KING'S CICM
CATALYSING INNOVATION

The King's Centre for Integrative Chinese Medicine

伦敦国王学院整合中医药学中心

KING'S College LONDON

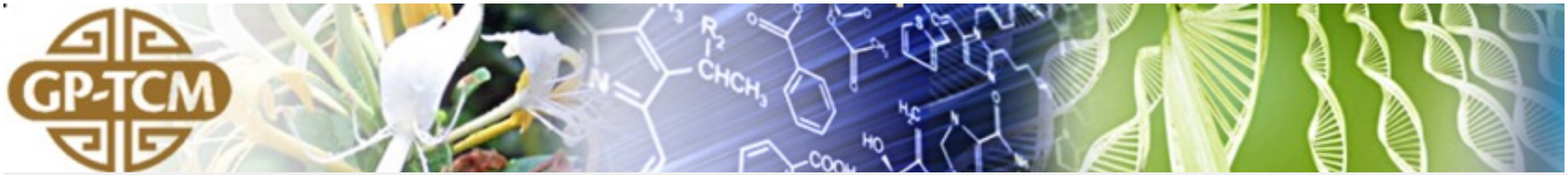
International Good Practice Guidelines and Standards in Research & Development of Chinese Herbal Medicine.

中草药研发的国际标准与规范

——纪念欧盟第七框架计划GP-TCM项目结题、 GP-TCM RA成立10周年

Dr Qihe Xu's PPT for his lecture at the School of Chinese Pharmacy, Beijing University of Chinese Medicine, 29th March 2023.

徐启河博士在北京中医药大学中药学院讲座PPT（2023年3月29日 · 中国北京）



中草药研发的国际标准与规范

——纪念欧盟第七框架计划GP-TCM项目结题、GP-TCM RA成立10周年

伦敦国王学院 徐启河

Qihe Xu, MD & PhD

Director, King's Centre for Integrative Chinese Medicine

Senior Lecturer in Renal Medicine & Pharmacology

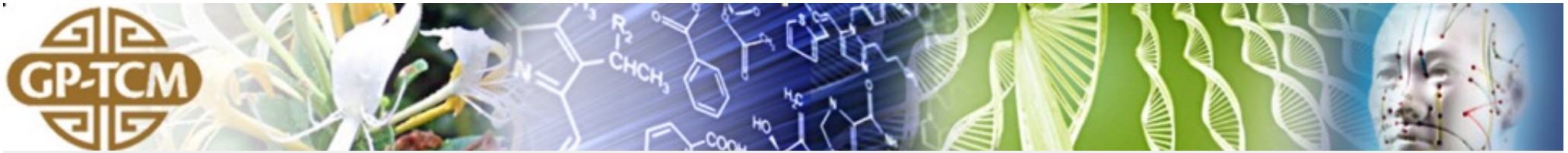
King's College London

E-mail: qihe.xu@kcl.ac.uk

特别感谢欧盟第七框架计划GP-TCM协作组的200位同仁们

SEVENTH FRAMEWORK PROGRAMME

KING'S College LONDON



GP-TCM背景

- 2007年，初到国王学院。准备研究中草药的抗纤维化、促纤维化活性。
- 向专家们请教中草药个方面的问题，发现他们的意见迥异;中草药领域似乎缺乏公认的是非、好坏。
- 孟子曰：“不以规矩，不能成方圆”。缺乏规范的领域令有兴趣研究中医药的“外行”无所适从，也导致整个领域的成果质量良莠不齐。

SEVENTH FRAMEWORK PROGRAMME

KING'S College LONDON

后基因组时代中医药研究的良好实践

Good Practice in TCM Research in the Post-genomic Era (GP-TCM，2009-2012)

- 2009年，成功竞得欧盟第七框架计划欧-中合作重点专项百万欧元资助，旨在建立队伍，协作攻关。
- 项目团队由25个国家的110个单位和200多名科学家组成，包括北中医的牛建昭、乔延江、董玲、王耘老师。

NIU Jianzhao

QIAO Yanjiang

DONG Ling

WANG Yun

Uzuner H, et al. TCM research in the post-genomic era: good practice, priorities, challenges and opportunities. J Ethnopharmacol. 2012;140:458-68.

10个专题组中，7个聚焦草药:

第一组：质量控制

第二组：提取与分析

第三组：毒理

第四组：体外药理

第五组：在体药理

第六组：临床研究

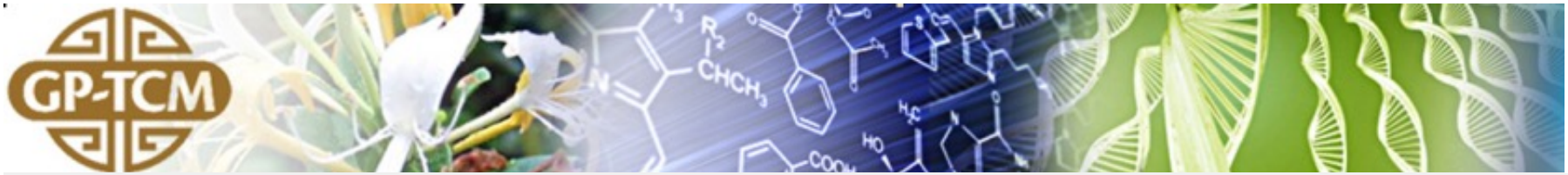
第七组：政策与法规研究

GP-TCM以“规范”为核心，探讨中医药现代化的若干方面

研究主题
- 历史回顾
- 现状分析
- 组学
- 规范与标准
- 机遇
- 挑战
- 优先领域
- 指导原则

The GP-TCM *J. Ethnopharmacol.* Special Issue (2012; volume 140, issue 3)

The quest for modernisation of traditional Chinese medicine. Xu Q, et al. BMC Complement Altern Med. 2013;13:132.



以“规范”为核心是中医药现代化的需要

- **中医药现代化就是中医药与时俱进，达到现代的标准与规范**

Xu *et al. BMC Complementary and Alternative Medicine* 2013, **13**:132
http://www.biomedcentral.com/1472-6882/13/132

(173 citations)

BMC
Complementary & Alternative Medicine

REVIEW Open Access

The quest for modernisation of traditional Chinese medicine

Qihe Xu[1*], Rudolf Bauer[2], Bruce M Hendry[1], Tai-Ping Fan[3], Zhongzhen Zhao[4], Pierre Duez[5], Monique SJ Simmonds[6], Claudia M Witt[7], Aiping Lu[4], Nicola Robinson[8], De-an Guo[9] and Peter J Hylands[10]

SEVENTH FRAMEWORK PROGRAMME

KING'S College LONDON

什么是“规范”？

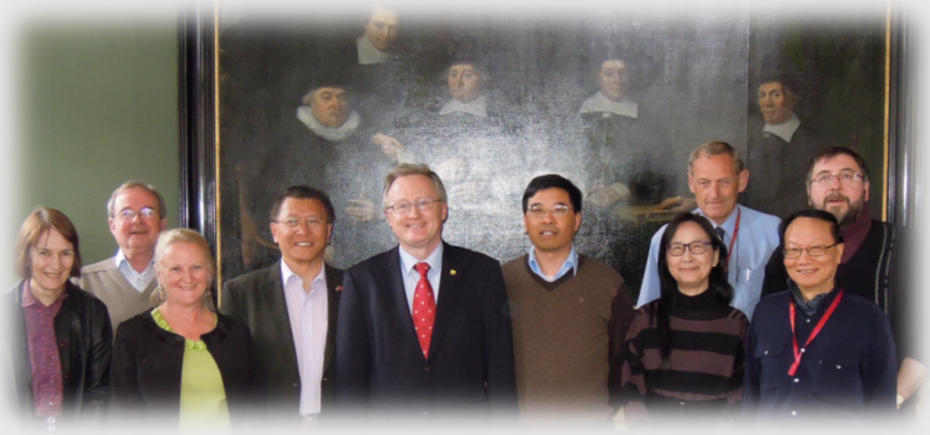
- 广义地讲：遵守国际公认的规则
- 技术层面：中医药相关的标准与指南
- 策略地讲：合作共享
- 实用的原则：求同尊异

Uzuner H, et al. J Ethnopharmacol. 2012;140:458-68 (94 citations)

为了“规范”建设、传播的可持续国际合作，中医药规范研究学会应运而生

Founding BoD members, 2012

(absent: De-an Guo and Aiping Lyu)



GP-TCM RA Presidents, 2012-2024

Rudolf Bauer
(2012-4)

De-an Guo
(2015-6)

Tai-Ping Fan
(2017-8)

Aiping Lyu
(2019-20)

Monique Simmonds
(2021-2)

Clara Lau
(2023-4)

技术标准与规范也要遵循求同尊异、和而不同的原则

标准与规范

GxP & Standards

- 国际同化度较高的标准与规范
  More internationally harmonised
- 具有国际影响力的区域性标准与规范
  Regionally harmonised, but with international importance

制订高同化度标准与规范的国际组织

- 国际标准化组织
  ISO
- 世中联
  WFCMS
- 世界卫生组织
  WHO
- GP-TCM、 GP-TCM RA 、学术期刊等
  International societies and journals…

ISO中医药技术委员会 (ISO/TC 249)

https://www.iso.org/committee/598435.html

- 2009-2023年， ISO与世中联等合作，发布了94个中医药原材料和生产成品质量、安全性和加工程序的国际标准。
- 32个国际标准正在制定过程中。

Prof. SHEN Yuandong

Chair, ISO/TC 249

Shanghai University of TCM

世中联不仅是ISO的合作伙伴，而且发表独立的国际标准

http://www.wfcms.org/index.php/list/52.html

No	WFCMS 国际标准与指南 (n=22 by Nov. 2022))	发布时间
22	SCM 55-2020 中药处方、调剂、给付与煎服要求—— 第 4 部分：中药煎服要求	2022-08-24
21	SCM 54-2020 中药处方、调剂、给付与煎服要求—— 第 3 部分：中药给付要求	2022-08-24
20	SCM 54-2020 中药处方、调剂、给付与煎服要求——第 2 部分：中药调剂要求	2022-08-24
19	SCM 54-2020 中药处方、调剂、给付与煎服要求——第 1 部分：中药处方要求	2022-08-23
18	SCM-C 0039-2020 温控红外灸疗垫	2022-05-05
17	SCM-C 0014-2019 糖脂代谢病（瘅浊）中西医结合诊疗技术规范	2022-05-05
16	SCM-C 0011-2018 牛胶原肽粉	2022-05-05
15	SCM0051-2019 国际中医远程会诊服务规范	2022-05-05
14	SCM-C 0008-2017 耳穴探测仪	2022-04-28
13	SCM0050-2019 国际中医远程教育服务规范	2022-04-28
12	SCM0041-2014 世界中医药学科体系类目	2022-04-28
11	SCM0027-2019 凉茶饮料	2022-04-28
10	SCM0026-2019 浮针疗法技术操作规范	2022-04-28
9	SCM0024-2018 标准化煎药中心基本要求	2022-04-28
8	SCM0023-2019 热敏灸技术操作规范	2022-04-28
7	SCM0020-2017 中医药健康旅游服务要求	2022-04-28
6	SCM0018-2017 国际中医临床实践指南 糖尿病	2022-04-28
5	SCM0012-2014 国际中医医师测试与评审规范	2022-04-28
4	SCM0010-2012 世界中医学专业核心课程	2022-04-28
3	SCM0008-2011 国际中医医师专业技术职称分级标准	2022-04-28
2	SCM0004-2010 诊所设置与服务标准	2022-04-28
1	SCM0003-2009 世界中医学本科（CMD 前）教育标准	2022-04-28

世中联国际标准：Many more WFCMS guidelines are being developed; some important drafts have been published.

Prof. LI Shao

Tsinghua University

Chair, WFCMS Specialty Committee of Network Pharmacology

Li S, et al. WFCMS Specialty Committee of Network Pharmacology.

Network Pharmacology Evaluation Method Guidance - Draft.

World J Tradit Chin Med 2021;7:146-54

https://www.wjtcm.net/text.asp?2021/7/1/146/310934

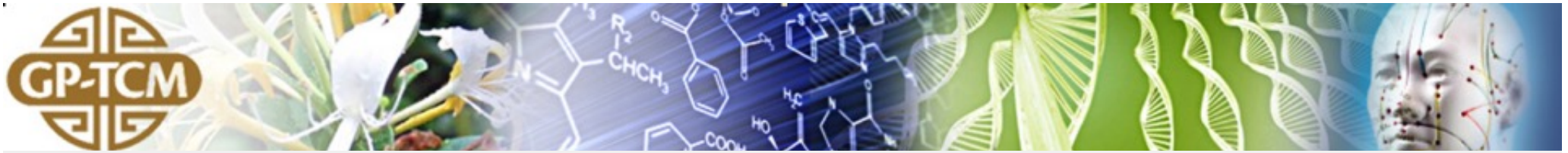
世中联与WHO引领中医术语标准化

WFCMS/WHO中医术语及其翻译标准化（2022, 08, 07）

- **WFCMS. International Standard Chinese-English Basic Nomenclature of Chinese Medicine, Beijing: People's Medical Publishing House. 2008; pp 1-789**（6526 terms）
- **WHO international standard terminologies on traditional medicine in the Western Pacific Region. 2007: pp1-356**（3543 terms）
- **WHO international standard terminologies on traditional Chinese medicine. 2022; pp1-453**（3415 terms）

WHO首次将传统医学诊断引入国际疾病分类 （2019）

- **WHO. Chapter 26. Supplementary Chapter Traditional Medicine Conditions - Module I.** ICD-11. International Classification of Diseases 11th Revision; The global standard for diagnostic health information. 1999; in effect, Jan. 2022.



WHO发布的标准和指南是GP-TCM研究的重要起点

1. WHO草药生产GMP（2007）

- WHO Guidelines on Good Manufacturing Practices (GMP) for Herbal Medicines. 2007, pp 1-72 (>60 citations)

2. WHO传统医学研究与评价的方法学一般指南 （2000）

- WHO General Guidelines for Methodologies on Research and Evaluation of Traditional Medicine. 2000; pp1-74 (>1000 citations)

SEVENTH FRAMEWORK PROGRAMME

KING'S College LONDON

GP-TCM 中药临床研究规范

Flower A, Witt C, Liu JP, Ulrich-Merzenich G, Yu H, Lewith G.
Guidelines for randomised controlled trials investigating Chinese herbal medicine.
J Ethnopharmacol. 2012;140(3):550-4.

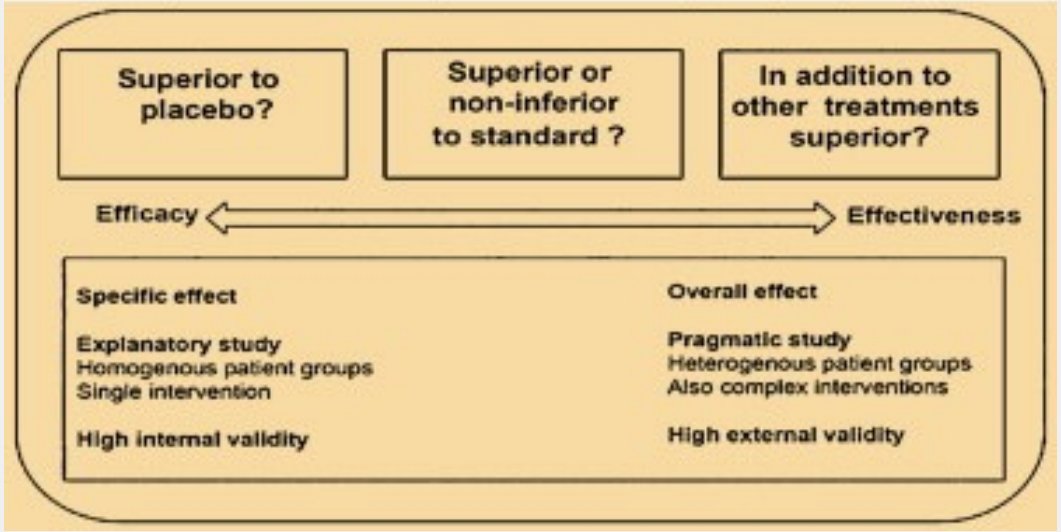
(92 citations)

Dr Andrew Flower

Prof. George Lewith

University of Southampton

The relationship between the research question and the corresponding study design (Witt 2009)



Prof. Jianping Liu

Beijing University of TCM

SEVENTH FRAMEWORK PROGRAMME

KING'S College LONDON

中药临床研究规范进展——

CONSORT中药复方临床研究规范（2017）

Prof. Zhaoxiang Bian
Chair, Clinical Studies Interest Group
GP-TCM RA

Cheng CW, Wu TX, Shang HC, Li YP, Altman DG, Moher D, Bian ZX; CONSORT-CHM Formulas 2017 Group. **CONSORT Extension for Chinese Herbal Medicine Formulas 2017: Recommendations, Explanation, and Elaboration.**
Ann Intern Med. 2017;167(2):112-121.

(174 citations)

繁体字版： Ann Intern Med. 2017 Jul 18;167(2):W7-W20. **(80 citations)**

简体字版： Ann Intern Med. 2017 Jul 18;167(2):W21-W34. **(13 citations)**

GP-TCM WP1/2

中药研究专业用词的规范

Chan K, Shaw D, Simmonds MS, Leon CJ, Xu Q, Lu A, Sutherland I, Ignatova S, Zhu YP, Verpoorte R, Williamson EM, Duez P.

Good practice in reviewing and publishing studies on herbal medicine, with special emphasis on traditional Chinese medicine and Chinese materia medica.

J Ethnopharmacol. 2012;140(3):469-75.

197 citations

J Ethnopharmacol 2012;140:469–75

Prof. Kelvin Chan
University of Sydney

Prof. Pierre Duez
University of Mons

Prof. Monique Simmonds
Royal Botanic Gardens

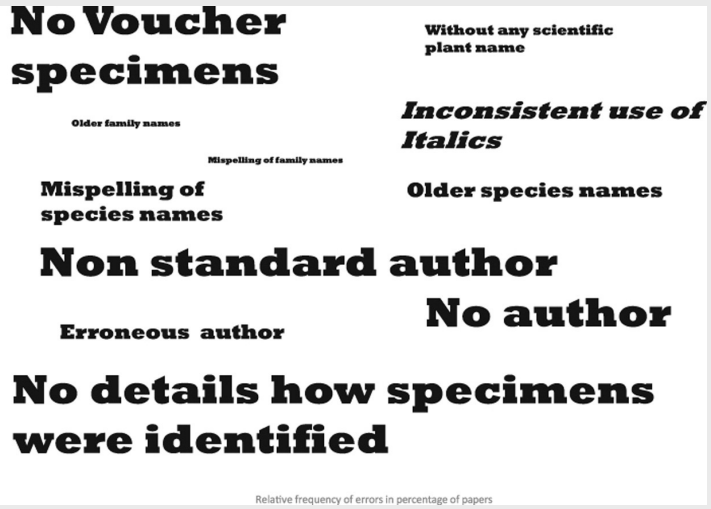
2 Years later…

规范解读：报告药用植物名称亟待解决的常见错误

Rivera D, Allkin R, Obón C, Alcaraz F, Verpoorte R, Heinrich M.
What is in a name? The need for accurate scientific nomenclature for plants.
J Ethnopharmacol. 2014;152(3):393-402.

(179 citations)

Graphical abstract
This paper explores the issues and impacts of ambiguous or erroneous use of botanical scientific nomenclature in ethnopharmacological studies



Prof. Rob Verpoorte
Leiden University

Prof. Michael Heinrich
University College London

世界植物在线植物名录2022年12月发布
代表着世界植物名称标准化最新进展

World Flora Online - The WFO Plant List

https://wfoplantlist.org/plant-list

- ***The Plant List*** **was published in 2010, last updated in 2013**
- **The WFO Plant List since 2018 and lately updated Dec. 2022**

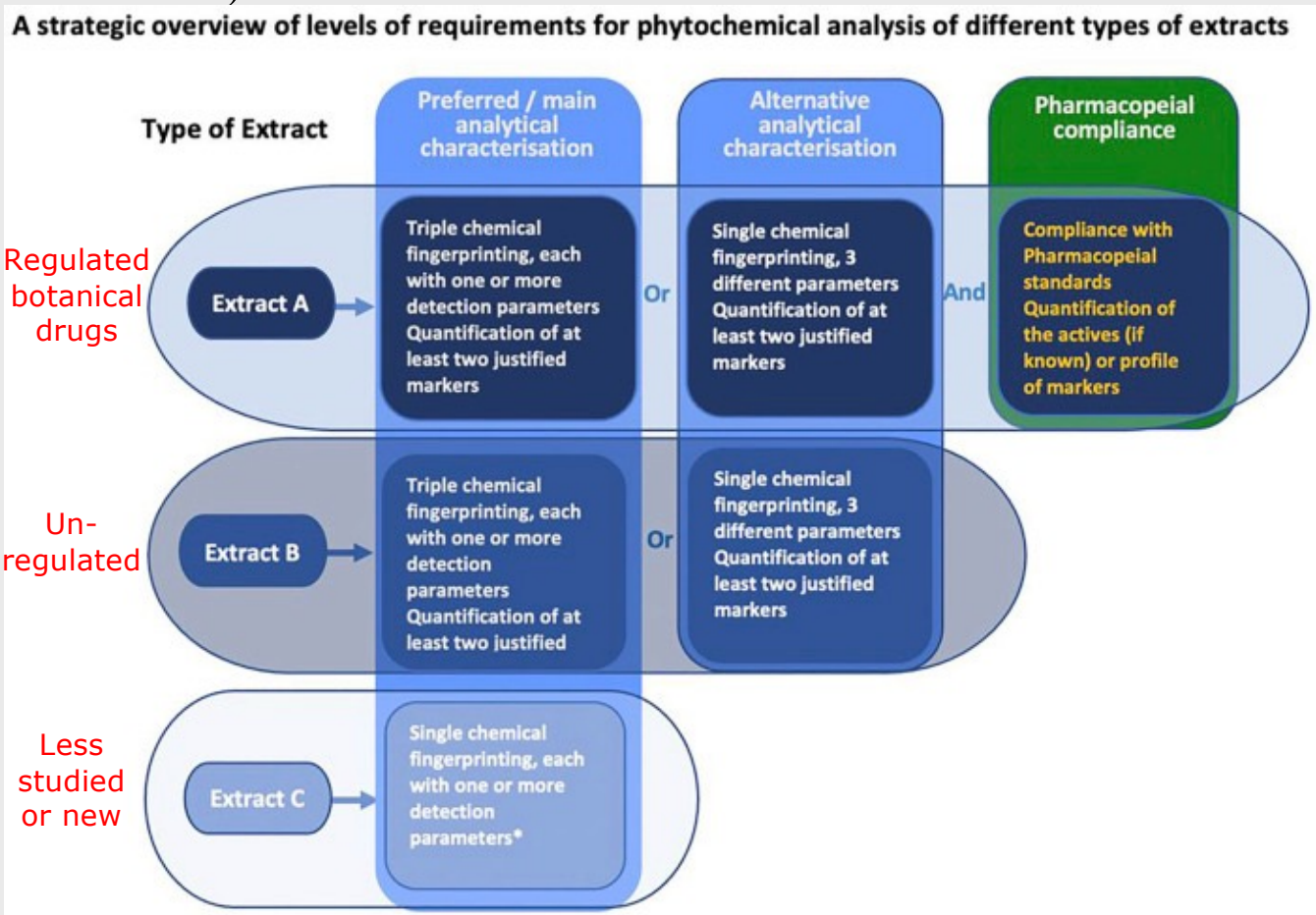
Prof. Monique Simmonds
Royal Botanic Gardens

药用植物鉴定、命名、提取、化学分析的指南

ConPhyMP业界共识声明（2022, “GP-TCM 指南 2.0”）

- Heinrich M, Jalil B, Abdel-Tawab M, Echeverria J, Kulić Ž, McGaw LJ, Pezzuto JM, Potterat O, Wang JB. **Best Practice in the chemical characterisation of extracts used in pharmacological and toxicological research: The ConPhyMP Guidelines.** Front Pharmacol. 2022;13:953205.
  - For all types of herbal preparations, a full specification of the plant material used for extraction is desirable (see Table 3).

Prof. Michael Heinrich
University College London



2019　第二十一卷　第九期　★Vol. 21 No.9

中药药理规范研究的思考*

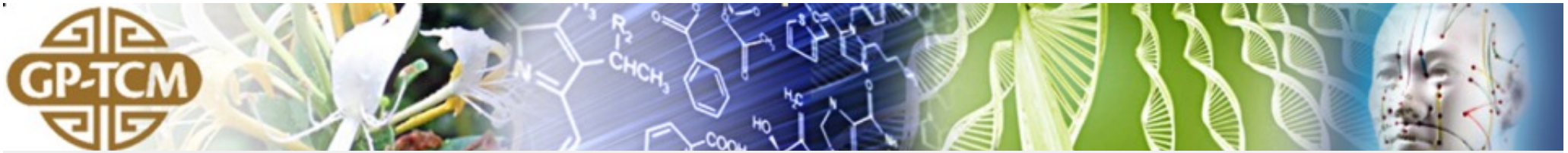
汪选斌[1**]，陆金健[2]

（1. 湖北医药学院附属人民医院生物医药研究院　湖北医药学院武当特色中药研究湖北省重点实验室　十堰 442000；2. 澳门大学中华医药研究院　中药质量研究国家重点实验室　澳门特别行政区　999078）

摘　要：用现代科学技术与方法对中药的药效、活性成分及作用机制进行研究始于上世纪20年代，从最初采用经典的植物化学模式对单味药进行研究，逐渐拓展到对药性理论、中药复方、配伍规律、治法治则及中医药理论的探讨，希望揭示中医药防治疾病的科学内涵，实现指导临床合理安全用药、发现新药、丰富和发展中医药理论的作用。近一个世纪以来，中药药理研究在理论、方法和技术上不规范，虽然取得了重要进展和大量研究成果，但也存在许多亟待解决的科学问题。本文试通过系统地梳理中药药理研究的成功经验和存在的问题，提出中药药理规范研究的定义，及其两个创新（思想创新和理论创新）和两个规范（方法规范和技术规范）。中药药理规范研究是创新前提下的规范以及规范基础上的创新辩证统一体，是创新—规范—再创新的不断循环发展。中药药理规范研究的提出希望能推动中药药理学学科向着更加规范、合理、科学的方向发展。

关键词：中药药理学　规范研究　思考　DNA模型

doi: 10.11842/wst.20190920004　　中图分类号：R285.6　　文献标识码：A



GP-TCM规范发表10周年落实情况的断面分析

10 Years after the publication of the GP-TCM guidelines

SEVENTH FRAMEWORK PROGRAMME

KING'S College LONDON

草药质控的指南落实情况令人担忧

Guidelines implementation is still far from satisfactory

KING'S College LONDON

Shepherd A, Brunckhorst O, Ahmed K, **Xu Q**. **Botanicals in health and disease of the testis and male fertility: A scoping review.** *Phytomedicine*. **2022**;106:154398.

- Only 9%-23% provided information on voucher samples, botanical authentication, extraction methods and chemical profiling!

草药临床研究规范落实也很堪忧

Poor guideline implementation in RCTs published in the past 5 years

KING'S College LONDON

- **Only 38% RCTs registered RCT protocols;**
- **Only 38% RCTs reported concealment of allocation and blinding of personnel** involved in the trial.
- **Only 43% RCTs reported** ADR satisfactorily.
- **Only 72% RCTs reported randomization methods.**
- **Only 78% RCTs reported ethical approval, but this was only 40% in those published in Chinese.**
- **Most RCTs reported written consent**— only 2 RCTs published in Chinese did not report informed consent.

Shepherd A, et al. *Phytomedicine*. **2022**;106:154398.

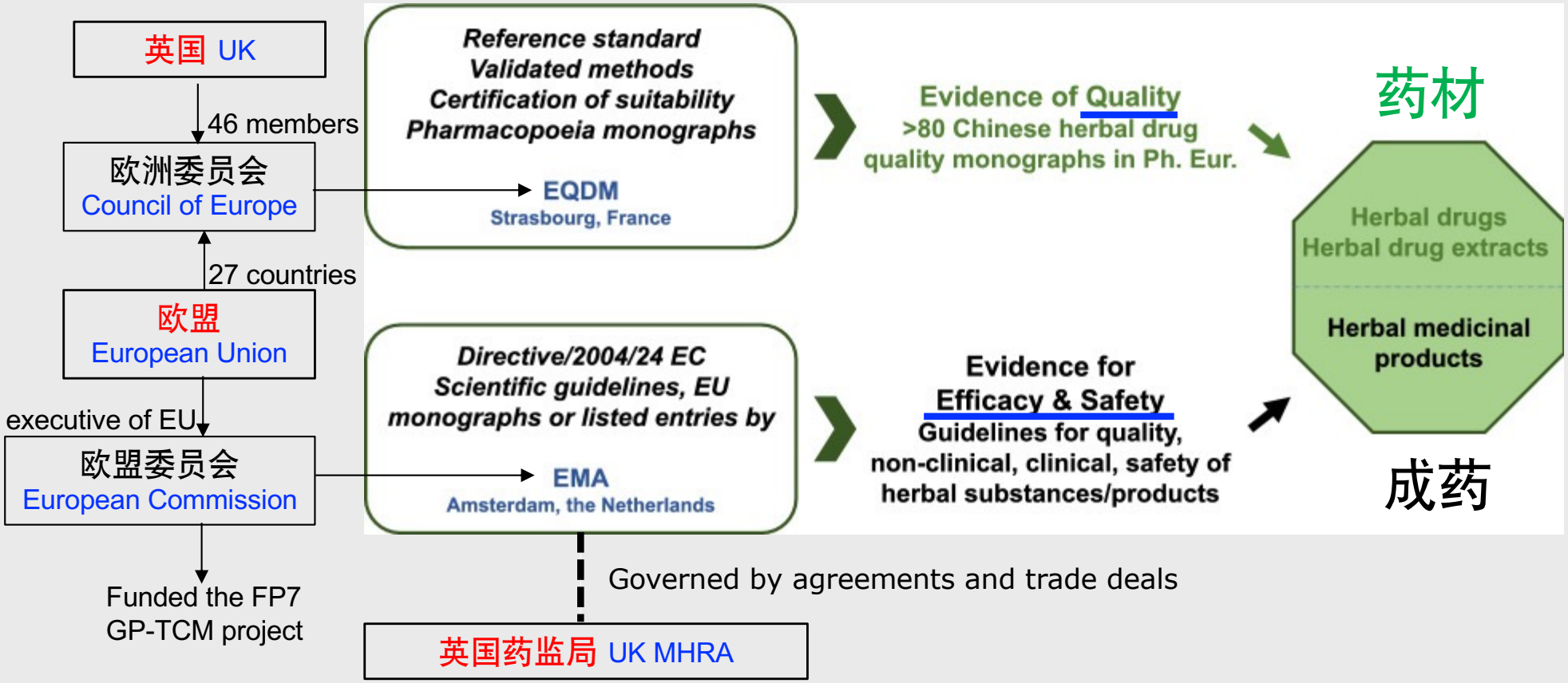
具有国际影响力的区域性标准与规范

- 药典，譬如：欧洲药典中药工作组
  e.g., Ph. Eur. TCM Working Party
- 欧洲药监局草药委员会
  EMA/HMPC
- 美国药品食品管理局
  The US FDA
- 国家中医药管理局《中成药治疗优势病种临床应用指南》
  NATCM-sponsored guidelines on proprietary TCM
- 杂志的指南与规范的学术探讨
  Journal guidelines &
  GxP academic fora

KING'S College LONDON

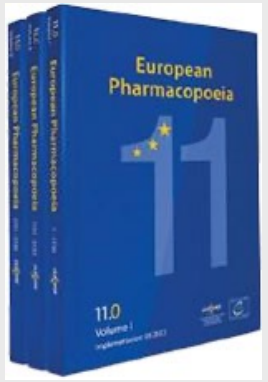
欧洲式标准与规范管理

1. 欧洲药品质量管理局 EDQM
   欧洲药典中药组 Ph. Eur. TCM Working Party → 药材 herbal drugs
2. 欧洲药监局草药委员会 EMA/HMPC → 成药 proprietary products



Wang M et al. Key quality factors for Chinese herbal medicines entering the EU market. Chin Med. 2022; 17: 29.

84味中草药进入了欧洲药典，占总草药数的1/3强



Prof. Gerhard Franz
Founding Chair of the Working Party
GP-TCM RA Regulatory IG Co-Chair

Prof. Rudi Bauer
Chair of the Working Party
GP-TCM RA Founding President

其它药典

- Chinese Pharmacopoeia (ChP)
- The Japanese Pharmacopoeia (JP)
- The United States Pharmacopeia- National Formula (USP-NF)
- The American Herbal Pharmacopoeia：

  56 standards of 15 TCM drugs by 2022.
- The Hong Kong Chinese Material Medica Standards

欧洲药监局草药委员会的成药归管办法

Since 2004, HMPs are regulated by HMPC/EMA under two categories:

1. **传统应用注册** (TUR): GMP+30y safe use
2. **市场许可** (MA): GMP + efficacy & safety established by RCT

TUR与MA的质量要求相同，但需要的注册材料不同，临床应用也不同

Table 3 Marketing authorization *vs.* simplified registration for herbal medicinal products in the EU

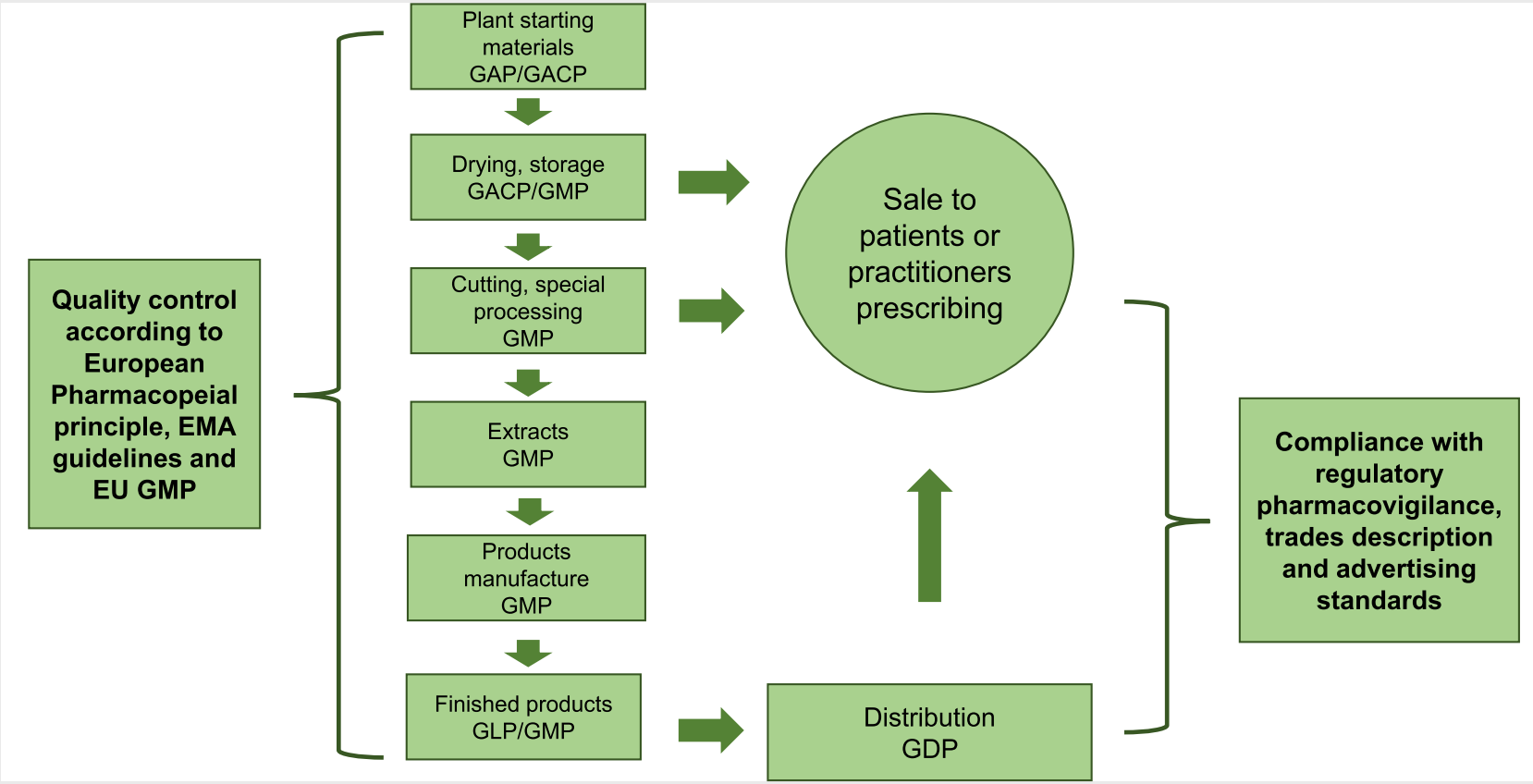
Categories	Market authorization for herbal medicinal products (2001/83/EC)	Simplified registration for herbal medicinal products (2004/24 /EC)
Indications	No specific limitations	Limited to self-medication and OTC
Traditional use evidence	No requirement for stand-alone or mixed application At least 10 years (medicinal use) for well-established use	30 years outside the EU including 15 years in the EU
Dosage form	No specific limitations	Limited to oral, external use and inhalation
Dossier requirements	Pre-clinical (new tests) and clinical data (new trials), or combined with some bibliographic data, Pharmacovigilance	Bibliographic documents, or safety tests, Pharmacovigilance
Quality control	GACP, GMP and CMC	GACP, GMP and CMC

OTC Over-the-Counter, *GACP* Good Agricultural and Collection Practice, *GMP* Good Manufacturing Practice, *CMC* Chemistry Manufacturing and Controls

Wang M et al. Key quality factors for Chinese herbal medicines entering the EU market. Chin Med. 2022; 17: 29.

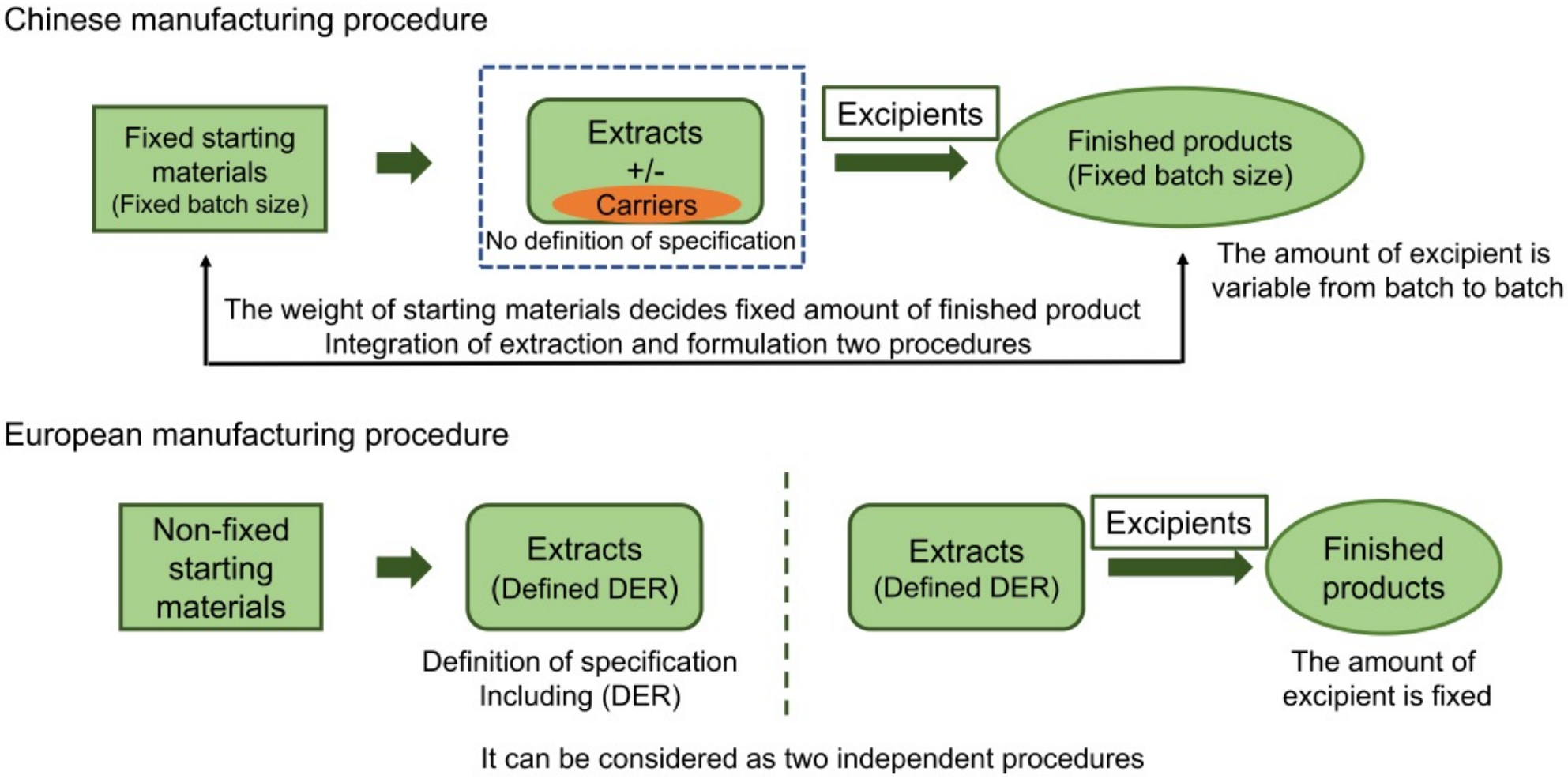
The GxPs (系列规范): From herbal drugs to finished products, there is a continuous process for quality control at each step from agriculture, collecting, laboratory testing, manufacturing to marketing.

- **GAP/GACP:** Good agricultural/collecting practice;
- **GLP:** Good laboratory practice;
- **GMP:** Good manufacturing practice; and
- **GDP:** Good distribution practice.



Wang M et al. Key quality factors for Chinese herbal medicines entering the EU market. Chin Med. 2022; 17: 29.

欧洲与中国对成药GMP质控程序要求的区别



Wang M et al. Key quality factors for Chinese herbal medicines entering the EU market. Chin Med. 2022; 17: 29.

七个中药传统使用注册

Dr Mei Wang
GP-TCM RA President-elect
Regulatory IG Chair

- **五个单味药**
  - 地奥心血康胶囊，荷兰
  - 丹参胶囊，荷兰
  - 愈风宁心片，荷兰
  - 凡诺华板蓝根颗粒， 英国
  - 凡诺华关节肌肉止痛片，英国
- **两个复方药**
  - 六君子丸, 德国
  - 逍遥片， 荷兰

Xiong Y, et al. **Market access for Chinese herbal medicinal products in Europe-A ten-year review of relevant products, policies, and challenges**. *Phytomedicine.* 2022;103:154237.

药材颗粒剂（Herbal drug granules）

- **TCM herbal drug granules:** granules manufactured based on single Chinese herbal drug via extraction with heating water, separation, concentration, dry, and granulation.
- **In most EU member states, TCM herbal drug granules are regarded as food supplements.**
- **In Germany, however, they are considered as "presentation medicinal products".** Therefore, quality monographs of TCM granules are in the process of establishment by the German Drug Codex, **a supplement book to the German Pharmacopoeia**.

- **06/2011:** NATCM and EDQM signed an MoU for cooperation in Beijing.
- **29/09/2011: Herbal drug granule** is a key focus of discussion at a joint workshop of the FP7 GP-TCM project and experts of the EDQM Ph. Eur. TCM Working Party, Strasbourg, France.

Group photo from the Joint Workshop

FDA“全证据”模式：成功注册的草药凤毛菱角

- 3个处方草药： **Only three approved prescription botanical drugs (2006; 2012; 2023)**
  - Sinecatechins, Veregen®;
  - Crofelemer, Mytesi™, is sourced from the red bark sap of the Croton lechleri tree that grows in the Amazon;
  - NexoBrid, a mixture of enzymes (凤梨酵素) from the stem of the *Ananas comosus* (pineapple plant) that dissolves dead tissue caused by a burn so that the healing can start.
- 少数几个非处方草药： **OTC botanical drugs** under the OCT botanical drug review: cascara, psyllium, senna, etc.
- **Dietary Supplement** cannot make a disease claim to diagnose, cure, mitigate, treat or prevent disease.

Wu C, et al. *J. Nat. Prod.* 2020, 83, 2, 552–562

Lee SL, et al. *Science* 2015;347 (6219 Suppl): S32-34.

国家中医药管理局 《中成药治疗优势病种临床应用指南》

- 是我国首部将使用对象主要定位于全科医师、西医师的中成药循证实践指南。
- 2015年10月立项，历史7年分批立题63个优势病种指南。
- 截止2022年7月已完成草案37项，公开发布29个指南。

国际学术期刊的指南

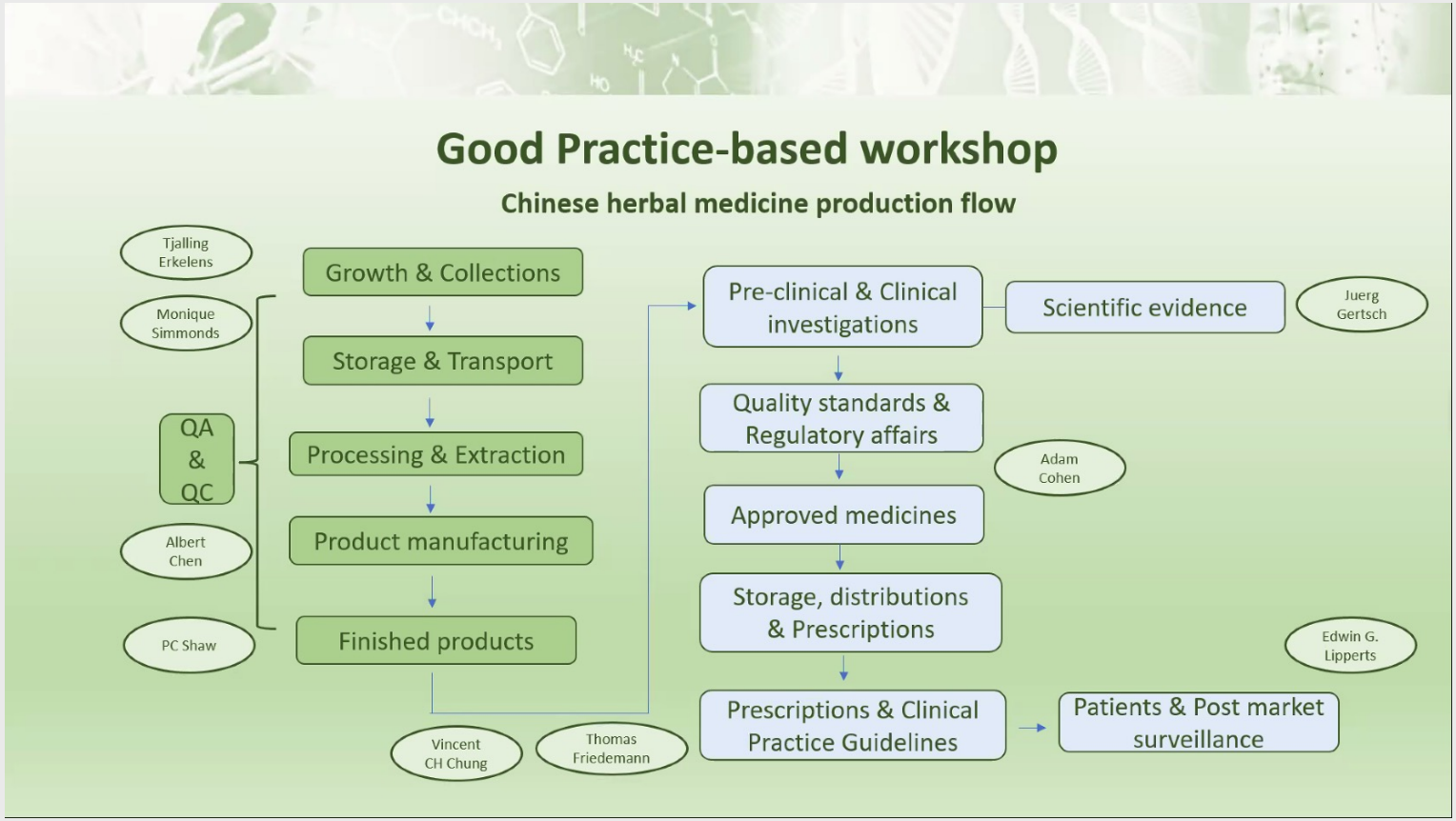
- *Br J Pharmacology*
- *Frontiers In Pharmacology – Ethnopharmacology*
- *Phytomedicine*
- *J Ethnopharmacology*
- *……*

规范的学术探讨: 为纪念学会成立十周年，GP-TCM RA 2022年11月29日成功举办了 《中医药规范讲座》网络会议

- 农业规范：Good Agricultural Practice (GAP)
- 实验室规范：Good Laboratory Practice (GLP)
- 生产规范：Good Manufacturing Practice (GMP)
- 流通规范：Good Distribution Practice (GDP)
- 临床规范：Good Clinical Practice（GCP）

Organiser: Dr Mei Wang
GP-TCM RA President-elect
Regulatory IG Chair

Organiser: Prof. Rob Verpoorte
Past GP-TCM RA BoD Member
Publication IG Chair



Open access to the GP-TCM RA GxP Workshop lectures:

http://www.gp-tcm.org/index.php/2022/10/01/gp-tcm-ra-good-practice-based-workshop/

中医药规范研究学会

The GP-TCM RA

http://www.gp-tcm.org

- **Free membership:**

  http://www.gp-tcm.org/index.php/membership/

- **Students' corner:**

  http://www.gp-tcm.org/index.php/student-section-corner/

- **Open-access newsletters:**

  http://www.gp-tcm.org/index.php/news/

- **7 interest groups** (4 on QC, Pharm/Tox, Clinical Studies, Regulation of Herbal Medicine; 1 on publication; and 1 on Good Clinical Practice Guidelines)

  http://www.gp-tcm.org/index.php/interest-groups/

结 束 语

- 近十年来，草药研究的国际和区域性标准与规范取得了不少进展。
- 与世中联合作，ISO发布了近百个中医药产品的国际标准；世中联独立发布了中药处方、调剂、给付与煎服、凉茶饮料等标准；WHO在中医诊断、学术术语、草药质控的标准化方面发挥引领作用；而以GP-TCM 为代表的欧-中合作是推动草药命名、提取、质控和临床研究规范的有生力量。
- 中国、欧洲与美国等的药监局、药典的相关标准化存在相互借鉴，但尚未达成一致。在《中成药治疗优势病种的临床应用指南》制定方面，国家中医药管理局发挥了重要的领导作用。
- 国际组织制定规范离不开专家个人，而规范的落实更是和我们每一位息息相关。让我们一起投身到规范制定、传播、落实与完善的队伍，为中医药现代化增砖添瓦！

Dr Qihe Xu（徐启河）

Renal Sciences and Integrative Chinese Medicine
Faculty of Life Sciences & Medicine
King's College London
Weston Education Centre
London SE5 9RJ
UNITED KINGDOM

qihe.xu@kcl.ac.uk

谢谢！