CTA/NDA Regulatory Landscape in China

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Disclaimer

The content of the following presentation represents solely author’s view and may not reflect any position of Roche or China Regulators.
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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• General introduction of China FDA/CDE & CTA/NDA review process
• CFDA guidance system and requirements for China CTA
• New policy trend
Current Regulation System

National Peoples Congress

Drug Administration Law (12/2001)
Scope and principles

State Council

Regulation for implementation of Drug Administration Law
infrastructure

CFDA

Drug Registration Regulation with Annexes (10/2007)
detailed requirements
and processes

Technical Guidelines
(final & draft)
CMC, pre-clinical, clinical, labelling, general.

Normative Documents (Written notices)
e.g. Special Review process (01/2009)
China – Clinical Trial Application (CTA) Review Process

CTA Dossier

CFDA (5wd) or PFDA (1-2ms)*

CDE Technical Review

Q & A

F2F meeting

Response to CDE Technical Review

Q & A

CDE Technical Review Result

CFDA Approval CTP

EC Approval

NIFDC/PIDC quality test (for imported/biologics)

Clock stop max 4 months

20-30 wd

Application in waiting queue

30 wd

80-90 wd
China – New Drug Application (NDA/BLA) Review Process

NDA Dossier with registration CTP

CFDA 5wd/ PFDA(1-2ms)

5 wd

NIFDC/PIDC Quality test of samples

60 (90) wd

CDE technical review

CDE technical review result

Clock Stop max 4 months

Q&A

F2F Meeting

40 - 50 wd

NDA Approval by CFDA

40 wd

Waiting in the queue

Can be requested by CDE

120-150 wd

Can be requested by CDE

5 wd

186 x 210

436 x 218

5 wd

425 x 274

Clock Stop max 4 months

60 (90) wd

Can be requested by CDE

186 x 210

436 x 218

5 wd

425 x 274

Clock Stop max 4 months

60 (90) wd

Can be requested by CDE

186 x 210

436 x 218

5 wd

425 x 274

Clock Stop max 4 months

60 (90) wd

Can be requested by CDE
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

**Imported Drug Pathway**
- Global Ph1
- Global Ph2
- Joint Global/China Phase 3
- CPP
- IDL CTA/CTP
- China NDA

**Local Manufacturing Pathway**
- Global Ph1
- Global Ph2
- Joint Global/China Phase 3
- China Ph1
- China Ph2
- China NDA
- 3+ years faster China Launch
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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

<table>
<thead>
<tr>
<th>ICH Guidelines</th>
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<tr>
<td>Stability Q1A-Q1F</td>
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<td>Analytical Validation Q2</td>
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<td>Impurities Q3A-Q3D</td>
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<td>Pharmacopoeias Q4-Q4B</td>
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<td>Quality of Biotechnological Products Q5A-Q5E</td>
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<td>Specifications Q6A-Q6B</td>
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<td>Pharmaceutical Quality System Q10</td>
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<td>Development and Manufacture of Drug Substance Q11</td>
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<td>Genotoxicity Studies S2</td>
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<td>Toxicokinetics and Pharmacokinetics S3A - S3B</td>
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<td>Chronic Toxicity Testing S4</td>
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<td>Reproductive Toxicology S5</td>
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<td>Biotechnological Products S6</td>
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<td>Safety Pharmacology Studies S7A - S7B</td>
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<td>Immunotoxicology Studies S8</td>
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<td>Anticancer Pharmaceuticals S9</td>
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<td>Photosafety Evaluation S10</td>
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<td>Single Dose Toxicity</td>
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<td>New Pharmaceutical Excipients</td>
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<td>Safety Testing of Drug Metabolites</td>
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<td>Nonclinical Evaluation of Pediatric Drug Products</td>
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<td>Local Tolerance Testing</td>
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<td>Integration of Toxicology Study Results</td>
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<td>FIH dose Estimating</td>
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<td>Clinical Safety E1-E2F</td>
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<td>Clinical Study Reports E3</td>
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<td>Clinical Trials E7-E11</td>
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<td>Clinical Evaluation by Therapeutic Category E12A</td>
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<td>Clinical Evaluation of QT E14</td>
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<td>Pharmacogenomics E15-E16</td>
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Special Requirements in CFDA Guidance before EIH

- Only the final reports are accepted for CTA submissions

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

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Helen Yang: Roche PDR

Na Yu: Roche PDR
Doing now what patients need next