A Change for promoting Innovation and Accelerating Approval

----An Ongoing Reform in Chinese Pharmaceutical Regulatory

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Why we have to change?

• Drug Quality
• R&D, Process, Distribution
• Regulatory team
• Low approval efficiency
Review Situation of CDE since 2003

- **DRR:** Drug Registration Regulation

- **No. of Applications**
- **Queue of Review**
- **No. of completed review case**

- **2005 version DRR**

- **2007 Version DRR**

- **Review backlog over 22,000**

- **Increase no. of external reviewer**

- **Grouping review**
Important Events

2015.7.22  CFDA: Self-inspection of Drug Clinical Trial Data

2015.8.9  State Council: Opinions on reforming the Review and Approval System for Drugs and Medical Devices with the objectives:
- Solve the backlog of registrations by the end of 2016 and realize the specified review and approval timeline within 2018
- Establish a more scientific and efficient review and approval system.

2016.8.10  CFDA: Bundling review and approval of packaging materials and pharmaceutical excipients

2016.10.26  CFDA: Priority review of medical devices for the diagnosis or treatment of rare diseases, malignant tumors, etc.

2017.5.11  CFDA: marketing authorization of new drugs and medical devices… etc.

2017.6.19  CFDA became an ICH member, clearly indicating that Chinese drug regulations are soon to be aligned with international ones

2017.10.8  State council: Opinion on Deepening the Reform of the Review and Approval System and Encouraging the Innovation of Drugs and Medical Devices

2017.10.10  CFDA: Decision on Adjusting the Management of Imported Drug Registration
Clinical Trial Management

- Modify the review and approval process, approval is only required for the first CTA
- Modify the review model to focus on the clinical value and clinical trial protocol
- Modify the supervision by implementing the reporting system, and suspension, reversion or termination of clinical trial
- Establish systemic, standardized and effective communication by assigning project managers for each application to facilitate the communication so as to improve the review quality and efficiency
- Establish priority review system to encourage the innovation and meet the urgent clinical needs

- Set up a review team, based on the claimed indication, which is led by clinical reviewers and composed of each discipline reviewers and project manager
- Conduct the review in accordance with the technical guidelines
- Establish Good Review Practice (GRP)
- Standardize technical review, on-site inspection, sampling and testing, communication, suspension and restart of clinical trials
- Conduct supervision on document completeness, compliance of registration procedures, standardization and definiteness of technical review conclusion
Biosimilar situation in China

- Clusters of companies develop same targets biosimilar
- Accessibility of reference drugs
- Challenges to regulatory agency
- International big pharma enter China
New Category of bio-products (being discussed)

- Fist in Class
- Biosimilar
- Need to prove to be better
- Biological products with established national standard (ChP)
Cell therapy

- Hospital technique or drug
- Chinese guideline is being drafted
- Leading companies enter China
- Regulation challenge: CMC
Points to discuss, before FIH

- Considerable flexibility the CMC data required
- Three batches consistency results are required
- Three viral clearance studies are required
- Container closure system certification are required
- EPC testing or UPB testing
Marketing Authorization

- Pre-filing Review System
  - Follow CTD format
  - All applications are submitted to CFDA directly
  - Conduct pre-filing review for the marketing authorization application to ensure the evaluability of the application documents.

- Marketing Authorization Holder System
  - Implement the MAH system
  - Clarify the main responsibility of the marketing authorization holder in drug registration and marketing

- Comprehensive Evaluation System
  - Establish a comprehensive evaluation system with technical review as the core, in combination with risk-based on-site inspection and sample testing
  - Accept foreign data to support MAA if meet China requirements
  - Accept application of new dosage form based on clinical needs
  - Implement conditional approvals

- Review and Approval Team
  - Includes external experts, lawyers, senior managers, auditors and etc.

- Improve Review Quality Management
  - Conduct the review in accordance with the technical guidelines
  - Establish Good Review Practice (GRP)
  - Standardize technical review, on-site inspection, sampling and testing, communication, suspension and restart of clinical trials

- Improve Review and Approval Management
  - Conduct supervision on document completeness, compliance of registration procedures, standardization and definiteness of technical review conclusion
Post-marketing Continuation and Supervision Management

Post-marketing Evaluation and Supervision System
- Establish the post-marketing risk information collection and analysis, pharmacovigilance, annual reports and other related systems by referring to FDA Risk Mitigation and Management Strategy (REMS) and EMA Risk Management Plan and annual reporting system
- Conduct re-evaluation for the post-marketing drugs to identify any potential and unknown safety risk for the first launched product

License Renewal System
- Continuous review and systematic evaluation of drug quality, safety, efficacy
- Submit license renewal application six months before the expiration of the license, and if no decision is made overdue after acceptance, the application will be regarded as approval

Annual Report System
- Marketing authorization holder should summarize and evaluate the variations and post-marketing safety information every year, and submit the annual report
Post-marketing Supervision

Change Management System
- Changes are categorized based on their potential influence and risk on quality, safety, efficacy, and filed through the appropriate regulatory pathway

Defined Timeline
- The timelines of specific registration procedure, e.g. acceptance, clinical trial, marketing authorization, variation, and license renewal, are defined clearly

Supervision and Management
- Clarify the management direction and responsibilities of the health authorities, explain the means of relief such as reexamination, and list various situation of abolished approval licenses

Legal Liability
- Clarify the responsibility pursuit and handling measures of health authority, technical departments and applicants when violating relevant laws and regulations
Draft Chinese Post-Approval Change Guideline

**Principle**
- Based on science and regulatory documents by CFDA. Refer to related documents from other agency. Responsibility, target and compliance, comparable study, related change, design space and plan to do the change.

**Established conditions**
- To be decided

**Requirements**
- To be decided
The reform started in 2015 has gone beyond drug review and approval to the reform of the entire medicines regulatory system. The ultimate goal of the reform is to integrate with global.

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