCC HbA1c Network study: as a member of IFCC HbA1c Network, we participated Seoul 1 and Seoul 2 study in 2020, Munich 1 and Munich 2 study in 2021, including inter laboratory comparison and value assignment. We keep our certification as Primary Reference Measurement Laboratory on HbA1c.

c) NCCL study: we participated reference inter-laboratory comparison study organized by National Center for Clinical Laboratory (NCCL). The measurands were Calcium and Triiodthyronin in 2020, 25-OH-Vitamin D3 and HCY in 2021. Results were satisfactory.

### (2) Shenzhen Mindray Bio-Medical Electronics CO., Ltd, China

a) In 2020&2021, Mindray participated the value assignment activities for candidate reference materials launched by National Institutes for Food and Drug Control (NIFDC), China. The measurands are as following:

- Total prostate specific antigen, tPSA;
- Free prostate specific antigen, fPSA;
- Glycoprotein CA125;
- Prolactin, PRL;
- Anti-thyroid peroxidase antibody, Anti-TPO.

b) In 2021, combined with the reference laboratory of Guangdong Province Traditional Chinese Medical Hospital, Mindray launched traceability research about the measurement of COVID-19 neutralizing antibody based on ID-LC- MS/MS platform.

c) In 2021, Mindray participated the value assignment activities for candidate reference material launched by National Center for Clinical Laboratories (NCCL), China. The measurand is Vitamin D in blood serum.

d) In 2021, Mindray participated the value assignment activities for candidate reference materials of specific proteins launched by Beijing Institute of Medical devices Testing (BIMT), China. The measurands are as following:

- C-reaction protein, CRP;
- Transferrin, TRF;
- Complement C3;
- Complement C4.

e) In 2021, Mindray participated the harmonization of C-reaction protein (CRP) measurement launched by National Institute of Metrology (NIM), China.

### (3) BeijingStrong Biotechnologies, Inc.(BSBE)

**a) Proficiency Testing Program:**

Every year, BSBE participates in the RELA International Proficiency Testing Program. 2020 and 2021, the number of projects participating in the RELA International Proficiency Testing Program has increased to 17. And all the results are satisfactory. So, the reference measurement capability of our reference laboratories can be demonstrated by participating in proficiency testing programs.

**b) Applications of reference measurement system in BSBE**

**① For the traceability of product calibrator**

We have studied deeply in the traceability of calibrators and formed a standardized operation process.

**Step1: Prepare of working calibrator**

First of all, collect a large number of clinical serum samples covered the high concentration and low , then mix the samples that concentrations similar and get different concentrations of serum(5-8 levels). after that detect of infectious diseases such as HIV, HbsAg and HCV in mixed serum, so serum containing infectious substances can be confirmed. And then filter the serum, dispense it to small units, and then seal it, lastly stored the serum in -80 °C refrigerator. This serum is used as working calibrator. (See Diagram 1)

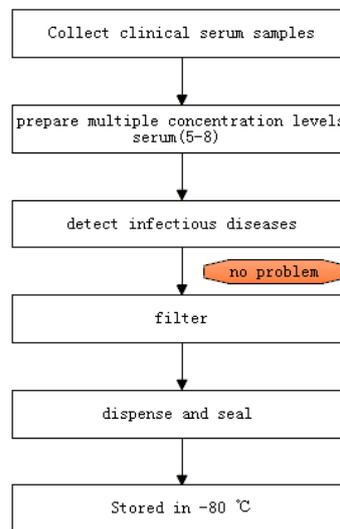


Diagram 1 The process of preparing of working calibrator

**Step2: Establish the chain of traceability**

We need to run the reference measurement procedure in BSBE reference measurement laboratory, and perform quality control with the reference material in order to confirm the validity of the reference measurement procedure, then assign a value to the serum using the validated reference measurement procedure. The chain of traceability was established according to ISO17511. (See Diagram 2)

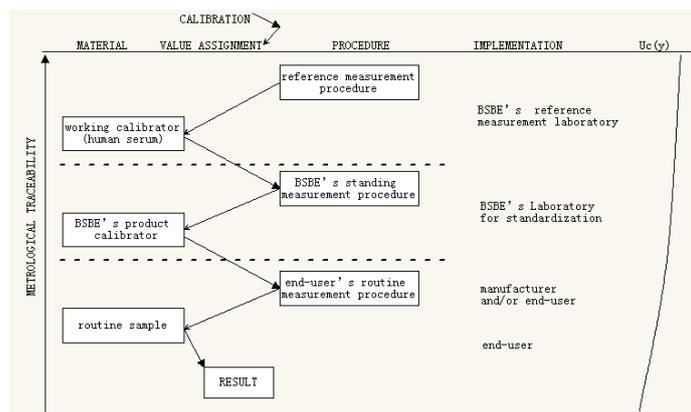


Diagram 2 The process of establishing the chain of traceability

Now, we have established about 20 reference measurement procedure in BSBE reference measurement laboratory. We also have prepared different concentrations of serum of each measurands. And the chain of traceability was established according to ISO17511.

In view of this, the routine testing system which is consistent with the BSBE calibrator, kit and automatic biochemical analyzer is traceable to the well confirmed reference measurement procedure, which can effectively ensure that clinical samples be accurately measured in the routine detection system, and will provide accurate results to clinicians and patients. The doctor can make an accurate diagnosis of the disease in time and provide effective treatment for the patients.

## 2. Planned activity(ies) in support of standardization in laboratory medicine

(Please outline R&D project(s) and/or programme(s) planned by your organization in the next two years including information on: new measurement area(s)/meaurands of interest for your organization; new CRMs and renewals of materials; development of methods (new measurands and improved measurement technique/principle); and extensions of your calibration measurement service(s) portfolio.)

### (1) National Institute of Metrology, China

NIM and BIPM plan to co-organize The Fourth TQ-MSQS International Conference (Therapeutics and Diagnostics: Measurements, Standards, Quality and Safety) in the year of 2022 at Chengdu city. Based on the valuable experiences that achieved from the previous three conferences that held from 2016-2020, NIM and BIPM will mainly focus on how to make a better relationship among IVD producers and reference laboratories in China. Meanwhile, lots of satellite symposiums will be held, which can establish a platform for end-users and standard researchers to discuss issues relating to measurement activities.

### (2) Maccura Biotechnology Co., Ltd. China Co., Ltd

In the next two years, Maccura will focus on reference material study and establishing new item reference methods, at the same time, doing products traceability well.

### (3) Reference Laboratory of Beijing Aerospace General Hospital

In the next two years, our laboratory is committed to the study of 25 hydroxyl vitamin standardization and related standard material development. In addition, we are interested in the lipase candidate reference procedure proposed by Japan. Many laboratory-to-lab exchanges have been cancelled or postponed due to the COVID-19 pandemic. Hope the situation will improve in the next two years.

### (4) Shenzhen Mindray Bio-Medical Electronics CO., Ltd, China

In the next two years, Mindray will focus on developing new RMP based on mass spectrometry, including:

a) Revising or modifying existing procedures to be more efficient and/or applicable under Mindray's measurement system, such as:

- i. FT3/FT4;
- ii. TC/TG/Apo A1/Apo B;
- iii. Folate/C-peptide/Insulin;
- iv. Uric Acid/Urine;
- v. Etc...

b) And developing new RMPs for some important measurands such as TSH.

### **(5) Shanghai Center for Clinical Laboratory**

a) We plan to establish methods on mass spec platform with measurands about C-peptide and Glycated albumin, etc. Extension of our calibration measurement services may be achieved by including more measurands into accreditation of ISO 15195 and by application of more into trueness verification programs.

b) We plan to establish the Yangtze River Delta regional reference laboratory network (7 laboratories have passed the ISO15195 accreditation of CNAS by the end of 2021) to further improve the equivalence of clinical laboratory test results.

c) We will continue to carry out education courses on standardization in laboratory medicine in Shanghai and nationwide.

### **(6) Beijing Strong Biotechnologies, Inc. (BSBE)**

In the next two years, we plan to build some reference measurement procedures covered metabolites, glycosylated proteins, vitamins, drugs on our reference measurement platforms. The projects we plan include ADA on the UV spectrophotometer platform; Cortisol, Cystatin C on the LC-MS/MS platform; Ca, Li, Mg, K, Na on the IC platform. And the research of protein reference method is a hot spot in the world, but at the same time it is a difficult point. In recent years, the research of protein reference method on the LC-MS/MS platform has been very deep. Our company is also very concerned about the research progress in this field. BSBE hope to strengthen the cooperation between reference laboratories and collaborative research.

## **3. Promoting traceability in laboratory medicine**

(Please describe activities your organization has undertaken during the last two years for promoting traceability in laboratory medicine including but not limited to a listing of your publication(s), presentation(s) and other communication(s) on traceability at international and national conferences or congresses, or other forums for clinical laboratory medicine)

### **(1) Maccura Biotechnology Co., Ltd. China Co., Ltd**

Assisting to promoting these meetings about traceability.

### **(2) Reference Laboratory of Beijing Aerospace General Hospital**

a. The 10th Academic Conference of Laboratory Medicine in Three Provinces and Two Cities of North China: How to use the reference system to improve the measurement ability of clinical laboratories.

b. Laboratory Medicine Standardization-Clinical Laboratory Accreditation Solution & Training course on clinical laboratory Methodology confirmation and Measurement Uncertainty Assessment: Basic theory of measurement uncertainty in medical laboratories and case sharing.

### **(3) Shanghai Center for Clinical Laboratory**

We actively cooperate with the Quality Control Center (QCC) of Medical Laboratory of University of Medicine Pharmacy at Ho Chi Minh city in Vietnam. Prof. Yi Ju was invited to give a video speech entitled " How SCCL ensures traceability in PT and stresses its importance to participants? " at the Workshop on the 10 years Celebration of QCC entitled: " Establish a Reference Laboratories Network in Viet Nam" on July 30, 2020.

#### 4. Reference laboratory networks /collaborations focusing on developing /implementing reference measurement systems

(Please describe your participation in laboratory networks, forums or professional/technical committees linked to reference measurements system development/implementation, and contributions to JCTLM Working Group activities.)

##### (1) Maccura Biotechnology Co., Ltd. China Co., Ltd

Maccura Biotechnology Co., Ltd. is the members of JCTLM Stakeholder Member.

##### (2) Shanghai Center for Clinical Laboratory

a) IFCC HbA1c Network: as a member of IFCC HbA1c Network, we participated its annual inter laboratory comparison study and value assignment for new calibrators.

b) IFCC working group on CGM: we participated in the discussion of the working group on continuous glucose monitoring. See the paper Standardization process of continuous glucose monitoring: Traceability and performance[J]. CCA, 2021, 515: 5-21.

##### (3) Shenzhen Mindray Bio-Medical Electronics CO., Ltd, China

Mindray are willing to participate and deeply involved into a series of committees and working groups as below:

- <https://www.ifcc.org/ifcc-scientific-division/sd-committees/c-tlm>;
- <https://www.ifcc.org/ifcc-scientific-division/sd-committees/c-stft>;
- <https://www.ifcc.org/ifcc-scientific-division/sd-working-groups/wg-sau>;
- <https://www.ifcc.org/ifcc-scientific-division/sd-working-groups/wg-sia>;
- <https://www.ifcc.org/ifcc-scientific-division/sd-working-groups/wg-tni>;
- <https://www.ifcc.org/ifcc-scientific-division/sd-working-groups/wg-pct>;
- <https://www.ifcc.org/ifcc-scientific-division/sd-working-groups/wg-ptnr>

##### (4) Beijing Strong Biotechnologies, Inc. (BSBE)

During 2020 to 2021, BSBE completed the “National Key R&D Plan of the Ministry of Science and Technology in the 13th Five-Year Plan”, Research on Traceability and Quality Evaluation of Biochemical IVD Reagents Related to Geriatric Diseases, with the purpose of developing the reference measurement systems in enterprise, developing reference materials and establishment of industry standards. Now, our company is actively establishing reference methods and actively participating in collaborative research among reference laboratories. We participated in collaborative research on homocysteine, testosterone reference methods and evaluate the matrix effective of reference material with National Institute of Metrology. Next, we will build reference laboratory networks with National Institute of Metrology and other enterprise.

#### 5. Open questions and suggestions to be addressed by JCTLM

(Suggestions on issues related to standardization and metrological traceability that should be considered by the JCTLM)

##### (1) Maccura Biotechnology Co., Ltd. China Co., Ltd

a. It would be better if the evaluation of Calibration and Measurement Capability (CMC) has a consistent standard document for guidance, for different clinical measurement areas, for review teams, for laboratories.

b. About multi-point calibrators, if reference material has only one concentration, how to do the traceability and assess the uncertainty?

c. If the concentration of the reference material is very low and is not suitable for calibration, how to do the traceability?

##### (2) Shenzhen Mindray Bio-Medical Electronics CO., Ltd, China

It would be better if the commutability information of secondary reference materials in JCTLM database could be provided.

**(3) Beijing Strong Biotechnologies, Inc. (BSBE)**

We are looking forward to the new ISO 17511 and harmonization standard releasing, hoping to promote traceability in laboratory medicine.