

EBF



中国生物分析协会

EBF – CBF

Knowledge Exchange

China Days

11-12 Sep 2014

Maritim Hotel - Berlin

Meet the Dragon

Key Points

- Joint meeting organized by:
 - EBF (Peter van Amsterdam, Margarete Brudny-Klöppel)
 - CBF (Daniel Tang, Dafang Zhong, Pei Hu)
- Knowledge Exchange (KNEX)
 - Reach out to stakeholders and interface partners
 - Small discussion meeting



- 41 Participants from 26 companies (Pharma / CRO / Consultant / Hospital / University)
- Intercultural Awareness
 - Chinese Culture Center Berlin

<http://www.europeanbioanalysisforum.eu>

China Bioanalysis Forum - CBF



中国生物分析协会

- Founded in Sep 2012
- Steering Committee – 7 members:
 - Academic: Prof. Dafang Zhong (SIMM), Prof. Hongliang Jiang (HUST)
 - Pharma/Biotech: Dr Kelly Dong (GSK)
 - Clinical Centers: Prof. Pei Hu (PUMCH), Dr Huichen Liu (BACH)
 - CROs: Dr Alicia Du (ChemPartner), Dr Daniel Tang (ICON, APAC)
- Expert Committee – 31 members:
 - Academic (6), Pharma/Biotech (9), Clinical Research (5), CRO (10), CFDA (1)
- Mission
 - 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.

Agenda of the Meeting

- *Doing business in China – (Intercultural Awareness)*
- *Quality Systems and Regulatory Processes*
- *Bioanalytical Guidelines*
- *Clinical studies*
- *Learning by doing*



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Quality Systems and Regulatory Processes

- **Jianan Wang (CFDI-CFDA)**
Regulatory oversight of drug clinical trial in China



- **Andrew Gray (MHRA)**
Is GLP an appropriate standard for laboratories that analyse samples from human clinical trials?



- **Philip Timmerman (Janssen R&D, on behalf of EBF)**
Bioanalysis in China: Working in the intersection of global regulations and OECD-GLP



Regulatory oversight of drug clinical trial in China

- Structure of CFDA – 3 Divisions
 - Food Supervision
 - Drug and Medical Device Supervision
 - General Administration
- Affiliated Organizations of CFDA
 - National Institutes for Food and Drug Control
 - State Pharmacopoeia Commission
 - Center for Drug Evaluation (CDE)
 - Center for Food and Drug Inspection (CFDI, 2014)
 -and several more....
- Local Food and Drug Administration
 - 31 Provincial FDA, Municipal & City-level FDA, County-level FDA
- Relevant laws and regulations and drug registration process
- Roles and responsibilities of CFDI for clinical trials and bioanalytical labs
- Key elements of inspections and common findings
- Focus on future inspection procedures and international cooperations

Bioanalytical Guidelines

- **Daniel Tang (ICON)**
Introduction of China Bioanalysis Forum (CBF)



- **Dafang Zhong**
(Shanghai Institute of Materia Medica)
Guidelines on Bioanalytical Method Validation in China



Background

- Current guidelines for bioanalysis in China
 - Chinese Pharmacopoeia 2000-2010
 - Included in BA/BE guideline (1 page)
 - CFDA guidelines 2005
- Objectives of the new guidance in ChP2015
 - A separate guidance for bioanalysis
 - Harmonized with international guidelines (EMA, FDA)
 - Detailed information
 - Meet future demands in China

Background

- Process of drafting the guidance in ChP 2015
 - Pharmacopoeia Commission (2010)
 - Subcommittee for Drug Formulation (2010)
 - Drafting group (2010)



Background

- Process of drafting the guidance in ChP 2015
 - EMA and FDA guidelines for reference
 - Published on a journal (2011) and conferences for consultation (2012)
 - CBF discussion and revision (2013)
 - Approved in the Subcommittee (2014)
 - Released on website (July 2014) for consultation (#9012, 13 pages)
<http://www.chp.org.cn/cms/newscen-ter/publicity/000904.html>

6666662 Drug Evaluation Research 第34卷第6期 2011年12月 -409-

· 专 论 ·

生物样品定量分析方法指导原则（草案）

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摘 要: 根据目前国际上对生物样品定量分析的相关指导原则, 建议《中国药典》修订和扩充现有的的的指导原则, 以适应新药开发和仿制药开发的需求。内容包括: 指导原则适用范围, 生物分析方法验证, 试验样品分析, 配体结合分析, 试验报告, 以及生物分析相关定义。其中, 对基质效应、已测样品再分析、稳定性考察等列出了详细的要求。

关键词: 生物样品分析指导原则; 生物分析方法验证; 基质效应; 已测样品再分析

中图分类号: R917 文献标志码: A 文章编号: 1674-6376(2011)06-0409-07

Guidance on Bioanalysis: Method validation and analysis of study samples (Draft)

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3. State Key Laboratory of Drug Delivery Technology and Pharmacokinetics, Tianjin Institute of Pharmaceutical Research, Tianjin 300193, China

Abstract: This is the draft version for the Guidance on Bioanalysis in China Pharmacopoeia, 2015 Edition. The recommendations are based on the current international guidelines and for adapting the requirements to the development of new drugs and generic drugs. It is composed of scope of the guidance, method validation, analysis of study samples, incurred samples reanalysis, ligand binding assays, reports, and definitions. Detailed requirements for matrix effect, incurred samples reanalysis, and stability investigation are introduced.

Key words: guidance on bioanalysis; method validation; matrix effect; incurred samples reanalysis

本指导原则是为中国药典 2015 年版附录准备的草案。其内容参考了中国药典 2010 年版指导原则（生物样品定量分析方法相关内容）^[1]；美国 FDA 指导原则（2001）^[2]，欧洲 EMA 指导原则（草案，2009）^[3]，以及中国 SFDA 指导原则（2005，生物样品定量分析方法相关内容）^[4-6]。目前，全球性的生物样品定量分析方法指导原则正在讨论中^[7-9]。

1 范围

对于新药开发和仿制药开发，准确测定生物基质（全血、血浆、尿）中的药物浓度非常重要，这些数据可用于资料申报。根据毒理学、药理学和生物等效性试验的结果做出关键性决定，以支持药品的安全性和有效性。因此，必须很好地表征、完整地验证和记录应用的生物分析方法。

本指导原则提供生物分析方法验证的要求，也涉及生物分析方法本身的特定方面，如临床前或临床试验样品的实际分析。还进一步指出，何时可能使用部分验证或交叉验证，替代一个生物分析方法的完整验证。

生物分析方法验证和试验样品分析应符合 GLP 原则。但是，由于临床生物分析试验处于 GLP 范围之外，所以开展临床试验的地点不需要作为国家 GLP 贯彻程序的一部分被监测。此外，对于在人体开展的临床试验，应该遵循 GCP 原则。

2 生物分析方法验证

2.1 分析方法的完整验证

对于任何分析方法，无论是新方法还是基于文献的方法，都应该进行完整的验证。

China Draft BMV Guideline

- Prof. Zhong provided an English version to EBF after the meeting



- EBF member comments were consolidated and sent to Prof. Zhong on Oct 31th

Clinical studies

- **Peter van Amsterdam (Abbott)**
*Introduction to the CTA & NDA
process in China*



- **Pei Hu**
(Peking Union Medical College Hospital)
Early Phase Clinical Studies in China



- **Huafang Li**
(Shanghai Mental Health Center)
Late Clinical Trials in China



Clinical Studies

- **Clinical Trial Application (CTA) / New Drug Application (NDA)**
 - Different processes for Import Drug License (IDL) application and International Multi-country Clinical Trial (IMCT) applications
 - Approval timelines for NCE's (RDPAC survey) are in the range of:
 - 24 / 36 month for IDL-CTA / IDL-NDA
 - 13 / 36 month for IMCT / IMCT-NDA
- **Clinical studies**
 - Only tested and qualified drugs can be used in clinical trails
 - Clinical studies can only be conducted in public hospitals certified by CFDA
 - Phase I clinical trials: - 2 Guidelines released in 2011 by CFDA
 - Clinical part and bioanalytical laboratory practise management
 - Late stage clinical trials:
 - The role of Administrative Office at the clinical site
 - Details to consider in preparation of the trial (feasibility, study team, IRB, consent issues, patient recruitment, bias in evaluation).
 - Opportunities and Challenges when conducting global trials in China
 - O: Subject pool, state-certified sites warrant consistent standards incl. qualified medical infrastructure, ...
 - C: Long regulatory approval process limit the chances to participate in global trials, shortage of qualified CRA and affect the quality of CT....

Learning by doing

- **Margarete Brudny-Klöppel (Bayer Pharma AG)**
How to Get the Business Started?

- **Fan Jin (Covance)**
*Opportunities and Challenges of
Conducting GLP Bioanalysis in China*



- **Johanna Beekman
(Bayer Pharma AG)**
*Bayer's experience in sample
exportation from China*



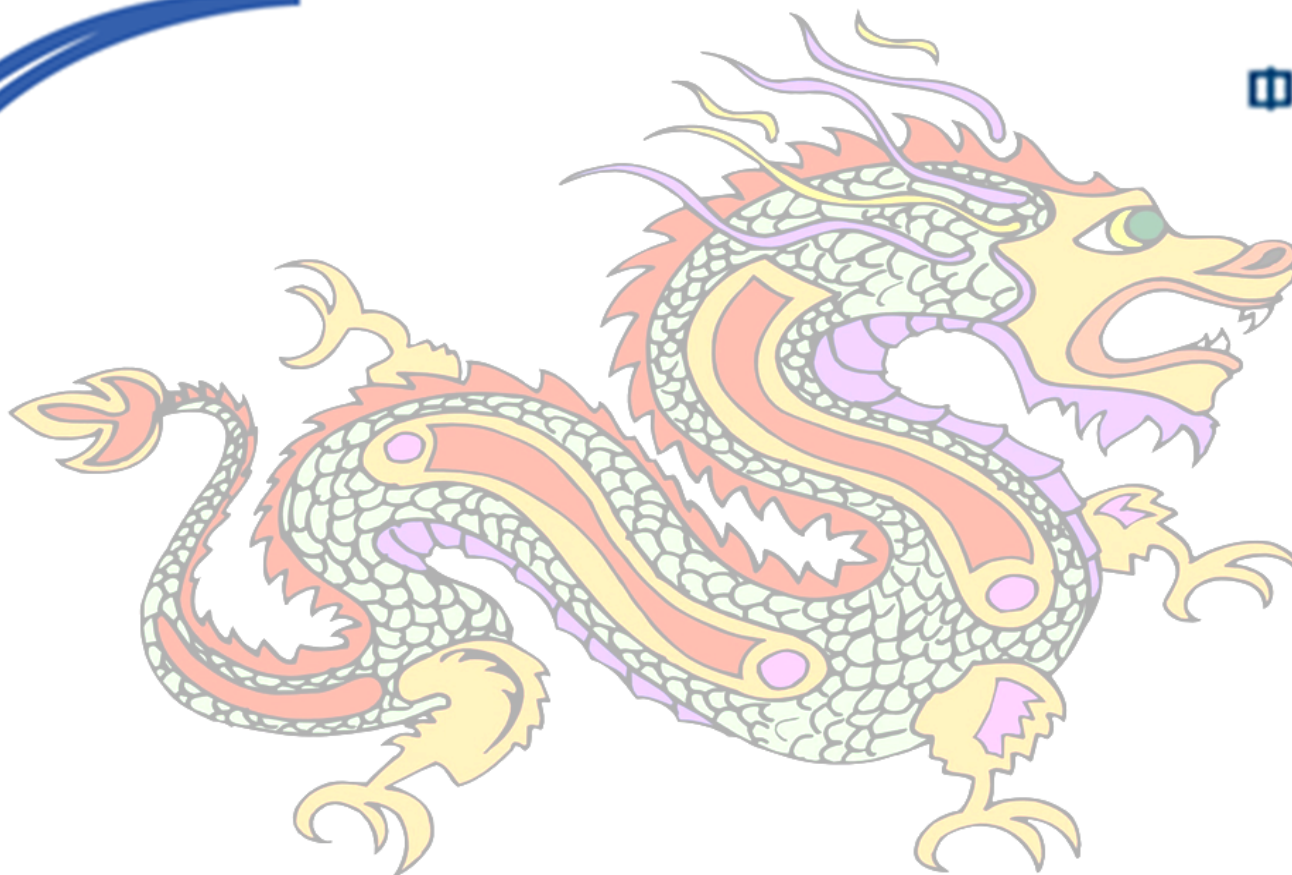
Learning by Doing

- Selection of an appropriate CRO
 - Application of an standardized procedure (preparation and conduct)
 - Unbiased evaluation based on predefined criteria (classification of the CRO, evaluation criteria and measures)
- Compliance and regulatory challenges
 - Facilities in China must have a CFDA GLP certificate before a claim of CFDA GLP compliance can be made for nonclinical safety studies.
 - CFDA has some special requirements on SOP, documentation, instrument calibration, QA inspection, protocol/report approval etc.
- Operational challenges
 - Import permit for biological samples and critical reagents i.e. antibodies
 - Lead time for special materials is about 4 weeks in China.
 - High turn-over rate of personnel
- Sample exportation challenges
 - There is no YES or NO concerning the export possibility
 - Complex application package with long review and approval times
 - No clinical site contracts can be signed before approval of sample exportation.

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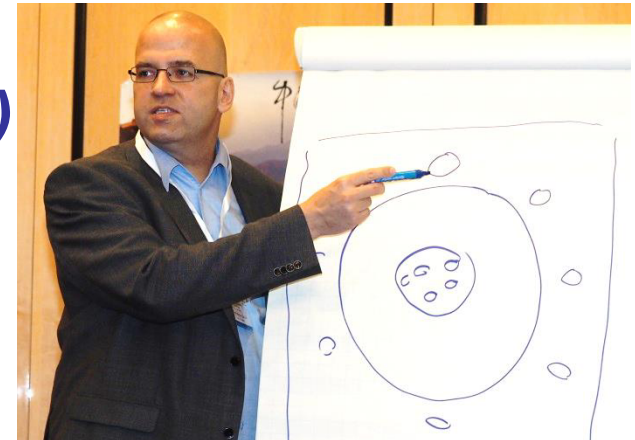
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Meet the Dragon ?

Doing Business in China – Intercultural Awareness

- **Christian Goedel**
(*SinaLingua, Heidelberg, Germany*)
Cross-Cultural Management

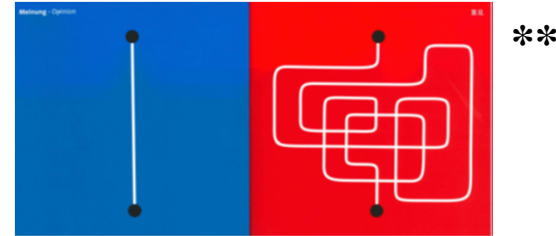


- **Yang Liu**
(*Yang Liu Design*)
East meets West –
Yang Liu's personal experience
on cultural differences

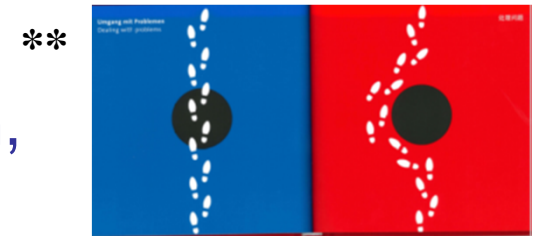


Doing Business in China – Intercultural Awareness

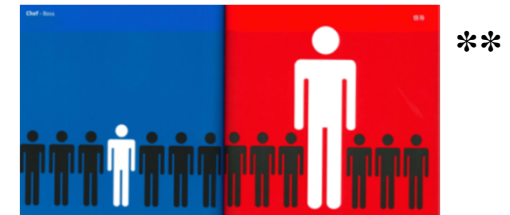
- Team building
 - Opinion, me, networking



- Communication
 - Dealing with problems, self promotion, being on time, preferred media



- Hierarchy and roles (Confucianism)
 - Boss, assigned place for everyone



Consequences for:

- Team discussion
- Communication with peers and Authorities
- Acceptance and respect of rules

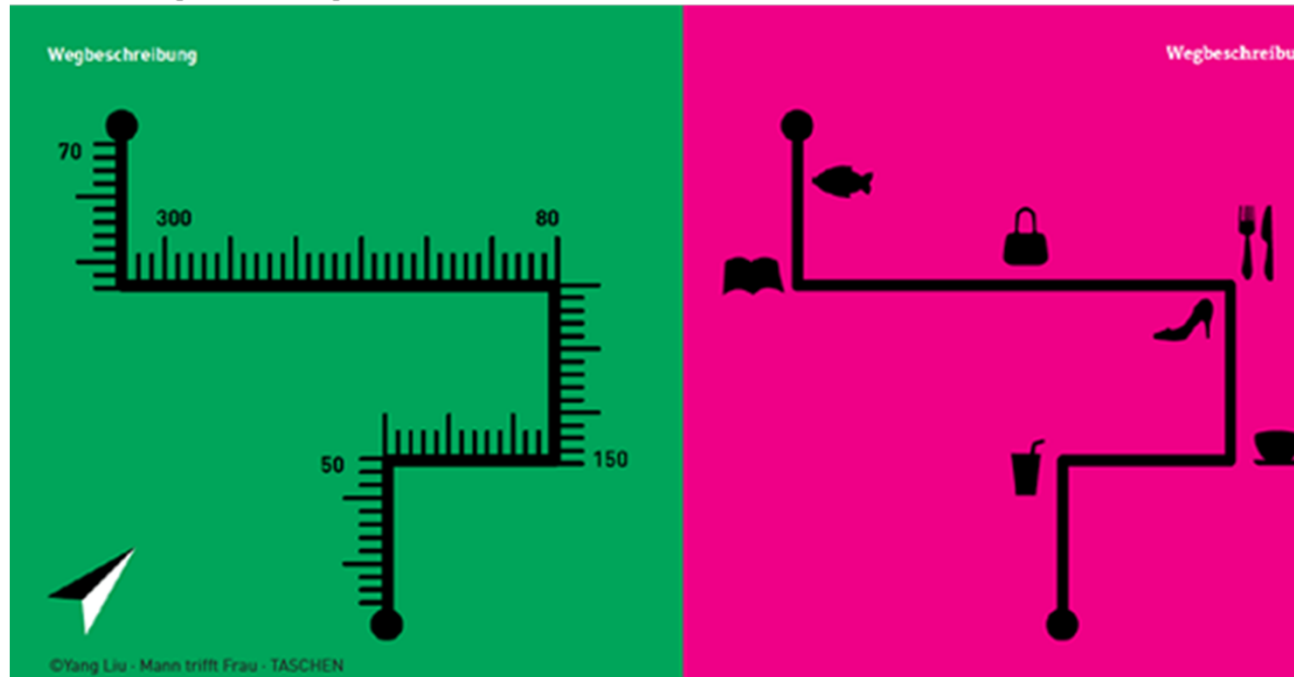
** Images shown are quotations from: ©Yang Liu 'Ost trifft West' (east meets West), Hermann Schmidt Verlag Mainz, 2014, 10th Print, ISBN 978-3874397339, www.yangliudesign.com

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... what else to consider?

➤ Differences between male / female?

Directions/Wegbeschreibung/对路的描写



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** Image shown is quotation from: ©Yang Liu 'Man meets Woman' (Mann trifft Frau), TASCHEN, 2014, ISBN 978-3836553995, www.yangliudesign.com

Slide Decks

- Are available on.....

knex2014.europeanbioanalysisforum.eu

Thank you!!