Introduction of China Bioanalysis Forum (CBF)

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Outline

- Background
  - Development of MNC Pharma, CRO and related BioA business
  - Review of Chinese bioanalytical regulations
  - Current status of GLP BioA lab in China
- Formation of China Bioanalysis Forum (CBF)
  - Mission, structure, ground rules etc
  - Recent activities
- CBF's involvement to prepare China Pharmacopeia BMV draft guidance

Background: Growth of MNC Pharma in China

"R&D center in China?" → *"in China, for China"* → *"in China, for Global"*

2001
ChemExplorer/Lilly Collaboration

2002
Nova Nordisk opened R&D center

2004
Roche opened R&D center

2005
PFE opened R&D center

2007
• GSK,
• Novastis
• AZ
opened R&D centers

2008
•Eli Lilly opened R&D center and closed Singapore center
•Genzyme invested $90m

2009
•Novartis - $1 Bn investment in China R&D
•JNJ opened R&D center
•Bayer invested 100m Euro for R&D center
•Nova Nordisk – $100m in China R&D
•Merck Serono invested $225m for R&D

2010
•S-A opened R&D center
•BMS move global R&D center from JP
•PFE opened second R&D center

Driving forces behind growth of MNC R&D centers:

- Huge market potential
- Large and growing talent pool
- Relatively low R&D cost
- CROs bring in technical know-how
- Viewed favorably by regulators (market access)

Background: Growth of CRO Business in China

Chemistry → *Biology* → *Preclinical Dev* → *Clinical Dev*

Local CROs

2000
Wuxi Chemistry based CRO

2001
ChemExplorer/Lilly collaboration

2003
Pharmaron

2004
Sundia
Medicilon

2005
BioDura - discovery
HDB- screening
Bridge Pharm - tox

2006-07
FMD – clinical
CrownBio - pharm model
Wuxi, ChemPartner, Sundia, Pharmaron
- integrated services

2007-08
Pharmlegacy - specialty animal model
Joinn, Tripod, Medicilon/MPIng t - tox

2000-02 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010-13

Global CROs

2003
Quintiles partnered with PUMCH
Eurofin opened central lab

2006
Frontage - BA/CMC

2007
Parexel acquired APEX
Covance - central lab/BA

2008
PPD partnered with PUL
CRL opened tox facility

2009
PPD acquired BioDura/Excel

2010-13
ICON acquired BeijingWits
Covance - Tox facility
CRL/Wuxi merger failed

- CRO business expansion is accelerating recently
- Local CROs – most on non-regulated areas
  Global CROs – most on regulated areas

Needs for Regulated Bioanalysis in China

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Preclinical Development

- Many GLP tox facilities in China have up-running, looking for GLP BA support.
- Many compounds discovered by MNC and domestic biotech have reached GLP tox stage.
- Foreign and local biotech companies are looking for low cost Preclinical Dev solutions.

Phase I Clinical

- Long approval time for FIH study is the main concern.
- Compounds from MNC R&D centers/ local biotech have reached Phase I. Many more are expected to come in the next few yrs
- Global clinical trials in China have increased in recent yrs

BE

- Drug registrations from foreign drug companies have exploded recently (small molecule/ vaccine/ antibody drugs)
- BE studies for local generic companies – going abroad.
- BE studies for global generic companies – cost saving

Later Phase Clinical

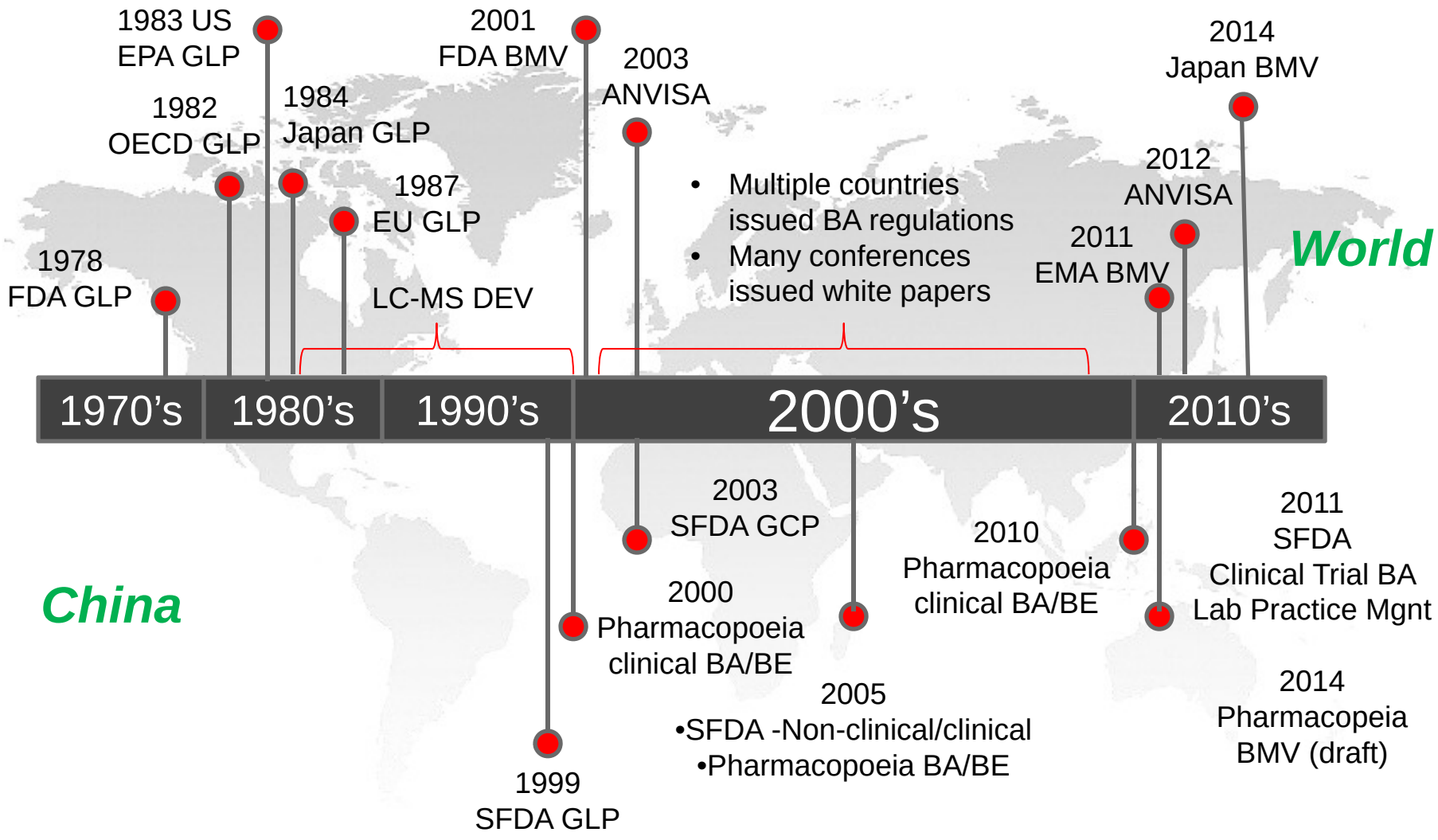
- Global clinical trials in China have increased substantially in recent years – Central lab

BA Support for ROW

One of most common ways for cost saving for many pharma/ biotech

Since the exportation of biological samples (especially human samples) is very difficult, bioanalysis of these samples will stay in China – request local bioanalytical and central labs

Historical Review of Regulations Related to Bioanalysis



Chinese Regulations on Bioanalysis

SFDA Guidelines	China Pharmacopoeia Guidelines
• Before 1999, bioanalysis rarely followed any guideline. • 1999, 2003 – Published the first GLP (1999) and GCP (2003) guidelines. • 2005 – Guideline on non-clinical development for chemical entity • 2005 – Guideline on clinical development for chemical entity	• 2000 - Guidelines on Clinical BA/BE studies • 2005 - Guidelines on Clinical BA/BE studies • 2010 - Guidelines on Clinical BA/BE studies • 2015 – Bioanalytical Method Validation Guidance (upcoming) *

* The first independent BMV guidance in China

Types of GLP Bioanalytical Labs in China

Lab Type	Scope	GLP/GCP Compliance
Labs associated with clinical centers	On-site phase I PK studies on site	Compliance to sFDA GCP requirements
Labs associated with drug safety evaluation centers (GLP Tox)	On-site GLP TK studies	Compliance to sFDA GLP requirements
Independent bioanalytical labs (global and domestic)	Both clinical and pre-clinical studies	Compliance to both sFDA/ international GLP/GCP requirements

Current Status of Regulated Bioanalysis in China

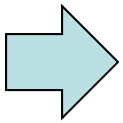
The degree of GLP compliance of bioanalytical labs in China varies substantially but has been improving rapidly

- Research institutes and clinical centers have accumulated many years' experience/learning on conducting GLP/GCP studies
- Global CROs have established their GLP labs in China with same quality systems as their foreign counterparts
- Many scientists with many years' GLP experience come to China and hold key positions in CROs and Pharmaceutical companies
- CFDA, instrument vendors, CROs and other non-profit organizations offer GLP trainings

Current Status of Regulated Bioanalysis in China

CFDA has tightened GLP/GCP regulations

- Starting from 2005, SFDA conducted on site audits for all nonclinical PK studies for IND application
- Starting from 2007, SFDA conducted on site audits for all clinical BA/BE studies
- Implemented more and stricter regulations (eg, Clinical Trial Bioanalytical Laboratory Practice Management, SFDA 2011)



However, there is still a big gap between Chinese and international GLP bioanalytical practice in general

Why CBF?

There is an urgent need to form a Bioanalysis focused group

- Preparation for fast development in drug R&D in China
- Regulatory considerations
  - CFDA regulations in bioanalysis
  - Harmonization of Chinese and international guidance in bioanalysis
- Platform to promote collaborations in bioanlaysis among industry, research institutes and clinical research
- Collate consensus and promote for Chinese bioanalysis at global level

Missions of CBF

- Encourage the scientific interactions between academia and industry in the field of bioanalysis in China

- Promote the harmonization of Chinese bioanalytical guideline with international bioanalytical guidelines

- Support the execution of regulated bioanalysis in China based on the industrial best practice

- Participate the harmonization and globalization of international guidance

- Provide the scientific education, technical training and talent development for young scientists.

Steering Committee (SC)

Academic

Professor Dafang Zhong
Shanghai Institute of Materia Medica (SIMM)

Professor Hongliang Jiang
Huazhong University of Science & Technology (HUST)

Pharmaceutical /Biotech

Dr Kelly Dong GSK, China R&D Center

Clinical Centers

Professor Pei Hu
Peking Union Medical College Hospital (PUMCH)

Dr Huichen Liu
Beijing Aerospace Central Hospital (BACH)

CRO

Dr Alicia Du ChemPartner

Dr Daniel Tang ICON, Asia Pacific

Expert Committee (EC)

Academic (6)

Prof Jinlan Zhang	IMM
Prof Xiaoyan Chen	SIMM
Prof Zhenqing Zhang	AMMS
Prof Haifeng Song	AMMS
Prof Taijun Hang	CPU
Prof Haiyan Xu	SYPHU

CRO (10)

Dr Zheming Gu	XBL, Nanjing
Dr Weiyi Zhen	Concord PharmTech
Dr Chengwei Fang	Phamaron
Dr Jingsong Xing	Wuxi AppTech
Dr Dongbei Li	Wuxi AppTech
Dr Zongping Zhang	Wuxi AppTech
Dr Luke Bi	Covance, China
Mrs Fan Jin	Covance, China
Dr John Lin	Frontage, USA
Dr Tee Zhang	Frontage, China

Pharma & Biotech (9)

Dr Eric Yang	GSK, USA
Dr Yang Wang	JNJ, USA
Dr Naidong Weng	JNJ, USA
Dr Wenzhe Lv	Roche, China
Dr Wenkui Li	Novartis, USA
Dr Shaolian Zhou	Novartis, USA
Mrs Xia Yin	Novast
Dr Lei Tang	Sanofi, USA
Dr Bing Kuang	Pfizer, USA

Clinical Research (5)

Prof Ji Jiang	PUMCH
Mr Cheng Yu	Xuhui Central Hospital
Dr John Li	TICH
Prof Heng Zheng	Tongji Hospital
Prof Mingji Wei	PUHSC

CFDA (1)

Mr Yuhu Zhang	CDE

Ground Rules of CBF

- CBF only represents a non-profit, science based organization, not individual SC or EC member

- Any official use of CBF logo or name in the meetings or publications etc should be approved by the SC

- Within CBF, we do not:
  - Exchange portfolio or IP information
  - Allow advertisements of members
  - Engage in business development

- Engagement in single vendor relationships is strictly limited and needs approval by the SC

Responsibility of SC

- Required to organize and attend regular teleconferences, yearly planning meeting and/or CBF symposium/conference

- Actively participate discussions, complete assigned tasks, represent CBF in the external conferences and interactions with other organizations

- Approve external presentations and publications

- Help identify the scientific topics/issues and organize focus teams for CBF as appropriate.

Ground Rules of EC

- There are no more than 2 representatives from each organization

- Each EC member should have at least 10 years of relevant experience in bioanalysis, deep understanding of bioanalytical regulations and can provide input to the bioanalysis related topics

- Share the passion to promote and contribute to scientific excellence in bioanalysis

Responsibility of EC

- Help provide scientific feedback to the Chinese and international bioanalytical guidance on behalf of CBF

- Might represent CBF at external conferences or publish CBF position papers

- Actively participate in the conferences/ workshops/symposiums organized or co-organized by CBF as program organizers or speakers

- Might involve in the collaborations between CBF and Chinese government agencies

Recent Activities of CBF (2013- 2014)

Regulatory activities

- Assisted to draft Bioanalytical Method Validation (BMV) Guidance for China Pharmacopeia (2015 version)
- Eight members participated GBC harmonization team (HT)
- On behalf of CBF, provided feedback to FDA draft guidance on BMV. Thirteen members attended CC V meeting in Baltimore in Dec 2013.
- As subject experts, several members participated the “Special Audits for BE studies” organized by CFDA.

Recent Activities of CBF (2013- 2014)

Conferences:

- Organized the first (Shanghai, Apr 2013) and the second (Beijing, Jun 2014) annual conferences.

- Invited speeches on EBF conferences to discuss the current status of bioanalysis and clinical research in China. (Barcelona, 2012/2013)

- Participated the discussion on harmonization of bioanalytical guidelines at JBF annual conferences (2013/2014)

- Co-organized regulated bioanalysis session at CPSA Shanghai conference (Shanghai, Apr 2013)

- Co-organized workshop of “Meet the Dragon”(Berlin, Sept 2014)

2nd CBF annual Conference (June 7-8, 2014)

Theme: Clinical research and large molecule bioanalysis

Session	Time	Topic	Speaker
Opening	9:00- 9:10 AM	Welcome	Dafang Zhong
CBF report	9:10 – 9:20 AM	CBF 2013-2014 Activities	Daniel Tang
Clinical Rsearch	9:20– 10:20 AM	Technical Evaluation of BE Studies from CFDA Perspective	Yuhu Zhang
		The Role of Phase I Clinical Studies in Drug R&D in China	Pei Hu
Break	10:20– 10:30 AM		
Large Molecule Bioanalysis	10:30– 12:00 PM	Challenges and Opportunities of Biosimilar Studies in China	Haifeng Song
		High Sensitive LC-MS/MS analysis for Peptides	Luke Bi
		Bioanalysis for Anti-Drug Antibody （ADA)	Dongbei Li

2nd CBF annual Conference (June 7-8, 2014)

Theme: Clinical research and large molecule bioanalysis

Session	Time	Topic	Speaker
Young Scientists Competition	1:15-3:15 PM	Six Presentations (three from North and three from South)	NA
Break	3:15 – 3:30 PM		
Regulatory Bioanalysis	3:30 – 4:30 PM	Update on New Non-Clinical Drug Pharmacokinetic Draft Guidance	Tao Sun
		Bioanalysis under GLP Regulations	Minjie Wei
Panel Discussion	4:30 – 5:30 PM	• Discussion on Challenges Bioanalysis in China from Technical and Regulatory Perspectives • Future Trends and Hot Topics of Bioanalysis • Career Development for Young Scientists	

Recent Activities of CBF (2013- 2014)

Publications:

- "Bioanalysis" Journal – Spotlight article
  - "Formation of CBF"
  - "Conference Report for 2nd CBF Annual Meeting"

- Published a series of "White Papers" related to regulated bioanalysis, especially on interpretation of the new China Pharmacopeia BMV guidance

Involvement of China Pharmacopeia BMV Guidance Preparation

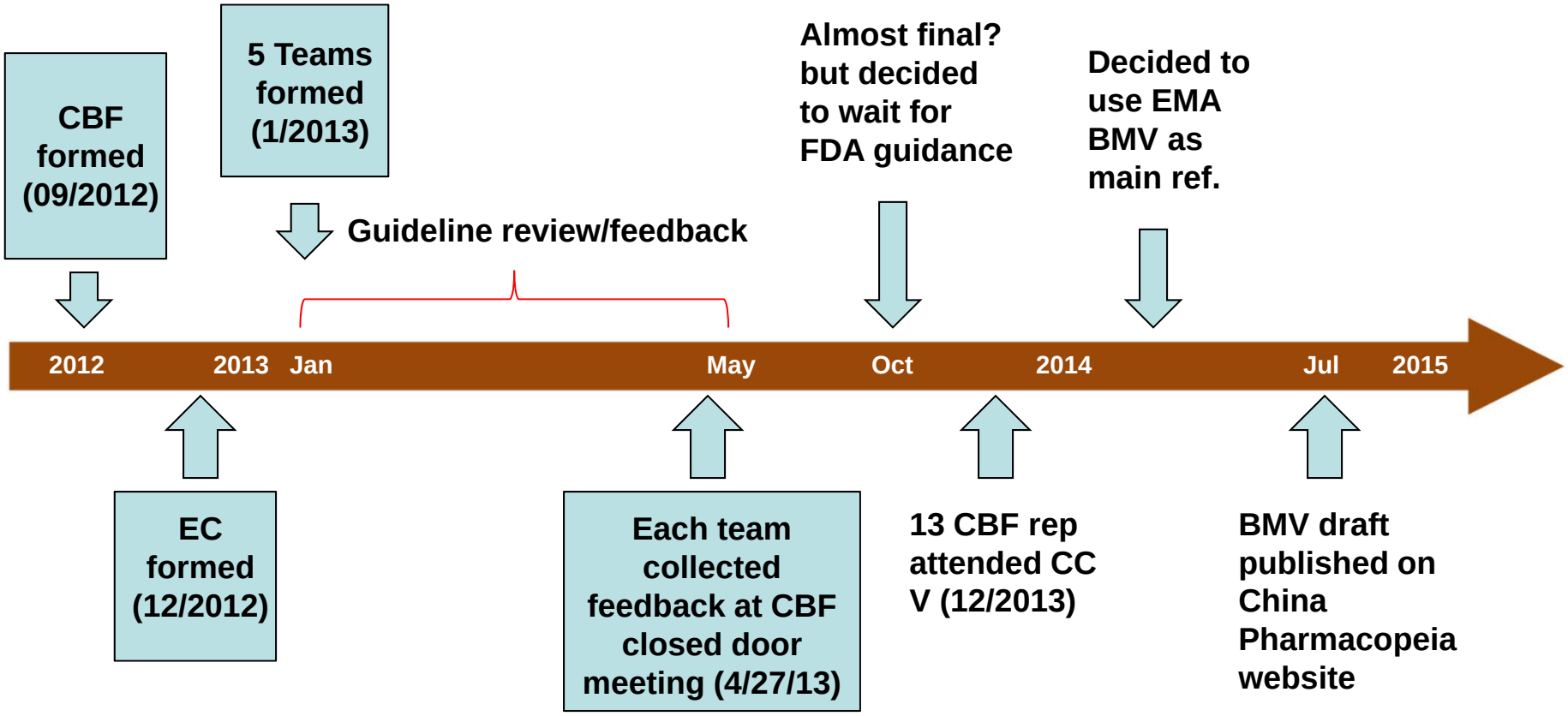
Main Considerations:

- Harmonize the existing terminology and introduce new terminology (in Chinese)
- Avoid re-inventing new requirements/terminology
- Consider the feasibility of certain requirements (from EMA/FDA guidance) in China
- Include LBA portion in the guidance
- Use EMA BMV (2011) guidance as main reference

Involvement of China Pharmacopeia BMV Guidance Preparation

Team	Topic	Team Leader	SC Sponsor	Team Member
1	Scope/ regulation, terminology, Reference std/Internal Std/reagent, sample management, documentation	Jinlan Zhang	Pei Hu	Wenzhe Lu,Naidong Weng,Tee Zhang,Luke Bi,
2	Full validation, partial validation, cross validation and the acceptance criteria	Zhemin Gu	Hongliang Jiang, Alicia Du	Eric Yang,Zongping Zhang,Chengwei Fang,Weiyi Zheng,Xiaoyan Chen,Jingsong Xing
3	Assessment of stability tests, Matrix effects	John Li	Kelly Dong, Alicia Du	Zhongping John Lin,Haiyan Xu,Zongping Zhang,Chengwei Fang,Heng Zheng,Weiyi Zheng,Xiaoyan Chen,Jingsong Xing
4	Sample analysis acceptance criteria, repeat analysis	Yang Wang	Huichen Liu, Dafang Zhong	Wenkui Li,Xia Yin,Luke Bi,Taijun Hang
5	Ligand binding assay	Haifeng Song	Daniel Tang	Huifen (Faye) Wang,Dongbei Li,Haiyan Xu,Heng Zheng,Lei Tang,George Wang,

Involvement of China Pharmacopeia BMV Guidance Preparation



Future roles of CBF and Chinese BioA Community

Stage 1 Regulatory Harmonization	Stage 2 Application	Stage 3 Actively Contribution
Harmonize Chinese guidance with major international guidelines	Interpretation of new guidance base on industry best practice Educate the BioA scientists and bring them to the international level	Actively participate new technology and innovative science development Contribute to scientific and regulatory discussion at global level

Q & A

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