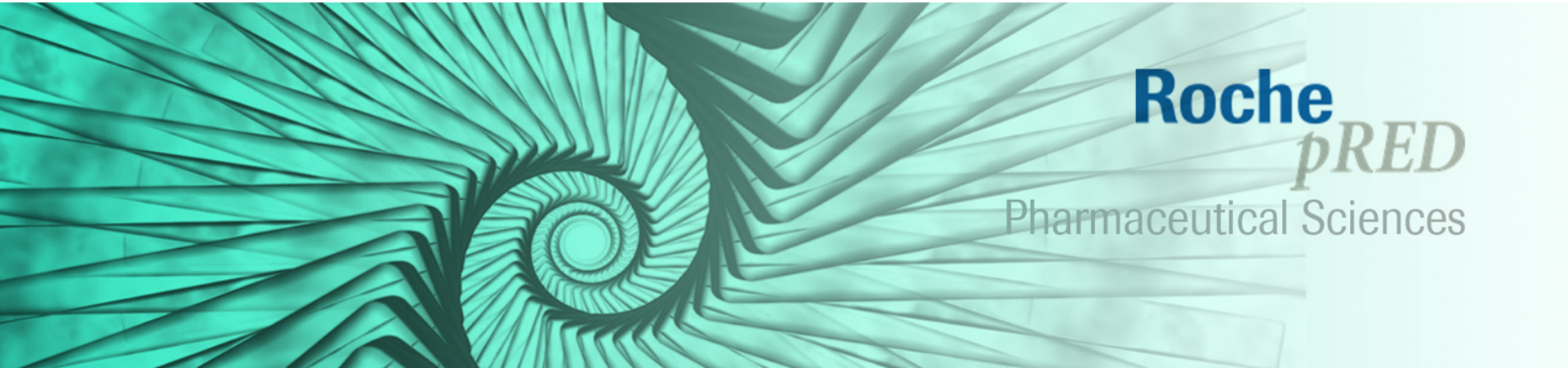
CTA/NDA Regulatory Landscape in China

Jack Xie, PhD, DABT

SOT 2016



Disclaimer

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Glossary

- CTA: Clinical Trial Application
- NDA: New Drug Application
- CTP: Clinical Trial Permit
- CPP: Certificate of Pharmaceutical Product
- IDL: Imported Drug License
- CFDA: China Food and Drug Administration
- PFDA: Provincial Food and Drug Administration
- CDE: Center for Drug Evaluation
- NIFDC: National Institutes for Food and Drug Control
- PFDC: Provincial Food and Drug Control

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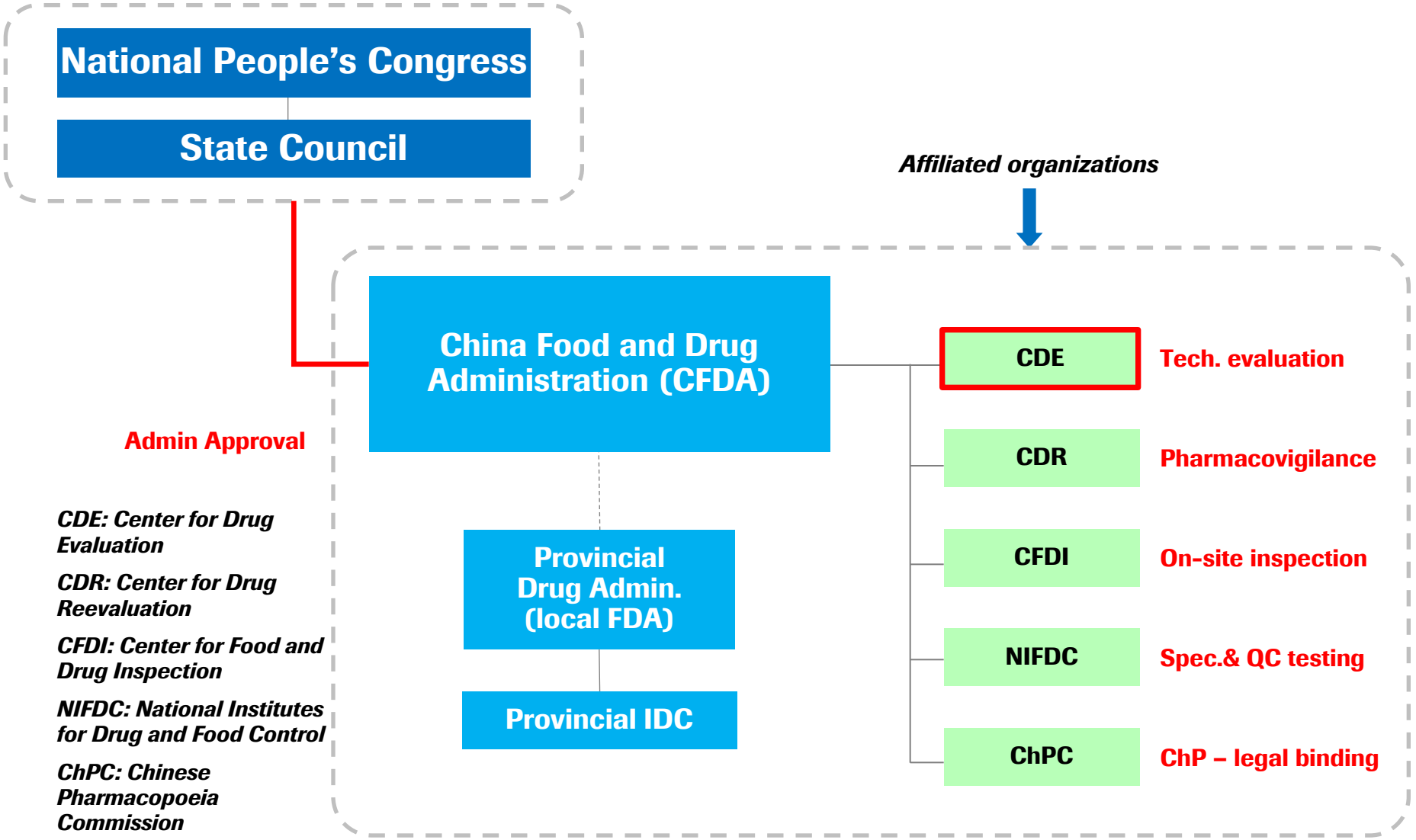
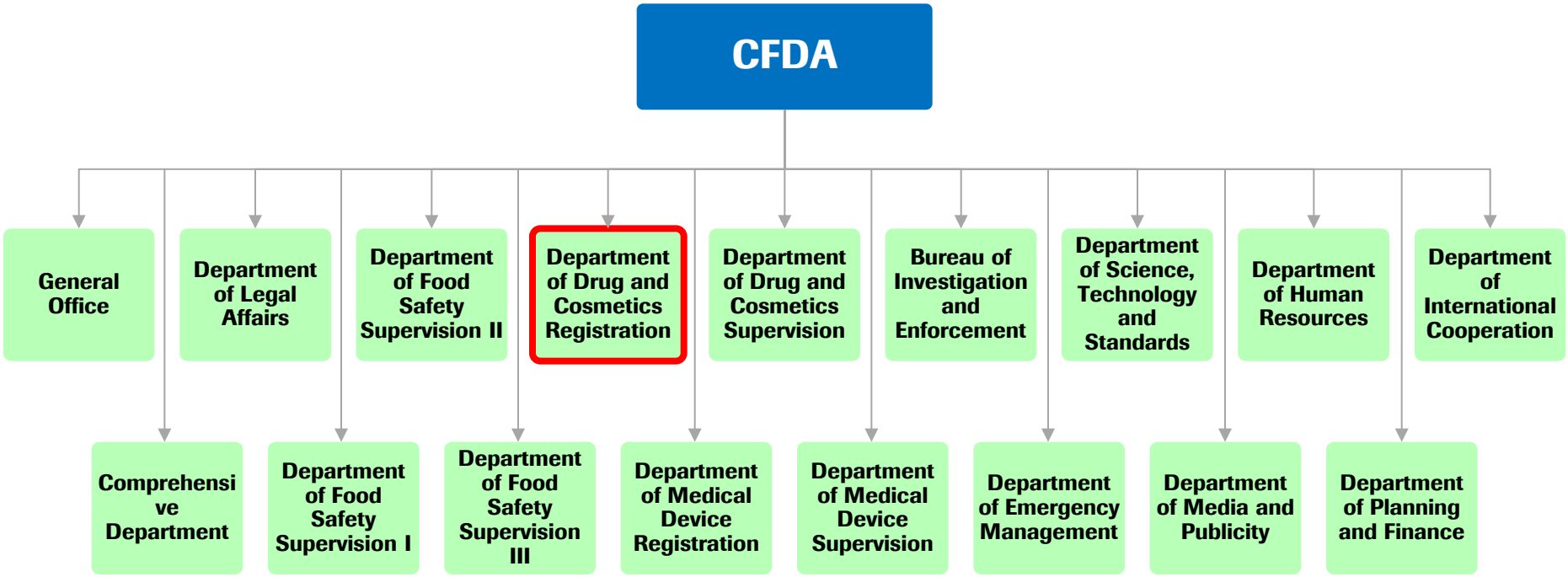
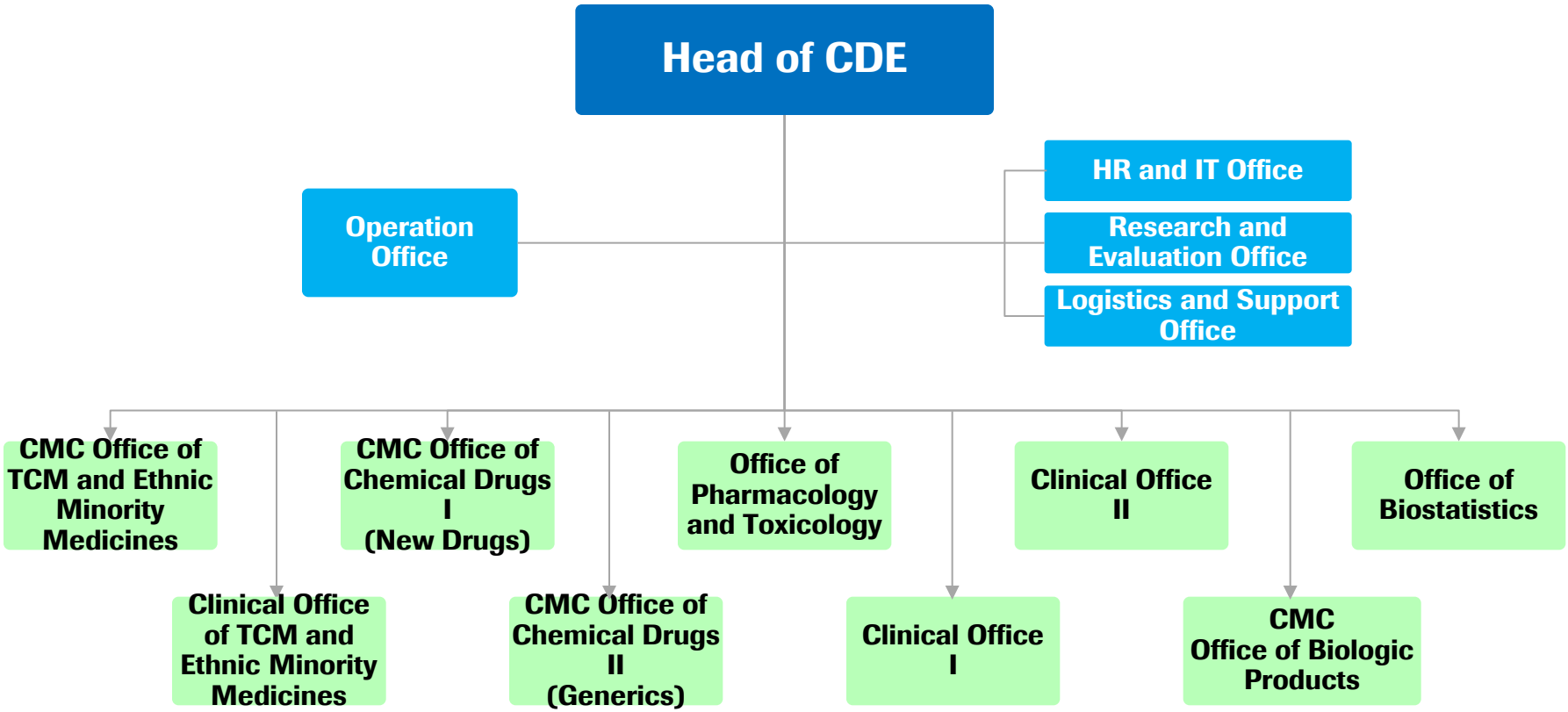
China Health Authorities Structure



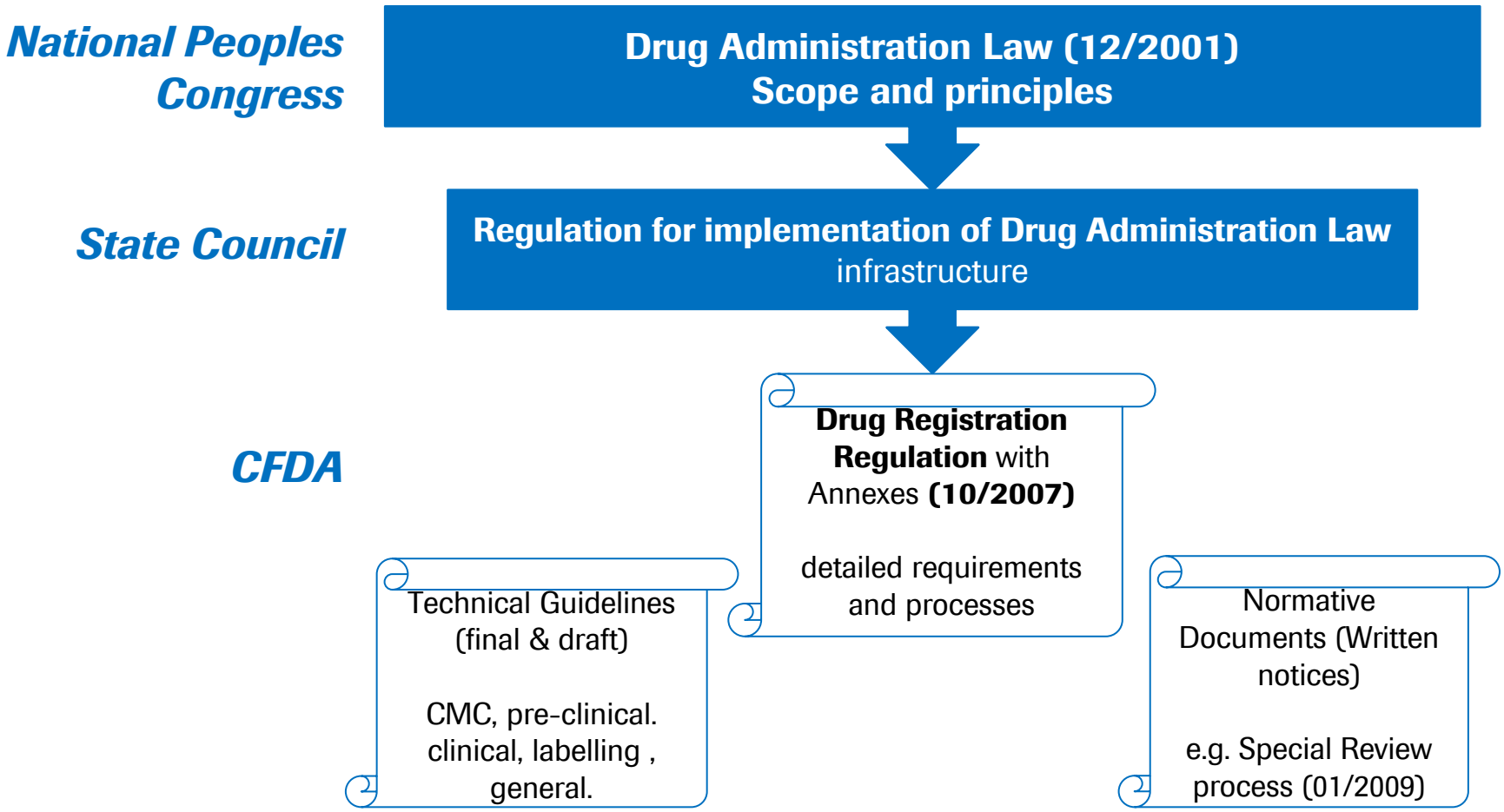
CFDA Organizational Chart



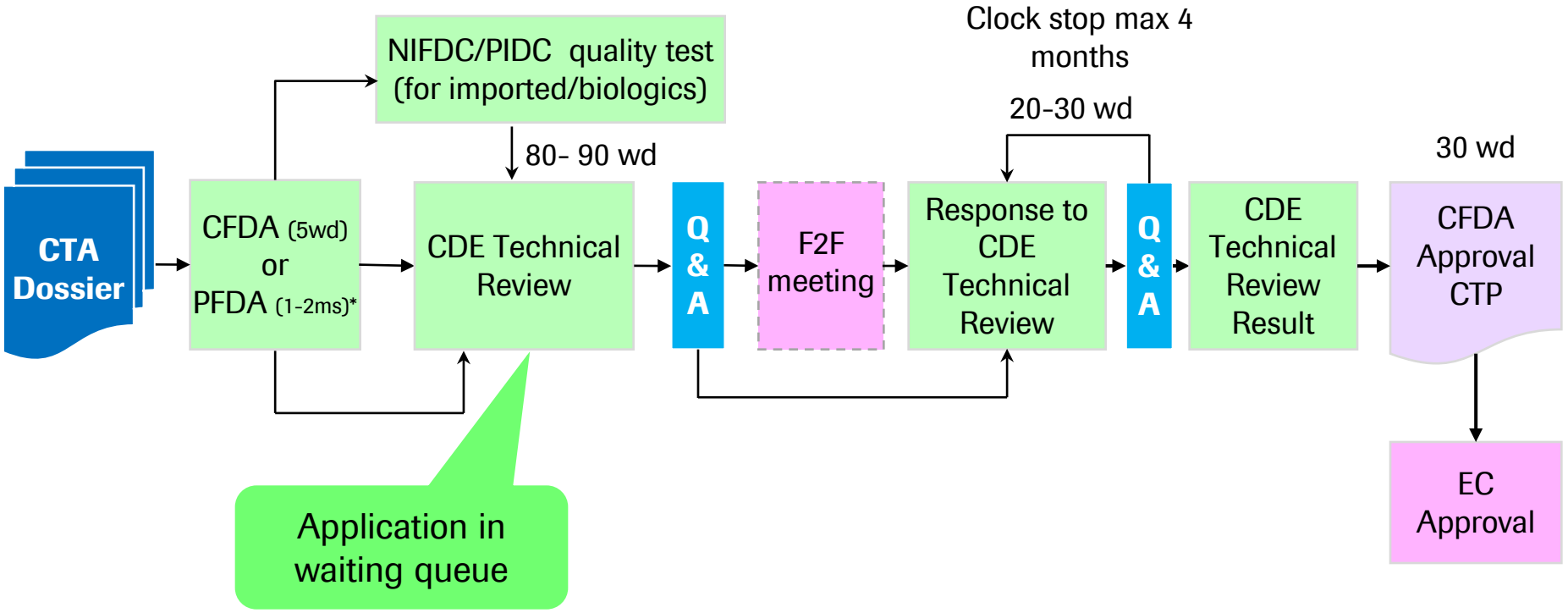
CDE Organizational Chart



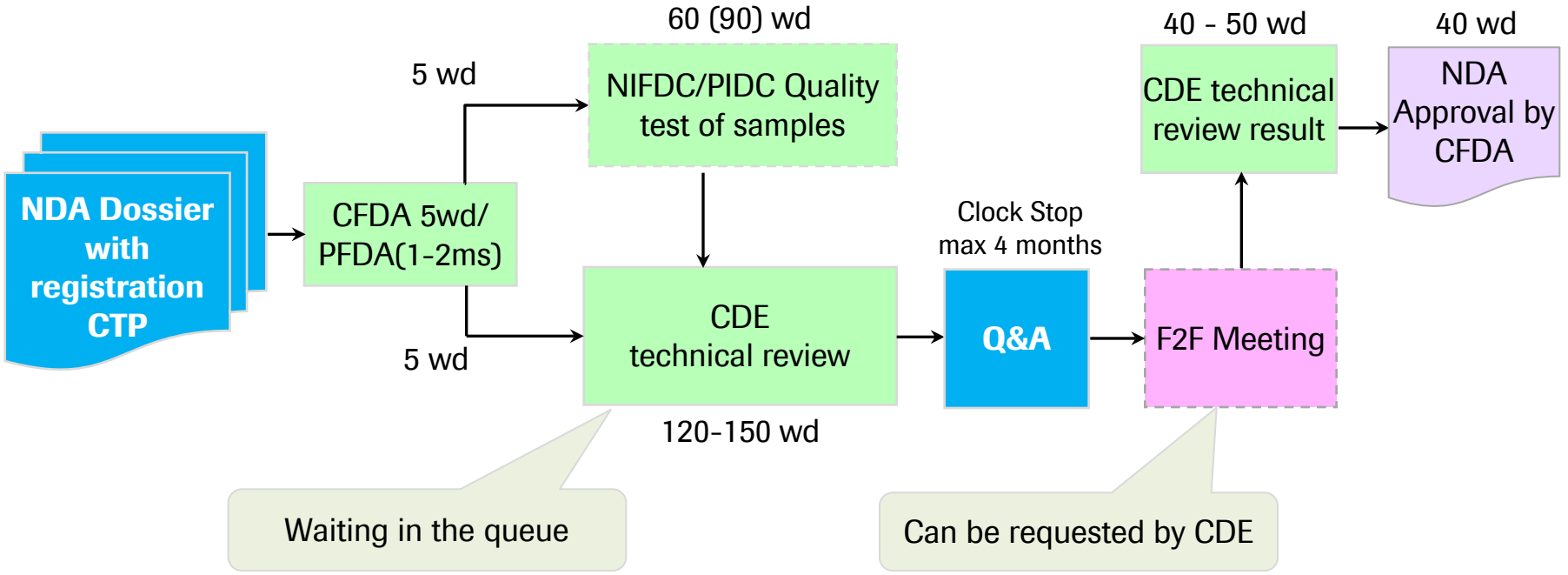
Current Regulation System



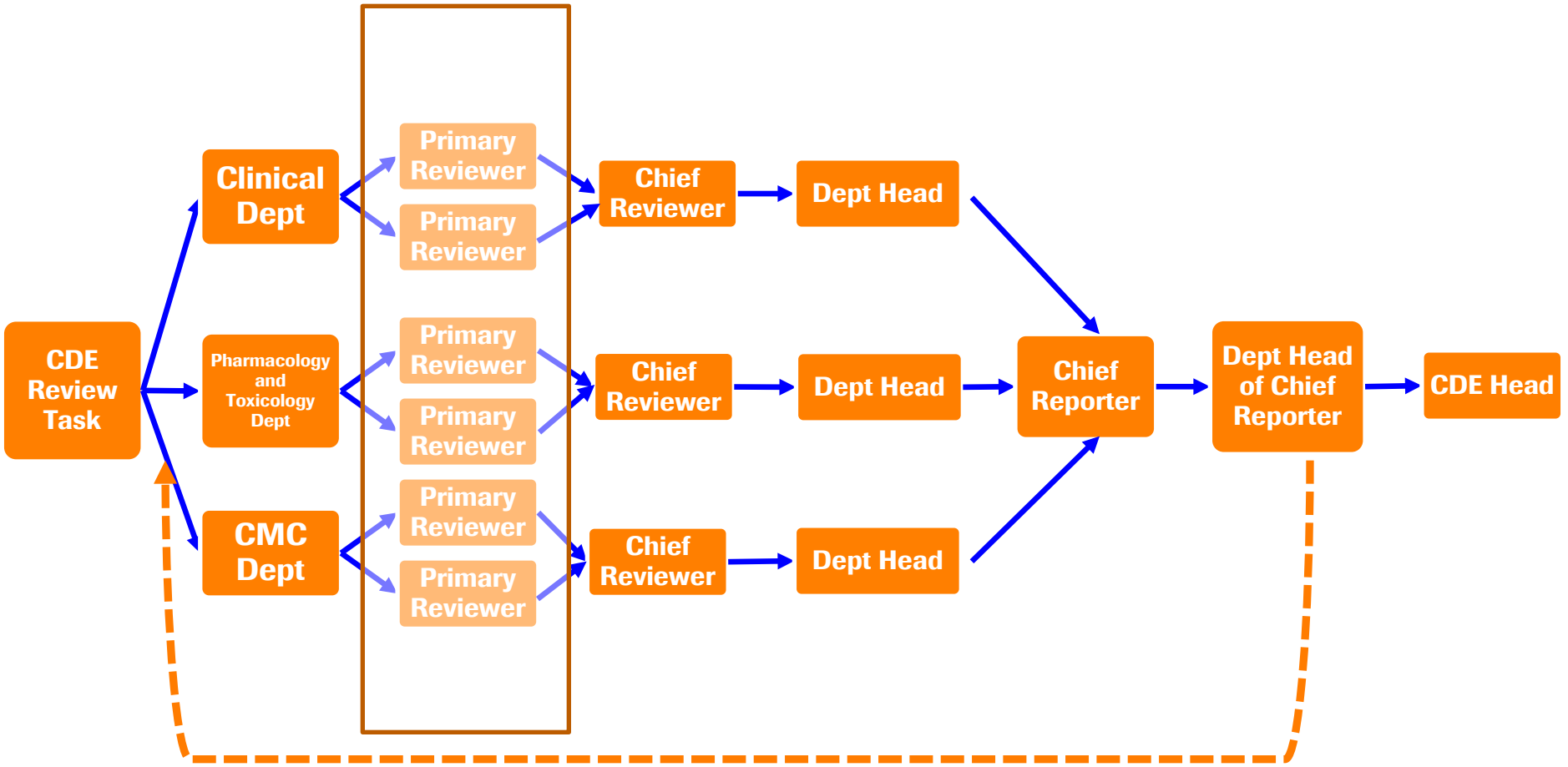
China – Clinical Trial Application (CTA) Review Process



China – New Drug Application (NDA/BLA) Review Process



CDE Personnel Allocation for the Innovative Drug Review



Communication of Drug Technical Evaluation (Draft)

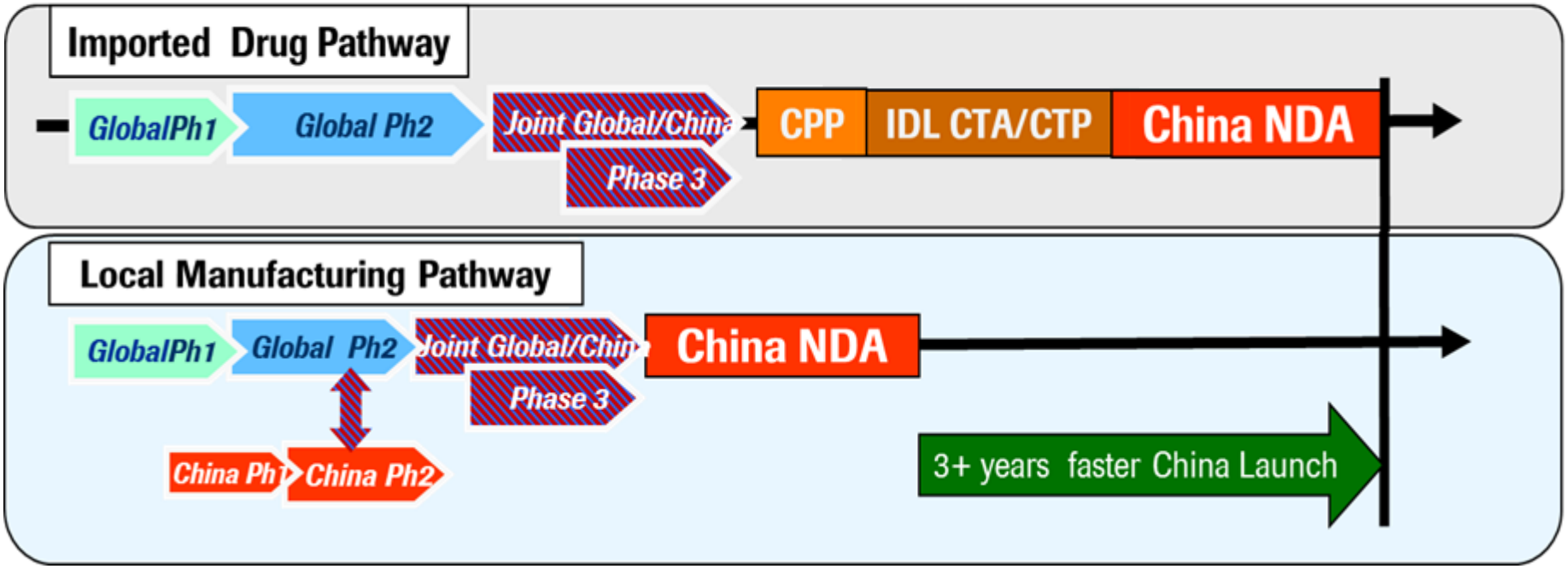
- Basically similar with FDA procedure

- (I) **Class I meetings** to **address critical issues** encountered in the process of clinical trials or to address major safety issues.

- (II) **Class II meetings** held in **the critical stages** of drug development:
  - § Pre-application meetings for Phase I clinical trial
  - § Meetings after the completion of Phase II clinical trial/prior to the initiation of Phase III clinical trial
  - § Meetings prior to the submission of NDA
  - § Meetings of risk evaluation and control

- (III) **Class III meetings**, other meetings that do not fall into Class I or II.
  - § Class III meetings can be proposed for special issues concerning improved new drugs and generic drugs

Current Timeline for Local Manufacturing & imported Pathways



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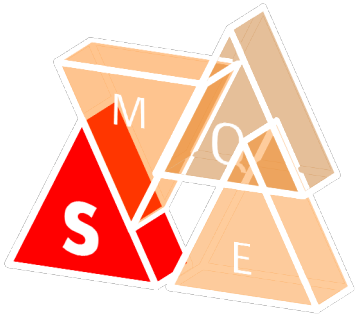
CFDA Guidelines

- All guidelines in different disciplinary (CMC, non-clinical, clinical etc.) for chemical drugs, traditional Chinese medicine, and biologics
- ICH basic concepts adopted
- In general following ICH guidance is acceptable if no counterparts in China
- www.cde.org.cn

Current Status I

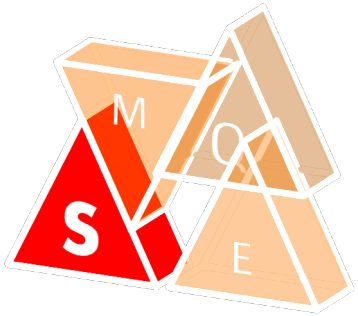
ICH Guidelines	Counterparts in China
Stability Q1A-Q1F	Yes
Analytical Validation Q2	Yes
Impurities Q3A-Q3D	Yes
Pharmacopoeias Q4-Q4B	--
Quality of Biotechnological Products Q5A-Q5E	Yes
Specifications Q6A-Q6B	Yes
GMP Q7	Yes
Pharmaceutical Development Q8	?
Quality Risk Management Q9	?
Pharmaceutical Quality System Q10	Yes
Development and Manufacture of Drug Substance Q11	Yes

Current Status II



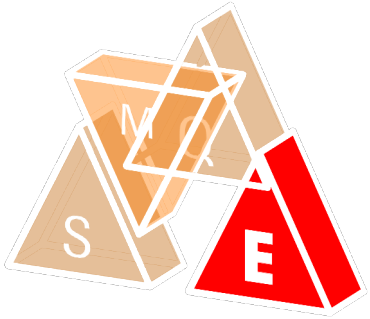
ICH Guidelines	Counterparts in China
Carcinogenicity Studies S1A - S1C	S1A only
Genotoxicity Studies S2	Yes
Toxicokinetics and Pharmacokinetics S3A - S3B	Yes
Chronic Toxicity Testing S4	Yes
Reproductive Toxicology S5	Yes
Biotechnological Products S6	Yes
Safety Pharmacology Studies S7A - S7B	Yes
Immunotoxicology Studies S8	?
Anticancer Pharmaceuticals S9	Yes
Photosafety Evaluation S10	Yes

Current Status III



Non-ICH Guidelines	Counterparts in China
Single Dose Toxicity	Yes
New Pharmaceutical Excipients	Yes
Safety Testing of Drug Metabolites	Yes
Nonclinical Evaluation of Pediatric Drug Products	Yes
Local Tolerance Testing	Yes
Integration of Toxicology Study Results	No
FIH dose Estimating	Yes

Current Status IV



ICH Guidelines	Counterparts in China
Clinical Safety E1-E2F	No
Clinical Study Reports E3	Yes
Dose-Response Studies E4	No
Ethnic Factors E5	No
GCP E6	Yes
Clinical Trials E7-E11	E9 only
Clinical Evaluation by Therapeutic Category E12A	Yes
Clinical Evaluation of QT E14	No
Pharmacogenomics E15-E16	No

Special Requirements in CFDA Guidance before EIH

- **Ø In vivo non-GLP DMPK studies using full validated BA methods and specific CFDA requirements**
- **Ø Tissue distribution studies in rodents**
- **Ø Reproductive tox studies**

- Only the final reports are accepted for CTA submissions

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Opinion of Reform of Medical Device and Medicinal Product Review and Approval System

State Council 2015 No 44 Document August 18, 2015

Major Objectives of the Reform:

§Improve the efficiency of review and approval

§Eliminate backlogs

§BE assessment of generics

§Priority review and approval of innovative drugs & innovative drugs with manufacturing site transferred to China

Bi Jingquan
New CFDA Commissioner

毕井泉 局　长 党组书记

简　历　毕井泉，男，汉族，1955年9月出生，黑龙江省庆安县人，1982年2月参加工作，1978年3月加入中国共产党，中央党校研究生学历，北京大学中国经济研究中心高级管理人员工商管理硕士。

1972.01—1976.01 黑龙江省庆安县民乐乡农村劳动
1976.01—1978.02 黑龙江省庆安县民乐乡政府经营管理站电管站工作
1978.03—1982.02 北京大学经济学系学习，获经济学学士学位
1982.02—1984.09 国家物价局农产品价格司工作
1984.09—1987.08 国家物价局农产品价格司综合处副处长
1987.08—1989.03 国家物价局农产品价格司综合处处长
1989.03—1994.03 国家物价局价格规划司副司长，综合司副司长
1994.03—1995.11 国家计划委员会价格管理司副司长
1995.11—1996.10 国家计划委员会收费管理司副司长（主持工作）
1996.10—1998.06 国家计划委员会工农产品价格管理司司长
1998.06—2001.07 国家发展计划委员会价格司司长
（期间：2000.03—2001.01，中央党校一年制中青年干部培训班学习）
2001.07—2003.04 国家发展计划委员会经贸流通司司长
2003.04—2005.09 国家发展和改革委员会经济贸易司司长
2005.09—2006.01 国家发展和改革委员会秘书长
2006.01—2006.06 国家发展和改革委员会副主任、党组成员兼秘书长
2006.06—2008.03 国家发展和改革委员会副主任、党组成员
2008.03—2015.01 国务院副秘书长、机关党组成员
2015.01— 国家食品药品监督管理总局局长、党组书记

分　工　负责总局全面工作，分管人事司。

Announcement of CFDA on Certain Policies for Drug Registration Review and Approval

(No.230 [2015])

- I. To promote the criteria for approval of generic drugs
- II. Streamlining the evaluation and approval of improvement new drugs
- **III. Optimized clinical trial application evaluation and approval**
  - § IND-like system procedure will be adopted
  - § Scientific rationale of clinical protocol and HV safety risk control will be the major concern of evaluation
  - § to strengthen the communication with applicant before CTA submission and during review
- IV. Allow the applicants to withdraw the applications failing to meet registration requirements
- V. Enhance efficacy and safety assessment
- **VI. Accelerating approval of drugs with urgent unmet medical needs**
- VII. Clinical Data Falsification will be severely punished

Priority Review/Approval (No.19 [2016]) --Scope

- **Drug with significant clinical value:**
  - § Innovative drug not yet launched in domestic and overseas market
  - § Innovative drug with manufacturing site transferred to China
  - § Drugs with advanced formulation technologies, innovative therapies, or sufficient clinical advantage
  - § Generic CTA for patent expiring <3 years; Generic NDA for patent expiring <1 year
  - § CTA/NDA to CFDA that filed & approved simultaneously with EU or US
  - § New drug listed in the National Major Science and Technology Projects

- **Diseases treatment with significant clinical advantage**

  AIDS/TB/Hepatitis/Rare disease/Malignant tumor/Pediatric drug/Diseases with high incidence or unique in elderly people

- **Others**

Special Acknowledgement

Qingli Wang: Executive Director, Office of Pharmacology & Toxicology, Center for Drug Evaluation, China Food and Drug Administration.

Helen Yang: Roche PDR

Na Yu: Roche PDR

Doing now what patients need next