Draft template for biennial activity report from JCTLM Member organizations

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.

Organization: NIM and 7 Organizations from China

JCTLM Member status: Yes

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Period covered: 2018 – 2019

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.)

During 2018-2019, with NIM China as the core, relying on CJCTLM , a lot of in vitro diagnostic reagent traceability work have been conducted by Chinese IVD companies and reference laboratories . Many reference materials, including proteins, metabolites, electrolytes have been developed. A series of reference methods were established, including C-peptide in serum, C-reactive protein in serum, homocysteine in serum, etc.

For more details, please refer to the introduction below.

1.1 Purity certified reference materials

Hormones purity	Hydrocortisone purity	GBW09221
	17α-hydroxyprogesterone purity	GBW09220
	17β-estradiol purity	GBW09223
	Estriol purity	GBW09224
	Estrone purity	GBW09225

	Vanilla mandelic acid purity	GBW09226
Hormones solution	17α-hydroxyprogesterone in methanol	GBW(E)090947
	17β-estradiol purity in methanol	GBW(E)090948
	Estriol-D3 in methanol	GBW(E)090949
	Estrone in methanol	GBW(E)090950
	Vanilla mandelic acid in methanol	GBW(E)090951
	17α-hydroxyprogesterone in methanol、Estriol-D3 and Estrone in methanol	GBW(E)090952
	17α-hydroxyprogesterone and hydrocortisone solution in methanol	GBW(E)090953

1.2 Matrix certified reference materials

Type	Name	Code
Hormones in human serum	Hydrocortisone in human serum（92.2ng/g）	GBW09833
	Hydrocortisone in human serum（107.6ng/g）	GBW09834
	Progesterone in human serum（1.09ng/g）	GBW09831
	Progesterone in human serum（21.89ng/g）	GBW09832
	17α-hydroxyprogesterone in human serum（0.51ng/g）	GBW09829
	17α-hydroxyprogesterone in human serum（1.65ng/g）	GBW09830
Vitamins and micronutrients	Folate and Insulin in Frozen Human Serum	GBW(E)090925
Proteins	Folate and Insulin in Frozen Human Serum	GBW(E)090925
Metabolites and substrates	Homocysteine in Frozen Human Serum (level 1)	GBW(E)091011
	Homocysteine in Frozen Human Serum (level 2)	GBW(E)091012
	Homocysteine in Frozen Human Serum (level 3)	GBW(E)091013
	Uric Acid in Frozen Human Serum (level 1)	GBW(E)090934
	Uric Acid in Frozen Human Serum (level 2)	GBW(E)090935
	Uric Acid in Frozen Human Serum (level 3)	GBW(E)090936
Electrolyte in serum	Potassium in Frozen Human Serum (level 1)	GBW(E) 090970
	Potassium in Frozen Human Serum (level 2)	GBW(E) 090971
	Potassium in Frozen Human Serum (level 3)	GBW(E) 090972
	Magnesium、Zinc、Iron and Copper in Frozen Human Serum (level 1)	GBW(E)090931
	Magnesium、Zinc、Iron and Copper in Frozen	GBW(E)090932

	Human Serum (level 2)	
	Magnesium、Zinc、Iron and Copper in Frozen Human Serum (level 3)	GBW(E)090933
	Alkaline phosphatase (ALP)	GBW(E)090920
	Aspartic acid transferase (AST)	GBW(E)090919
	Human papillomavirus type 18 deoxyribonucleic acid (HPV18DNA)	GBW(E)090957
	Human papillomavirus type 16 deoxyribonucleic acid (HPV16DNA)	GBW(E)090956
	Hepatitis C virus (HCV DNA) Ribonucleic Acid Serum	GBW(E)090628
	Hepatitis B virus (HBV DNA) deoxyribonucleic acid Serum	GBW(E)090627

1.3 Reference measurement methods

Analyte	Approach	Matrix
C-reactive protein	ID-LC- MS/MS	Serum
C peptide	ID-LC/ MS/MS	Serum
Uric acid	ID-GC MS	Serum
Homocysteine	ID-GC MS/ID-LC- MS/MS	Serum
25-OH-Vitamin D3	ID-LC- MS/MS	Serum
Estriol	ID-LC-MS/MS	Serum
5-Methyltetrahydrofolic acid	ID-LC/ MS/MS	Serum
Potassium	ID-ICP MS	Serum
Magnesium	ID-ICP MS	Serum
17α-hydroxyprogesterone (17-OHP)	ID-LC-MS/MS	High-purity material, Calibration solution, Serum
HCY	ID-LC-MS/MS	High-purity material, Calibration solution, Serum
25-OH-VD3	ID-LC-MS/MS	High-purity material, Calibration solution, Serum
Testosterone	ID-LC-MS/MS	High-purity material, Calibration solution, Serum
Adenosine deaminase (ADA)	Candidate reference method for the Measurement of Catalytic Activity Concentrations of ADA at 37 °C	High-purity material, Calibration solution, Serum

1.4 Calibration (reference) measurement services

Analyte	Approach	Clients	Time	Matrix
25-OH-vitamin D	ID-LC-MS/MS	National Center for Clinical Laboratories (NCCL)	2019.01-2019.02	
Chloride	Ion Chromatography	National Center for Clinical Laboratories (NCCL)	2019.01-2019.04	
Sodium	Ion Chromatography	Beijing Chao-yang Hospital	2019.07-2019.10	
Potassium	Ion Chromatography			
Calcium	Ion Chromatography			
Total Propein	Spectrophotometry			
Glucose	Spectrophotometry			
Total Bilirubine	Spectrophotometry			
GGT	IFCC reference measurement procedure (37 °C)			
Sodium	Ion Chromatography	Beijing Chao-yang Hospital	2018.07-2018.10	
Potassium	Ion Chromatography			
Calcium	Ion Chromatography			
Total Protein	Spectrophotometry			
Glucose	Spectrophotometry			
Total Bilirubine	Spectrophotometry			
GGT	IFCC reference measurement procedure (37 °C)			
AMY	IFCC reference measurement procedure (37 °C)	European Commission Joint Research Centre	2018.05-2019.06	
Testosterone	ID-LC-MS/MS	National Institute of Metrology，China	2017.11-2018.05	
Homocysteine	ID-LC-MS/MS			

17β-estradiol	ID-LC-MS/MS			Calibration materials, control specimens and human serum
Creatinine	ID-LC-MS/MS			Calibration materials, control specimens and human serum
total protein	Biuret Colorimetric assay			Calibration materials, control specimens and human serum

1.5 Publications

Authors	**Title**	**Journal, issue, page**
Peng Xiao, Hongmei Li, Xianjiang Li and Dewei Song	Analytical barriers in clinical B-type natriuretic peptide measurement and the promising analytical methods based on mass spectrometry technology	Clinical Chemistry and Laboratory Medicine 2019 Jun 26;57(7):954-966
Min.Shen, Xiaodong Yang, Lin Wang.	Establishment and performance evaluation of candidate reference measurement procedure for serum total homocysteine by liquid chromatography-tandem mass spectrometry	Laboratory Medicine. 2018.33:1018-1025
Jihua Zou, Min Shen, Man Zhang	An improved reference method for serum cations measurement by ion chromatography	Clinical Laboratory Analysis. 2018. DOI: 10.1002/jcla.22429
Jihua Zou, Min Shen, etc	Evaluation of IVD quantitative procedures' accuracy(truness and precision)	Science Press, in printing
Professional committee of clinical mass spectrometry laboratory medicine, laboratory physician branch, Chinese medical doctor association(one of authors)	Consensus of method development and validation of liquid chromatography-tandem mass spectrometry in clinical laboratories.	Laboratory Medicine.2019, 34(3):189-196.
Professional committee of clinical mass spectrometry laboratory medicine, laboratory physician branch, Chinese medical doctor association(one of authors)	Consensus on the application of mass spectrometry in the detection of microelements in clinical laboratories.	Laboratory Medicine.2019, 34(8):677-681.

Professional committee of clinical mass spectrometry laboratory medicine, laboratory physician branch, Chinese medical doctor association(one of authors)	Consensus on the application of MS/MS technology in the screening of the newborn's amino acid, organic acid and fatty acid oxidation metabolic disorders in clinical laboratories.	Laboratory Medicine.2019, 34(6):479-485.
J. Zou, M. Zhang, M. Shen, M. Tu,B. Zou	Establishment and evaluation of candidate reference measurement procedure for serum electrolytes （potassium sodium calcium and magnesium） based on ion chromatography	Laboratory Medicine. 2017. 32: 143-148. (in Chinese)
J. Jia, M. Tu, M. Shen, J. Zou, M. Zhang	Uncertainty Evaluation of serum cations concentrations measured based on ion chromatography as reference measurement procedure	Laboratory Medicine. 2016. 31: 1087-1092. (in Chinese)
B. Zou, J. Zou, M. Shen, M. Zhang, L. Wu, M. Tu	Establishment of reference measurement procedures for serum electrolytes based on ion chromatography	Laboratory Medicine. 2015. 30: 1250-1256. (in Chinese)
B. Zou, J. Zou, X. Yang, M. Shen, L. Wu	Development of a candidate reference measurement procedure for the Determination of Serum 25-Hydroxyvitamin D using isotope-dilution liquid chromatography-tandem mass spectrometry	Clinical Chemistry 2016 AACC Annual Meeting and Clinical Lab Expo
B.Zou,J.Zou,M.Shen,M.Zhang, L.Wu,M.Tu	Ion chromatography as candidate reference method for the determination of chloride in human serum	Clinical Chemistry 2015, 61(10) AACC Annual Meeting and Clinical Lab Expo
B.Zou,J.Zou,M.Shen,M.Zhang, L.Wu,M.Tu,Y.Yan	An improved reference method for serum cations measurement by ion chromatography	Clinical Chemistry 2015, 61(10) AACC Annual Meeting and Clinical Lab Expo
PENG Xu, ZOU Yingshu, YANG Zongbing, WANG Jun.	Qualititative analysis of 5-methyltertrahydrofolate in human serum by ID-LC-MS/MS.	Chinese Journal of Clinical Laboratory Science. 2018, 36(3),161-165.
KANG Juan, WANG Huiru, SUN Jingsheng, WANG Jun, CHEN Wei.	Establishment of clinical reference measurement laboratory using blood cell analysis as an example	Laboratory Medicine. 2018, 33(2):177-181.
Li Shengmin， Chai Chuanke，Zou Yingshu,Peng Xu, Yang Zhong, Wang Jun.	A new Density Measurement Device for trace Serum or Blood.	Chinese Journal of Medical Device, 2018, 31(23):49-51
Peng Xu, Zou Yingshu, Wang Jun.	Determination of Unconjugated Estriol in Human Serum by ID-LC/MS/MS	Chinese Journal of Medical Device,2019, 32(9):43-45
WANG Jun, DAI Lei-ying, YANG Zhong, ZHAO Bing-feng, LI Zheng, WANG Hui-ru.	Study for Performance Evaluation Protocol of Automatic Luminescence Immunoassay Analyzer	Chinese Journal of Luminescence. 2019, 40(1):122-129.

Xianzhang Huang, Qiaoxuan Zhang , Songbai Zheng, Jianbing Wang, Liqiao Han, Haibiao Lin, Peifeng Ke, Junhua Zhuang, Zhimin Cao	Measurement of human serum unconjugated estriol without derivatization using liquid chromatography-tandem mass spectrometry candidate reference method and compared with two immunoassays.	Analytical and Bioanalytical Chemistry, 2018, 401(24): 6257-6267.
Liqiao Han, Xiaoting Huang, Lu Zhang, Qiaoxuan Zhang, Jianbing Wang, Haibiao Lin, Jun Yan, Junhua Zhuang, Xianzhang Huang	Candidate reference measurement procedure for determination of urea in serum by liquid chromatography-tandem mass spectrometry.	Journal of Pharmaceutical and Biomedical Analysis, 2019, 162: 124-129.
Qiaoxuan Zhang, Lu Zhang, Haibiao Lin1, Zhiliang Cai, Jun Yan, Qiqin Wang, Liqiao Han, Jianbing Wang, Peifeng Ke, Junhua Zhuang, Xianzhang Huang.	Evaluation of a bracketing calibration-based isotope dilution liquid chromatography–tandem mass spectrometry candidate reference measurement procedure for 17α-hydroxyprogesterone in human plasma.	Analytical and Bioanalytical Chemistry, 2019, DOI: 10.1007/s00216-019-02086-5.
Qiaoxuan Zhang, Zhiliang Cai, Yingyi Liu, Haibiao Lin, Qiqin Wang, Jun Yan, Liqiao Han, 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 17β-estradiol by isotope dilution liquid chromatography tandem mass spectrometry	Microchemical Journal, 2019, DOI: 10.1007/S0026-265X(19)31814-4
Liqiao Han, Xiaoting Huang, Jianbing Wang, Haibiao Lin, Qiaoxuan Zhang, Yongmei Gu, Keqi Sun, Yongdan Yang, Jun Yan, peifeng Ke, Xianzhang Huang, Junhua Zhuang	Optimization of an enzyme-coupling method by spectrophotometer for serum adenosine deaminase: As a candidate reference method	Analytical Biochemistry 587 (2019) 113462
Yi Ju, Qing Li, Liping Tang.	Hemoglobin A1c standardization in China.	Chin J Lab Med, 2018,41(11): 804-807.
Yi Ju, Qing Li, Zhonggan Jin.	Uncertainty assessment of HbA1cLC-MS.	Chinese Journal of Clinical Laboratory Science, 2018,36(12):923-926.
Qing Li, Yi Ju, Hewen Sun, etc.	Isotope dilution liquid chromatography mass spectrometry quantification of serum apolipoprotein E and its phenotyping,	Chin J Lab Med, 2019,42(8): 629-633.
Qing Li, Yi Ju, Hewen Sun, etc.	Peptides releasing study of serumapolipoprotein A-I and apolipoprotein B by ID-LC-MS,	Chin J Lab Med, 2018,41(11): 870-874.
Qing Li, Yi Ju, Hewen Sun, etc.	Digestion efficiency of serum apolipoprotein C by liquid chromatography tandem mass spectrometry assay,	Chinese Journal of Clinical Laboratory Science, 2018, 36(10):747-750
Qing Li, Yi Ju, Hewen Sun, etc	Optimization of ID-LC-MS/MS candidate reference method on serum apolipoprotein A-I and apolipoprotein B	Chinese Journal of Clinical Laboratory Science,2018,36(12):899-902.

Zhonggan Jin, Yi Ju, etc	,.Establishment of an isotope dilution chromatography tandem mass spectrometry reference method for Hcy and its application,	.Chin J Lab Med, 2019,42(10): 858-862.
Zhonggan Jin, Yi Ju, Qing Li, etc.	Analysis on the results of creatinine,uric acid and urea determination trueness verification in Shanghai,	2016.Labratory Medicine, 2018,33(4): 348-352.

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

（1）National Institute of Metrology, China

a. In 2018, NIM organized 9 reference laboratories in China to establish a reference method for homocysteine(HCY), and investigated the commutability of Hcy, testosterone

b. In 2018, NIM organized six reference laboratories to jointly determine the EQA samples of HCY by LC-MC/MS method, and through the ability verification of 102 hospitals organized by Shanghai Center for Clinical Laboratory, to find out the causes of unqualified laboratories, and to calibrate the measurement system of the laboratory with reference materials, so that the compliance rate increased from 73% to 98%.

c. Three CRMs (Electrolytes in frozen human serum) were accepted in JCTLM database. This Certified Reference Material (GBW08124-08126) is primarily intended for use in calibration and validation of procedures in clinical analysis of electrolytes in human serum or plasma. This CRM also can be used for calibrating automatic analyzers and direct-reading ion-selective electrode(ISE) analyzers.

d. In 2019, NIM Value assignment using the Reference Measurement Procedure for E2 and E3 Reference Materials.

e. Based on the ACRM meeting , NIM organized KRISS and NMIJ value assigned for alpha fetoprote(AFP).

f. In 2019, NIM organized 6 reference laboratories in China to investigated the commutability of CRP pure reference material and serum reference materials.

（2）Maccura Biotechnology Co., Ltd

a. 2018, GDHTCM: Value assignment using the Reference Measurement Procedure for 14 kinds of Reference Materials.
b. 2018, NIFDC: Value assignment using the Reference Measurement Procedure for TBIL Reference Materials
c. 2019, IRMM: Value assignment using the IFCC Reference Measurement Procedure for AMY Reference Materials
d. 2019, NIM: Value assignment using the Reference Measurement Procedure for E2 and E3 Reference Materials.
e. 2019, NIM: Evaluation of commutability of testosterone and homocysteine in serum.

（3）Shanghai Center for Clinical Laboratory

a. Participation of RELA, IFCC HbA1c Networkand NCCL study.

RELA study: in 2018, 24 measurands got involved in RELA study, including HbA1c, Glucose, Cholesterol, Urea, Uric acid, Creatinine, Triiodthyronin, Thyroxin, Cortisol, Testosterone, Progesterone,

Estriol, Estradiol-17β, 25(OH)VD3, Digoxin, Sodium, Calcium, Potassium, Lithium, ALT, AST, ALP, AMY and GGT.In 2019, the number increased to 26 with addition of LDH and CK. Results were satisfactory.

IFCC HbA1c Network study: as a member of IFCC HbA1c Network, we participated Chicago 1 and Chicago 2 study in 2018, Barcelona 1 and Barcelona 2 study in 2019, including inter laboratory comparison and value assignment. We keep our certificationas Primary Reference Measurement Laboratory on HbA1c.

NCCL study: we participated reference inter-laboratory comparison study organized by National Center for Clinical Laboratory (NCCL). The measurands were LDH, CK and Progesterone in 2018, Progesteroneand uric acidin 2019.Results were satisfactory.

b. Value assignment services:

a) Trueness verification programs (TVP): Our center's TVP: in 2018, it included HbA1c, Creatinine, Urea, Uric Acid, AST,ALT,GGT,ALP,LDH and Calcium. In 2019, it includedALT, AST, GGT, ALP, LDH, AMY, CK, Ca, Na, HbA1c, Creatinine, Urea, Uric Acid and Cortisol.
b) NCCL's order: in 2018, it was on HbA1c.
c) Guangdong Hospital of Traditional Chinese Medicine's order: in 2018, we assigned values to their reference materials on the following measurands, such as estradiol, creatinine, ALT,AST,ALP,AMYand GGT.
d) National Institute of Metrology's order: Testosterone and HCY for scientific research.

c. On-going development of RMP includes apolipoproteins, HCY, Cyc-C, 17OH progesterone, et . On-going development of RM includes 25(OH)VD3 and 25(OH)VD2.

d. Measurands include HbA1c, Glucose, Cholesterol, Urea, Uric acid, Creatinine, T3, T4, Cortisol, Testosterone, Progesterone, estradiol, estrogen, 25(OH)VD3, digoxin, sodium, calcium, potassium, lithium, ALT, AST, GGT, LDH, AMY, CK and GGT.

（3）BeijingStrong Biotechnologies, Inc.(BSBE)

Overview of BSBE's reference measurement laboratory

a. Research platform:

BSBE's reference measurement laboratory has been approved by CNAS Medical Reference Laboratory at 2019.1.9, is accredited in accordance with ISO/ICE17025+ISO15195. Laboratory have two reference measurement procedures research platform:the UV spectrophotometer （Agilent Cary 100）and the LC-MS / MS (AB Sciex API 5500) .

b. The established reference measurement procedures:

On the UV spectrophotometer platform, we have established 11 reference measurement procedures, include seven enzyme such as AMY, ALP, ALT, AST, LDH, GGT and CK, as well as 3 small molecule metabolites: urea, uric acid, glucose and the total protein reference measurement procedures.

The LC-MS / MS platform was built in the end of 2016, till now 7 reference measurement procedures have been established include Homocysteine, free estriol, Testosterone, Creatinine, HbA1C , Total cholesterol, Uric Acid.

platform	spectrophotometer platform	LC-MS / MS
1	ALT	Homocysteine
2	AST	free estriol
3	AMY	Testosterone
4	ALP	CRE
5	CK	HbA1C
6	LDH	CHO
7	GGT	UA
8	TP	
9	UREA	
10	UA	
11	GLU	
12	CRE	

c. Proficiency Testing Program:

Every year, our lab participate in the RELA International Proficiency Testing Program. From 2017 to 2019, the number of projects participating in the RELA International Proficiency Testing Program has increased significantly from 5 to 13 . And all the results are satisfactory. So, the reference measurement capability of our reference laboratories can be demonstrated by participating in proficiency testing programs. For example 2018 RELA result

RELA 2018						
项目	sample	value	$U_c(k=2)$	Equivalent limit（%）	Target value	Bias
ALT	RELA-A	1.779	0.029	±5.25	1.795	-0.89%
	RELA-B	2.925	0.044	±5.25	2.971	-1.55%
AST	RELA-A	1.651	0.023	±5.25	1.657	-0.36%
	RELA-B	5.402	0.077	±5.25	5.511	-1.98%
AMY	RELA-A	7.109	0.217	±5.25	7.268	-2.19%
	RELA-B	8.089	0.245	±5.25	8.192	-1.26%
GGT	RELA-A	1.289	0.046	±5.25	1.307	-1.38%
	RELA-B	2.435	0.087	±5.25	2.473	-1.54%
LDH	RELA-A	5.184	0.079	±4.50	5.236	-0.99%
	RELA-B	2.756	0.043	±4.50	2.758	-0.07%
ALP	RELA-A	3.437	0.127	±5.25	3.431	0.17%

	RELA-B	4.46	0.162	±5.25	4.435	0.56%
TP	RELA-A	6.686	0.135	±2.50	6.694	-0.12%
	RELA-B	6.015	0.124	±2.50	6.014	0.02%
CK	RELA-A	5.886	0.104	±5.0	5.952	-1.11%
	RELA-B	5.442	0.095	±5.0	5.448	-0.11%
GLU	RELA-A	4.14	0.085	±3.75	4.294	-3.59%
	RELA-B	6.383	0.09	±3.75	6.562	-2.73%
UA	RELA-A	468.7	2.779	±3.25	458.893	2.14%
	RELA-B	424.7	2.47	±3.25	419.693	1.19%
Estriol	RELA-A	17.17	0.269	±10.0	16.710	2.75%
	RELA-B	33.25	0.545	±10.0	32.451	2.46%

d. Applications of reference measurement system in BSBE

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 ℃ refrigerator. This serum is used as working calibrator.(See Diagram 1)

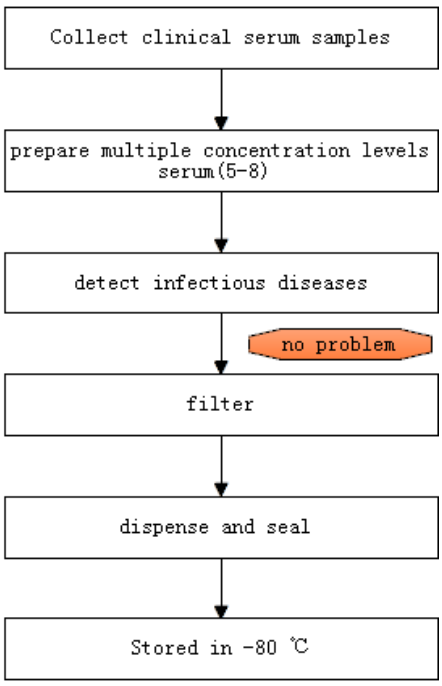

Diagram 1：The process of preparing of working calibrator

Step2: Establish the chain of traceability

We need to run the reference measurement procedure in BSBE’s 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)

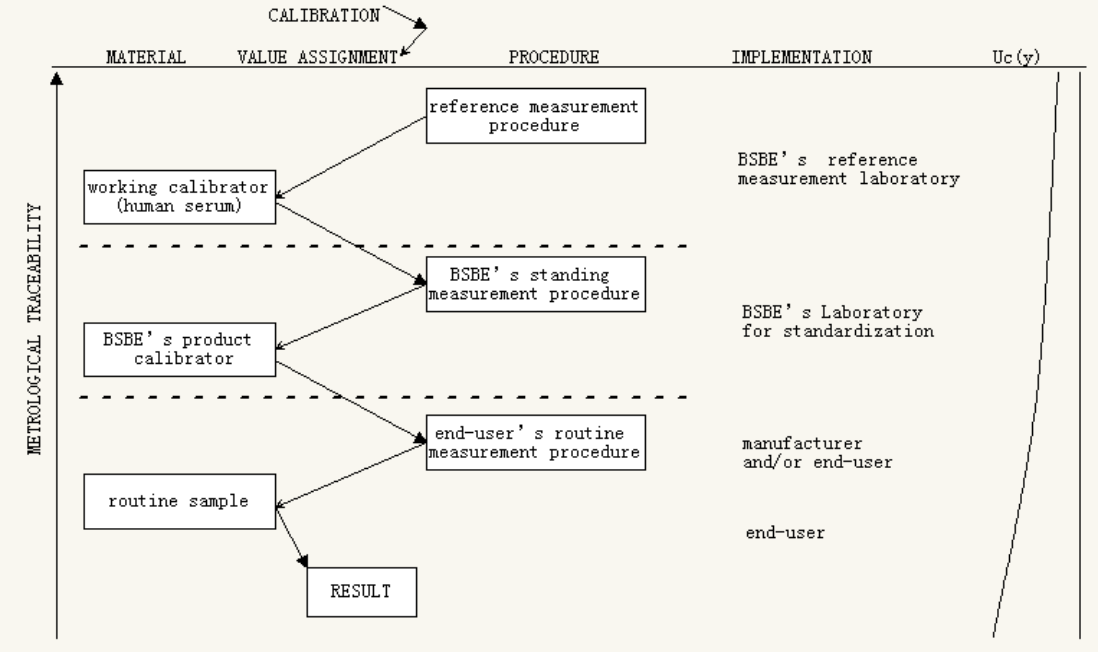

Diagram 2：the process of establishing the chain of traceability

Now, we have established 19 reference measurement procedure in BSBE’s 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 BSBE’s calibrator, BSBE’s kit and BSBE’s the 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.

e. Evaluate product quality

Autobio upholds the tenet of "committed to the penetration and improvement of medical laboratory technology, serving for human health" and strives to provide both cost-efficient and high-quality products to medical laboratories. We established two reference laboratories according to ISO17025 and ISO15195 in 2018 and participated in RELA activities since the year 2014.

We have established about 22 reference measurement procedures include ALT, AST, GGT, AMY, CK, LDH, ALP, Glu, TP, TBIL, UA, Urea, K, Na, Ca, Mg,T4,Cor,uE3,ALD, Testosterone and Progesterone. In the past 5 years, we got excellent results in RELA activities.

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

In the next two years, NIM will focus on newborn screening markers, cardiovascular and cerebrovascular diseases, tumors and other important diseases, develope a batch of high-order reference materials and reference methods, established the reference laboratory network for C-reactive protein and other test indicators, and provided better traceability services for the EQA.

（2）Beijing Institute of Medical Device Testing (BIMDT)

In the next two years, our organization plans to develop the reference methods and material including glycated haemoglobin (HbA1c), folate, some non-peptide hormones like 17-hydroxyprogesterone, progesterone.

（3）Guangdong Provincial Hospital of Chinese Medicine (GPHCM)

We plan to develop the new measurands by LC-MS/MS: human serum T3 and T4, HbA1c, Cystatin C and urinary albumin;And also we want to develop the new CRMs about human serum ALT, AST, GGT, ALP, TP, TBIL, Urea, Creatinine, Unconjugated Estriol and 17β-Estradiol et al. in China.

（4）Shanghai Center for Clinical Laboratory

First, we plan to establish methods on mass spec platform with measurands about apolipoproteins, HCY, Cyc-C, 17OH progesterone, 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. Besides, we also plan to develop RM on 25(OH)VD3 and 25(OH)VD2. Second, we will start more continual educational courses on standardization in laboratory medicine in Shanghai and nationwide. Third,we will publish more papers on method development and application.

（5） Maccura Biotechnology Co., Ltd

The next two years, Maccura plans to establish the reference method of FT3, FT4, TC, Digoxin, TG, Glu, Theophylline and Ions, meanwhile, study the traceability of these products. About the reference measurement services, Maccura plans to expand the following areas: Blood cells, Non-peptide hormones, Proteins, and Ions.

Maccura plans to produce domestic secondary reference material for uric acid,creatinine, T3, T4, FT3 and FT4 in the next two years.

（6）BeijingStrong Biotechnologies, Inc.(BSBE)

In the next two years, we plan to build some reference measurement procedures covered metabolites, glycated hemoglobins, hormones, proteins,vitamins on our reference measurement platforms. The projects we plan include TB, on the UV spectrophotometer platform, 25-OH-VD , Cortisol, Estradiol,Aldosterone, Cystatin C,17-hydroxyprogesterone on the LC-MS/MS 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.

(7) MedicalSystem Biotechnology Co., Ltd

In the next two years, we will develop the reference measurement procedures including Aldosterone, Progesterone, Total thyroxine (TT4), Blood cell counting (e.g. red blood cell count(RBC), hemoglobin (HGB), white blood cell count (WBC), hematocrit (Hct) and platelet (PLT)), etc.

（8）Autobio Diagnostic Co., Ltd

In the next two years, we plan to develop 12 reference measurement procedures include T3, FT3, FT4, rT3, E2, HbA1c, HCY, CP, INS, 25-OH-VD, 17α-OHP, CG. Building two reference laboratories accredited by CNAS and joining the JCTLM list.

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) National Institute of Metrology, China

a. 2018 Protein and Peptide Therapeutics and Diagnostics: Research and Quality Assurance International Workshop-- Measurement and Standards, Quality and Safety

PPTD is a “Protein and Peptide Therapeutics and Diagnostics” international workshop held every two years by the NIM, BIPM and NIFDC. In 2016, the first PPTD workshop was held in Chengdu, China, with

approximately 450 attendees from international organizations, national metrology institutes, academic institutions and industry.

Over four hundred participants attended the "Protein and Peptide Therapeutics and Diagnostics: Research and Quality Assurance (PPTD-2018)" Workshop held in Chengdu (China) from October 10 to 12, 2018, which was organized by NIM (China). It brought together metrology institutes, academic researchers, IVD and reagent manufacturers, regulators and pharmaceutical industry and clinical and government laboratories to present developments in establishing metrological traceability for in vitro diagnostics for accurate patient care.

The three-day workshop attracted over 80 presentations and 50 posters covering three sessions: Advanced Methods for Peptide and Protein Drug Characterization and Quality Assurance; Standards and Advances in Peptide and Protein Diagnostics; Advances and Challenges in IVD Standards and Research.

The workshop was organized under the auspices of the Joint Committee for Traceability in Laboratory Medicine (JCTLM), presenting developments in measurement methods and standards for characterizing therapeutic proteins and peptides.

It focused on the importance of measurement standards and metrology for supporting in vitro diagnostic and pharmaceutical industries as well as underpinning innovative research and the development and quality of new products.

b. "BCEIA 2019 branch of chemical metrology and reference materials"

Beijing Conference and Exhibition on Instrumental Analysis (BCEIA) is a highly specialized international analytical instruments conference and exhibition in China, which was organized for the first time in 1985, and successfully held 17 times on biennial basis up to now.The 'Chemical Metrology and Reference Material' sub-session we will be holding is one of its 10 parallel sessions of BCEIA 2019. Under the theme of 'Metrology for Worldwide Mutual Trust and Prosperity', it includes topics as follows:New Techniques for Reference Materials，Food Safety Measurement，Clinical Diagnosis and Biological Medicine，Environmental Analysis and Measurement. There are several report focus on the IVD tracebility from PTB, NMIJ HSA and China.

(2) Beijing Institute of Medical Device Testing (BIMDT)

Our organization promoted the conversion of traceability-related international standards and are applying the RMP certification. Meanwhile, our organization developed about 20 IVD product industrial standards, in which, traceability were required for the development of these products.

（3）Guangdong Provincial Hospital of Chinese Medicine (GPHCM)

In 2018, we have assigned values of ALT, AST, GGT, ALP, TP and TBIL for Guangdong center for clinical laboratory. And these frozen human serum samples were used for trueness verification of liver function in 53

clinical laboratories in Guangdong Province. In 2018, we also assigned values of HCY and uE3 for the master calibrators in Mindray. In 2019, we also assigned values of Creatinine, HCY, for the master calibrators and calibrated RBC, WBC, PLT, Hb and Hct of the Automatic blood cell analyzer in Zybio Inc.In 2019, we also calibrated RBC, WBC, PLT, Hb and Hct of the Automatic blood cell analyzer in Shenzhen DUMIND BIOTECH.

（4） Maccura Biotechnology Co., Ltd

Conference papers and Speeches at the meetings:

a. Protein and Peptide Therapeutics and Diagnostics: Research and Quality Assurance International Workshop, October, 2018.
   Speeches: Application of mass spectrometry for metrological traceability in IVD manufacturers.
   Conference posters: Determination of serum chloride by ion chromatography, Precise Determination of Calcium in Serum by Simulated Isotope Dilution Method of Inductively Coupled Plasma Mass Spectrometry, Effect of different antibody dosage on platelet reference measurement results.
b. 14th Annual Meeting of the Laboratory Medical Reference System. November, 2018.
   Speeches: The metrological traceability of immunochemical chemiluminescence and uncertainty study.
   Conference papers: The establishment of ID-UPLC/MS/MS method for the measurement of Creainine in human serum and its application in IVD metrological traceability and Application of Blood Cell Reference Method in Traceability of Commercial Calibrators.

Sponsor of Meetings:

c. Protein and Peptide Therapeutics and Diagnostics: Research and Quality Assurance International Workshop(PPTD), October 12nd-14th, 2018, Chengdu Sichuan, China.
   Speech: Application of mass spectrometry for metrological traceability in IVD manufacturers.
d. The 6th National Symposium on Integrated Traditional Chinese and Western Medicine in Laboratory Medicine, June 28th to 29th, 2019, Chengdu China.
   Conference papers and Speech: The metrological traceability and standardization of immunoassay.
e. The 8th Academic conference of laboratory medicine in three northeastern provinces, August 17h to18th, 2019, Haerbin China.
   Conference papers and Speech: The metrological traceability of immunochemical chemiluminescence assay kits.

（5）Autobio Diagnostic Co., Ltd

We have done some work to promote the standardization of clinical laboratory test results. In the recent 2 years, we developed dozens of master calibrators. We have participated in the verification of some Chinese pharmaceutical industry standards, such as ‘Evaluation of measurement uncertainty of calibrators for in vitro diagnostic kits’ and so on.

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）National Institute of Metrology, China

a. Ms.Bei Xu and Dr. Dewei Song are the members of JCTLM Database Working Group. They Participate in JCTLM database review every year.

b. CJCTLM is a professional technical committee established by NIM, which is responsible for the traceability of Chinese laboratory medicine. It is responsible for organizing relevant institutions in China to carry out the activities of Metrology traceability and reference laboratory. The Secretariat is located in NIM.

In recent years, CJCTLM has organized a number of traceability work in laboratory medicine, including the commutability verification of Hcy, testosterone and CRP, the organization of EQA of Hcy in 102 hospitals, and the promotion of reference laboratories to establish reference methods for estriol and Hcy.

(2) MedicalSystem Biotechnology Co., Ltd

We have participated in RELA (IFCC External Quality assessment scheme for Reference Laboratories in Laboratory Medicine) every year since 2010. In RELA 2017and 2018, we have participated 24 measurands (including Enzymes, Metabolites and substrates, Proteins, Electrolytes, 25-OH-vitamin D3, Testosterone, Aldosterone etc.) with satisfactory results. In 2017, we also have participated in the inter-lab collaborative research for the detection of serum estriol by using a candidate reference method (based on ID-LC-MS/MS method) which was organized by Guangdong Provincial Hospital of Chinese Medicine in PR China. In 2019, for National Center for Clinical Laboratories (NCCL), we provided measurement service for the samples of 25-OH-vitamin D (ID-LC-MS/MS).

（3） Beijing Institute of Medical Device Testing

We participated in RELA comparison actively every year and got satisfied results on the reference measurements of enzymes and substrates. Moreover, we have successfully organized the inter-lab comparison using blood cell counting reference methods several times in our country.

（4） Guangdong Provincial Hospital of Chinese Medicine (GPHCM)

We have taken part in the RELA laboratory networks and China National Center for Clinical Laboratories' Medical reference measurement laboratory quality evaluation.

（5）Maccura Biotechnology Co., Ltd.

a. Participate in the RELA experiment of IFCC and the Chinese reference laboratory Proficiency Testing each year;
b. Participate in the reference laboratory network of China; Participate in the evaluation of ADA reference measurement accuracy, 2018.

c. The member of National Clinical Medicine Metrology Technical Committee, China.
d. Assist JCTLM, BIPM and NIM in organizing the PPTD meeting in Chengdu, China, 2018.
e. Participate in the traceability project organized by National Institute of Metrology, China, 2019
f. Participate in the National Glycohemoglobin Standardization Program(NGSP),2019
g. Participate in the IFCC reference measurement system for HbA1c.

（6） Shanghai Center for Clinical Laboratory

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

B. Participation of certification campaign for the new CRM for alpha-amylase: ERM-AD456/IFCC**.**In 2018-2019, we participated the value assignment activity for ERM-AD456/IFCC which was organized by JRC.

（7） BeijingStrong Biotechnologies, Inc.(BSBE)

2018-2019, Our company completed the "G20 project" of Beijing Municipal Commission of Science and Technology, 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 built reference laboratory networks with National Institute of Metrology and other enterprise.

（8）Autobio Diagnostic Co., Ltd

We participated in RELA activities include ALT, AST, GGT, AMY, CK, LDH, ALP, Glu, TP, TBIL, UA, Urea, K, Na, Ca, Mg,T4,Cor,uE3,ALD, Testosterone and Progesterone. We also participated in the collaborative research of the estriol project organized by Guangdong Provincial Hospital of Traditional Chinese Medicine

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)

Note: The information of this report will be accessible publicly on the relevant JCTLM Members webpage, unless the author of the report states otherwise. In the case the organization does not authorizes the publication of the report in part or full, the author will add a statement to clarify which part(s) of the report will /will not be rendered public.

（1）Beijing Institute of Medical Device Testing

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

（2） Maccura Biotechnology Co., Ltd

About the evaluation of Calibration and Measurement Capability (CMC), whether there can be a consistent standard document for guidance, for different clinical measurement areas, for review teams, for laboratories?

The offered measurands of RELA can be increased as soon as possible?

（3）Shanghai Center for Clinical Laboratory

If JCTLM list on reference measurement procedure could expand more quickly, it would help its downstream application and benefit traceability establishment for more measurands.

（4） BeijingStrong Biotechnologies, Inc.(BSBE)

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

（5）Autobio Diagnostic Co., Ltd

We hope JCTLM will promote the development of more reference measurement procedures.