IND Review Process and Consulting System in China

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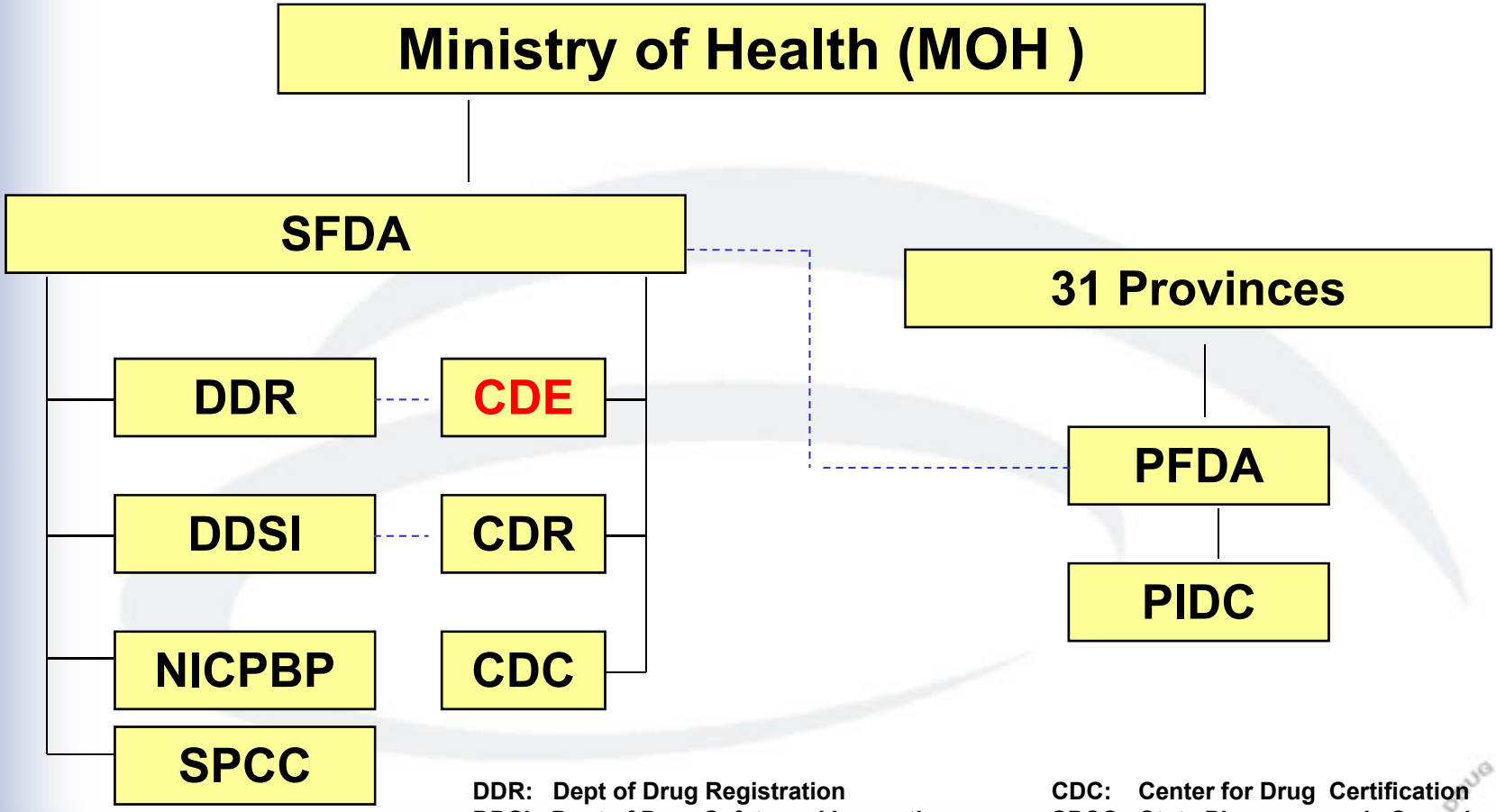
Disclaimer

The opinions included herein are those of the presenter, and do not necessarily reflect those of the CDE ,SFDA

Major Topics

- ☞ China's drug administration system
- ✓ IND Procedure
- ✓ NDA Procedure
- ☞ CDE organization and review process
- ✓ IND review process
- ✓ Consulting and Communication
- ☞ Challenges & Opportunities

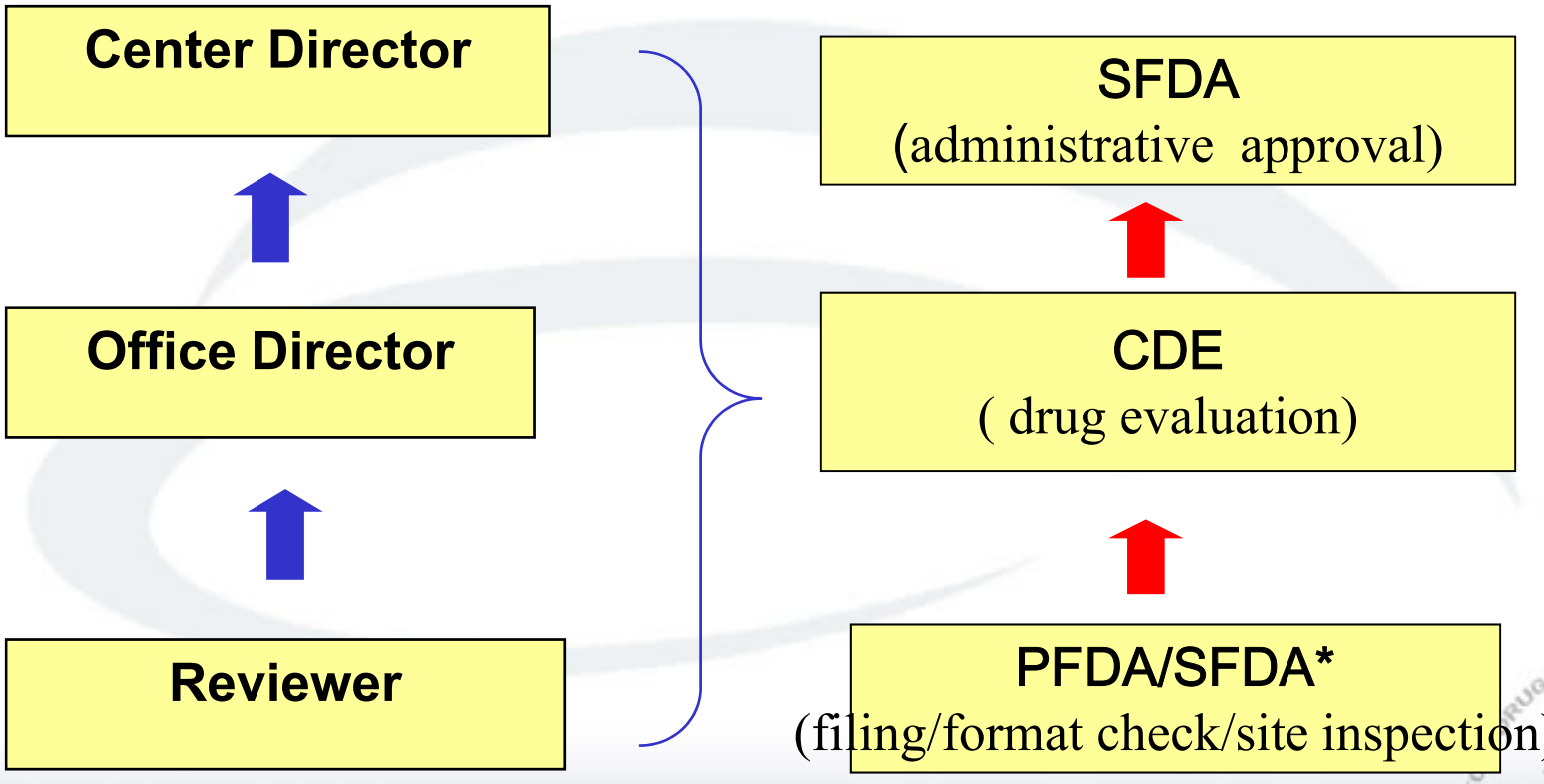
China's Drug Administration System



DDR: Dept of Drug Registration
DDSI: Dept of Drug Safety and Inspections
CDR: Center for Drug Re-evaluation
NICPBP: National Institute for the Control of Pharmaceutical & Biological Products

CDC: Center for Drug Certification
SPCC: State Pharmacopoeia Commission of China
PFDA: Provincial Food & Drug Administration
PIDC: Provincial Institute for Drug Control

Decision-making Process



*for domestic application, the dossier should be submitted to PFDA; while for the import application ,directly to SFDA office.

Registration Categories of Chemical Drugs

--According to Drug Registration Regulation 2007

1. **New drug never marketed in any country**
   - synthesis or semi-synthesis¥natural sources or by fermentation¥Optical isomer¥fewer components from marketed multi-component drug¥New combination products¥
   - ***a newly added indication***
2. **Changed administration route and not marketed in any country**
3. **Drug marketed ex-China**
4. **Changed acid or alkaline radicals or metallic elements**
5. **Changed dose form, but no change of administration route**
6. **Drugs following national standard**

Application Types of Chemical Drugs

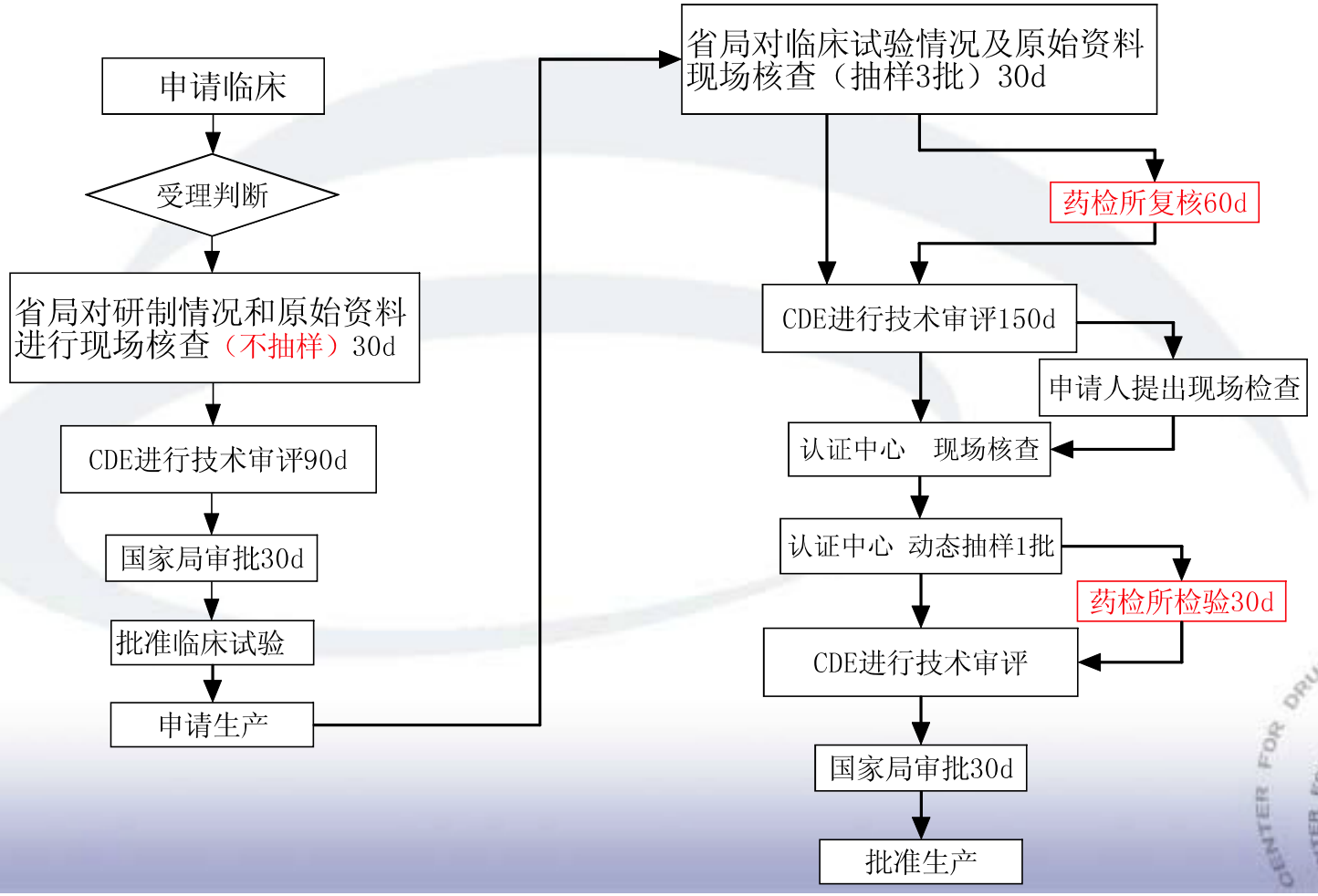
--According to Drug Registration Regulation 2007

1. **New Drug Application (IND and NDA)**
2. **Generic Drug Application**
3. **Import Drug Application**
4. **Supplemental Application (post-approval Change)**
5. **Renewal Application**

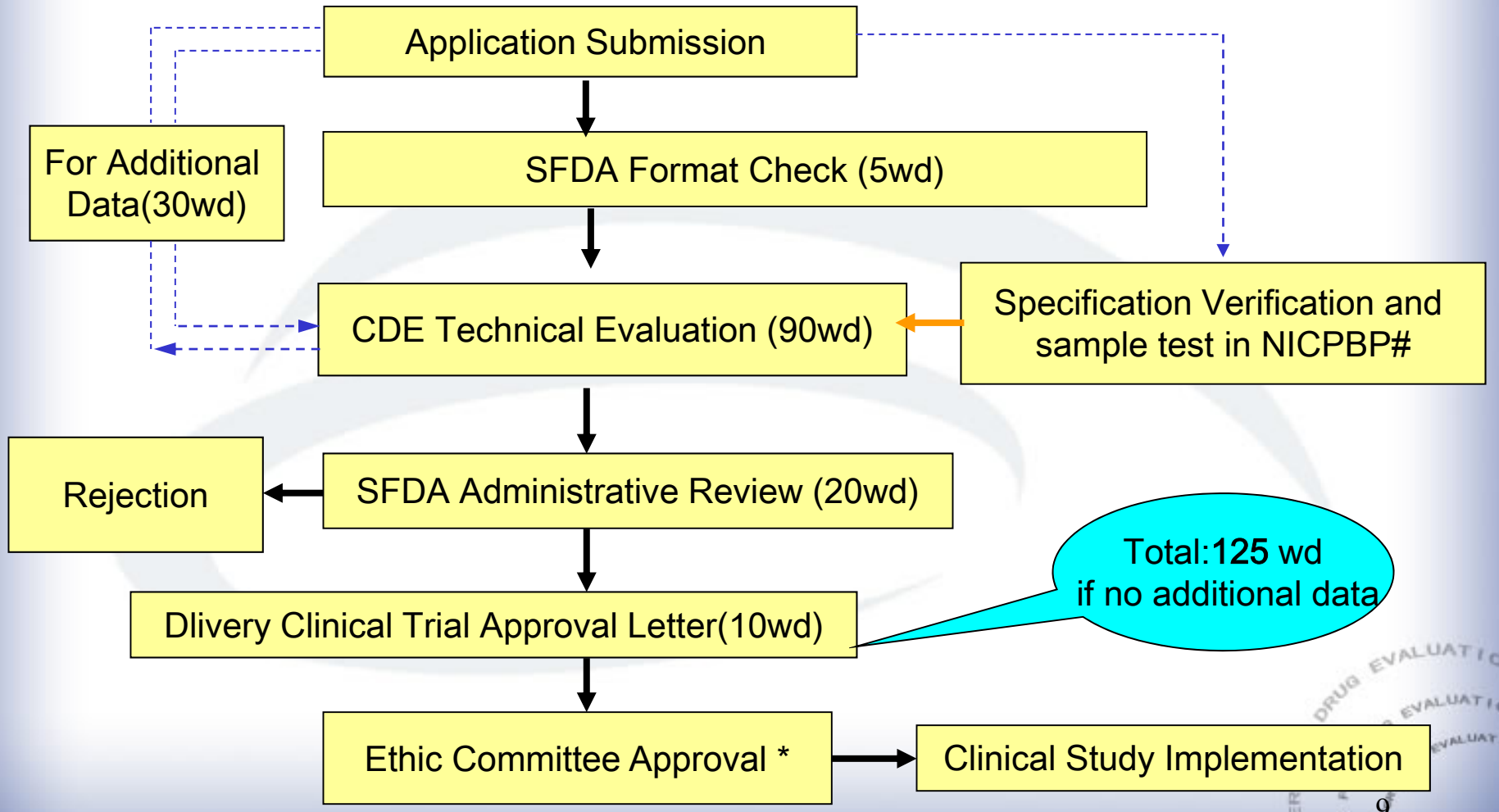
New Drug Application Procedure

IND　　NDA

新药报批程序（28号令）



Application Procedure for Import New Drug — Clinical Trial application



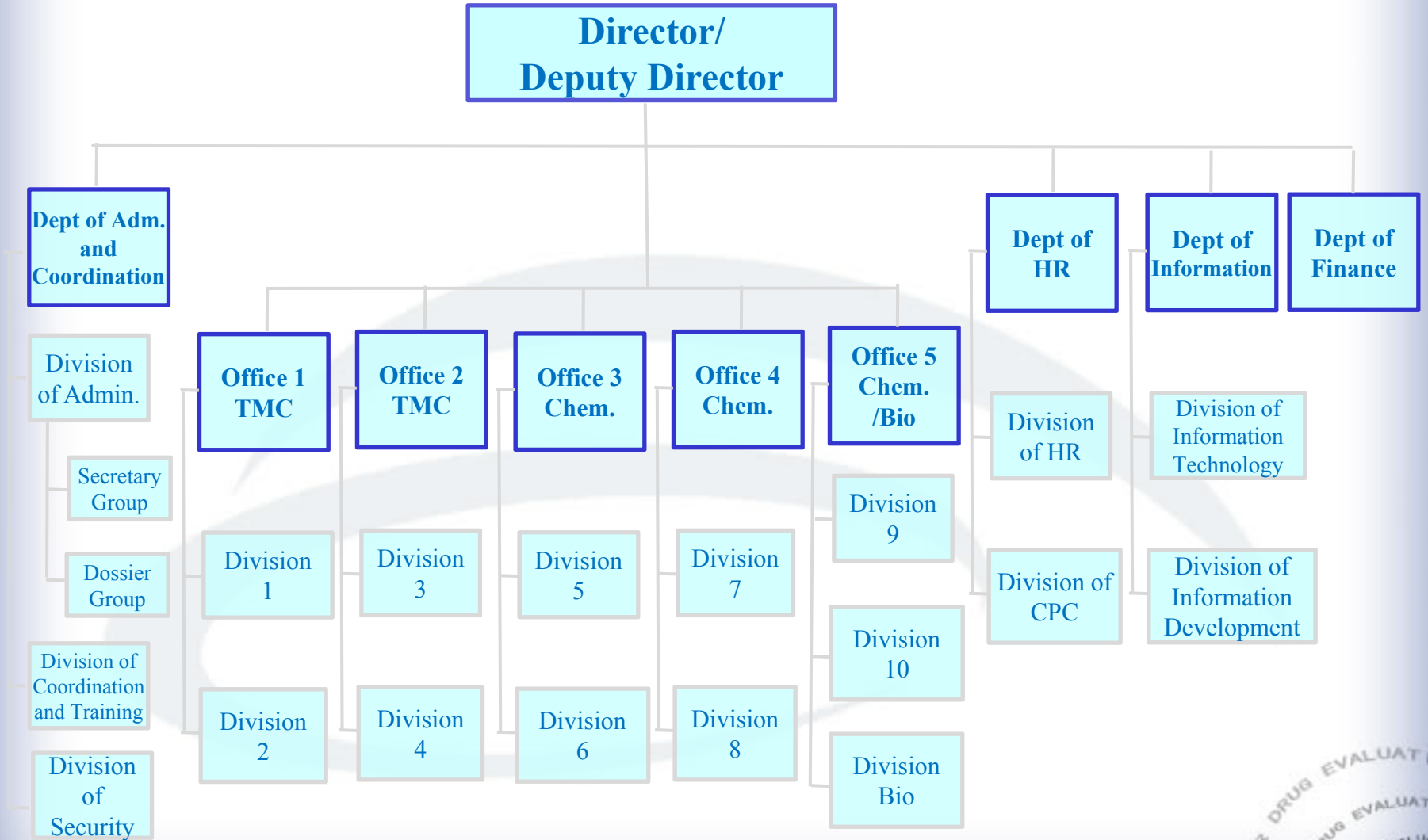
* Not time requirement, depending on study site schedule.
# Not necessary for chemical drug MRCT

CDE Responsibility

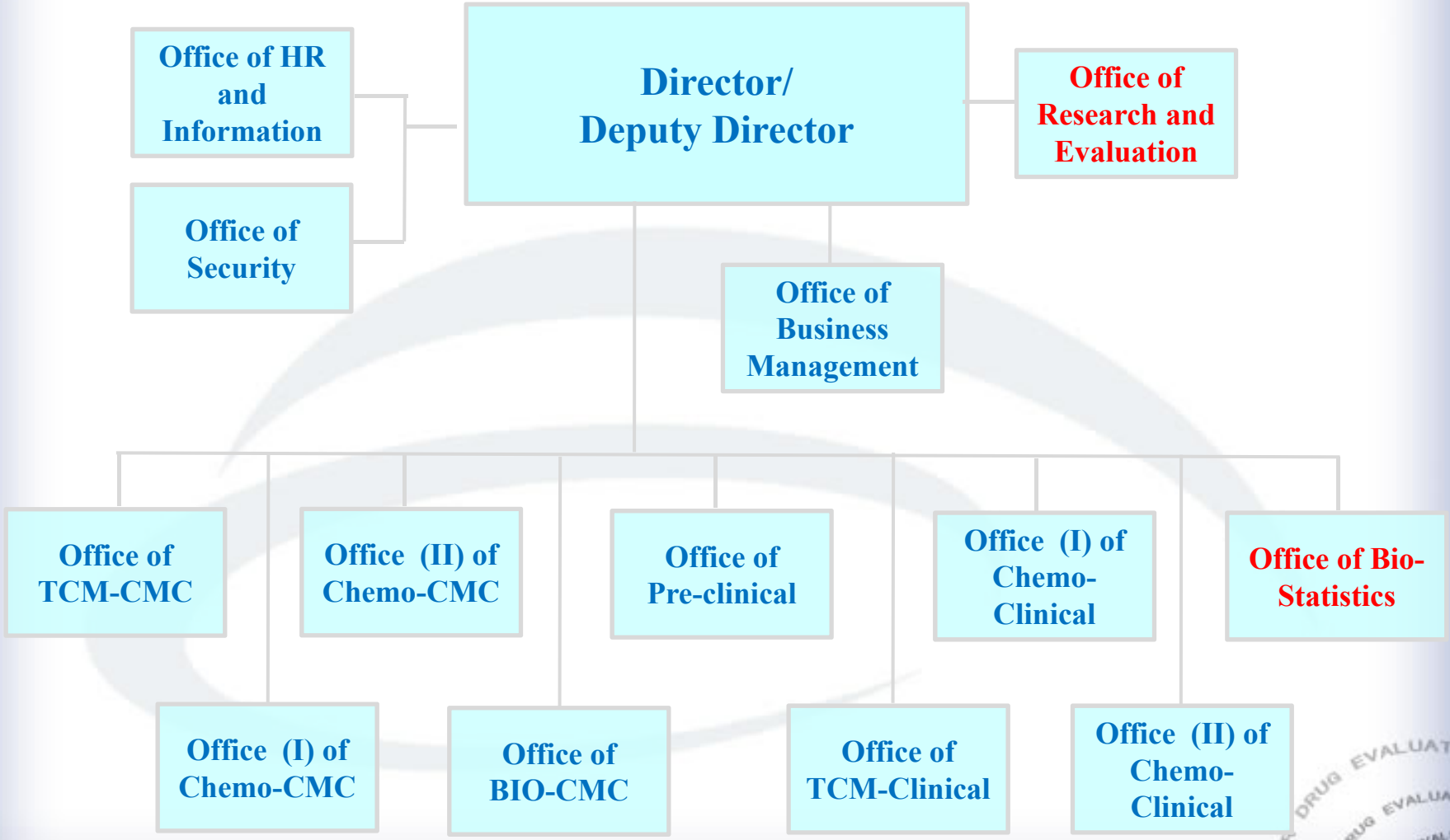
Main responsibilities:

- **Both IND and NDA**
- **Chemical products, biologic products, including vaccines, and TCM , including botanical drugs**
- **Administrative review and approval stay with SFDA department of drug registration**
- **Post-marketing review stays with Center for Drug Re-evaluation**

CDE Organization Structure (before 2011.2)



CDE Organization Structure (since 2011.2)



CDE Review Process（since 2011.3.23）

Assign review process by application types*:

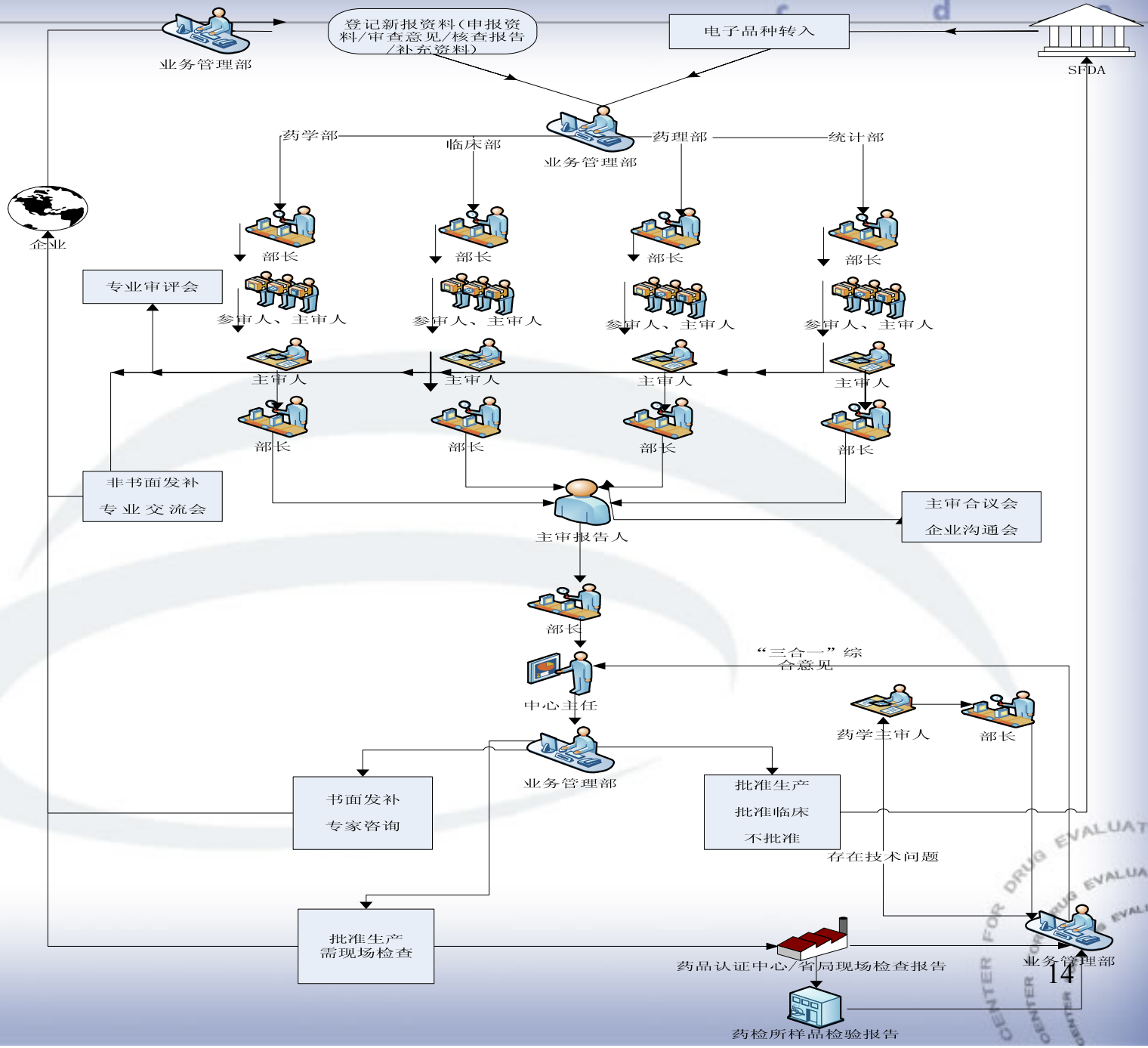
- **Parallel —New drug application**
- **Single-discipline —Generic drug and Supplemental application**
- **Sequential —Generic drug and Supplemental application**

（Shift from single discipline process when multiple disciplines needed）

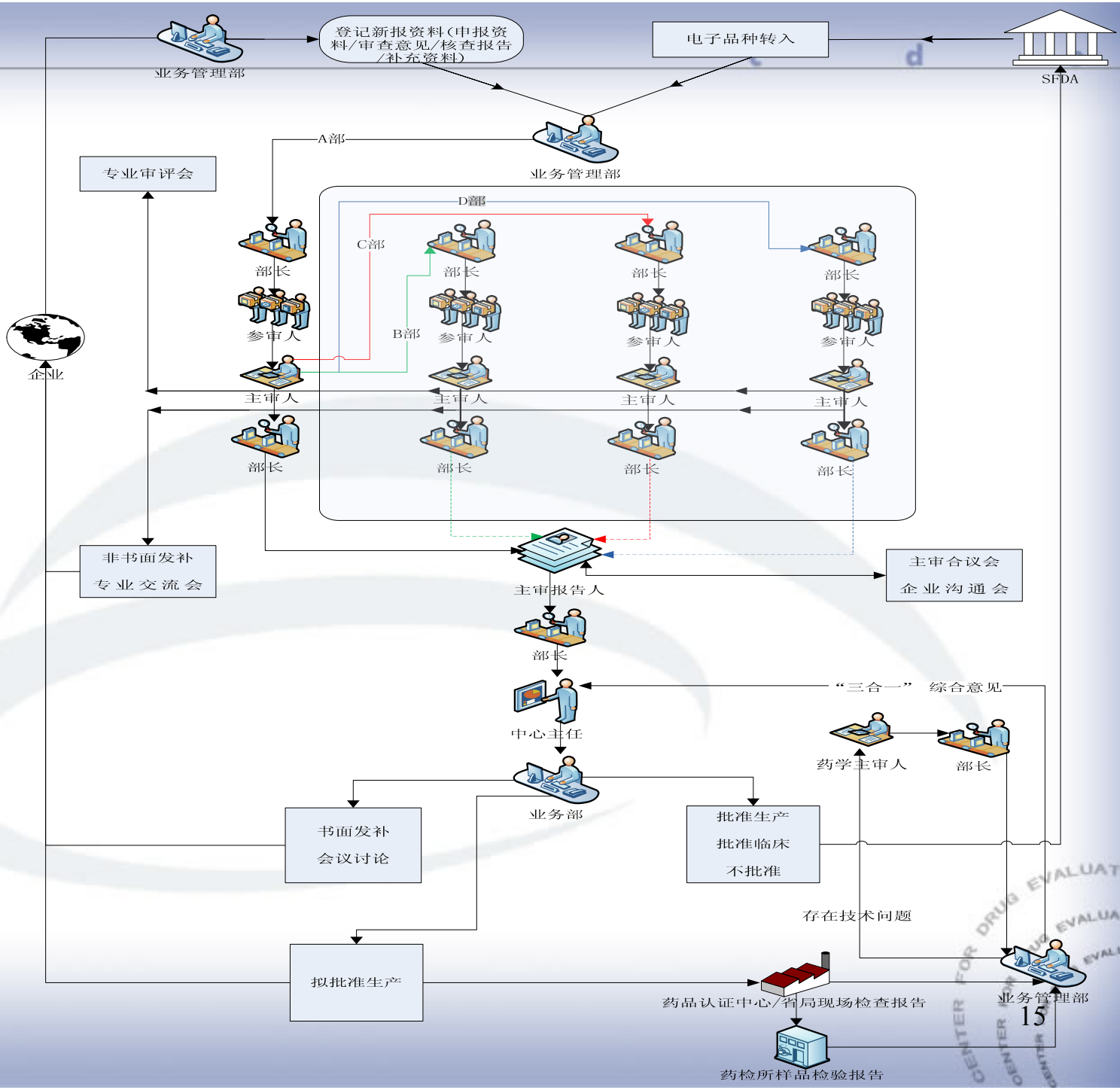
- **Simplified —Supplemental application**

*before 2011.2,one process for all

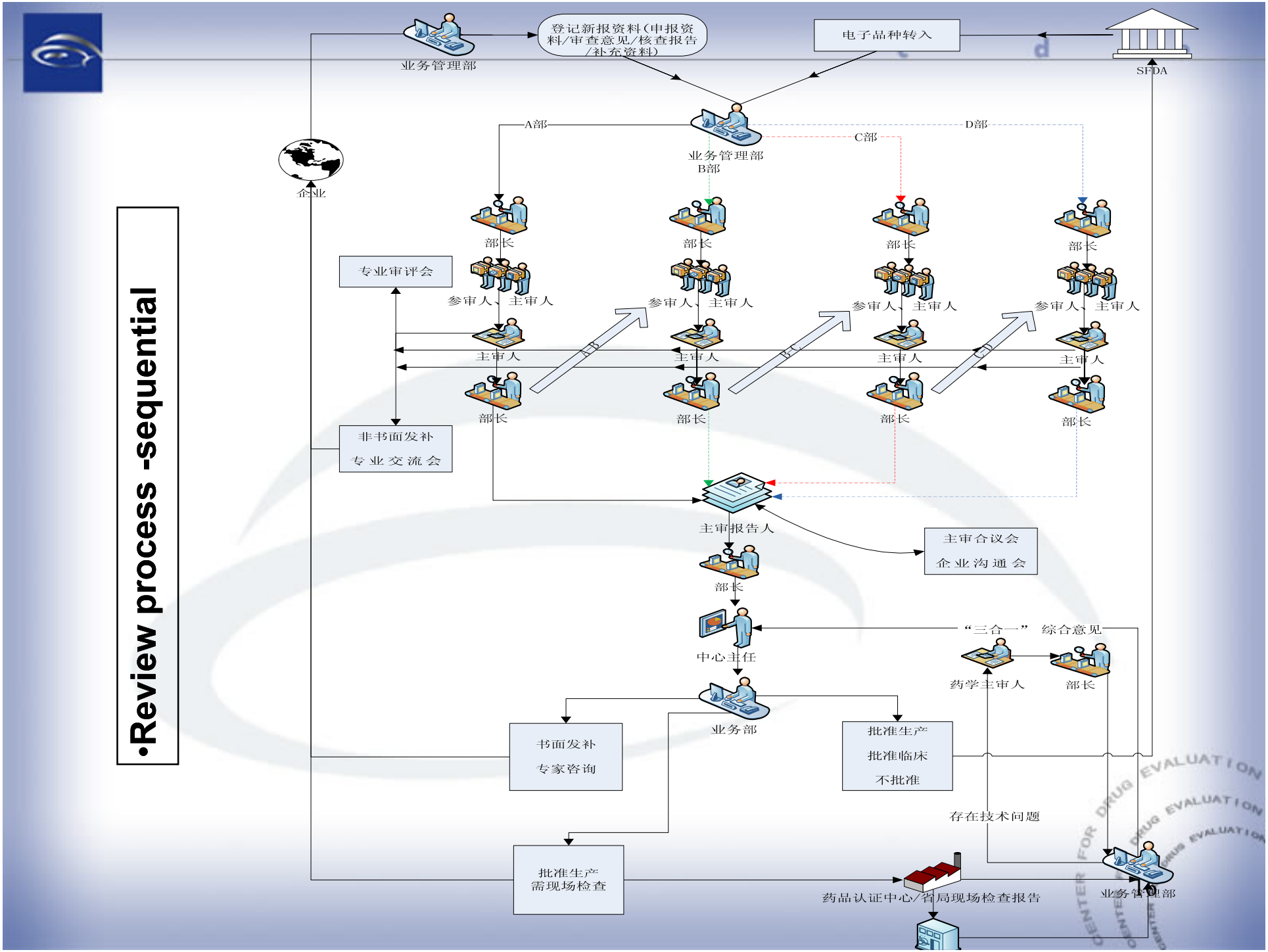
•Review process -parallel



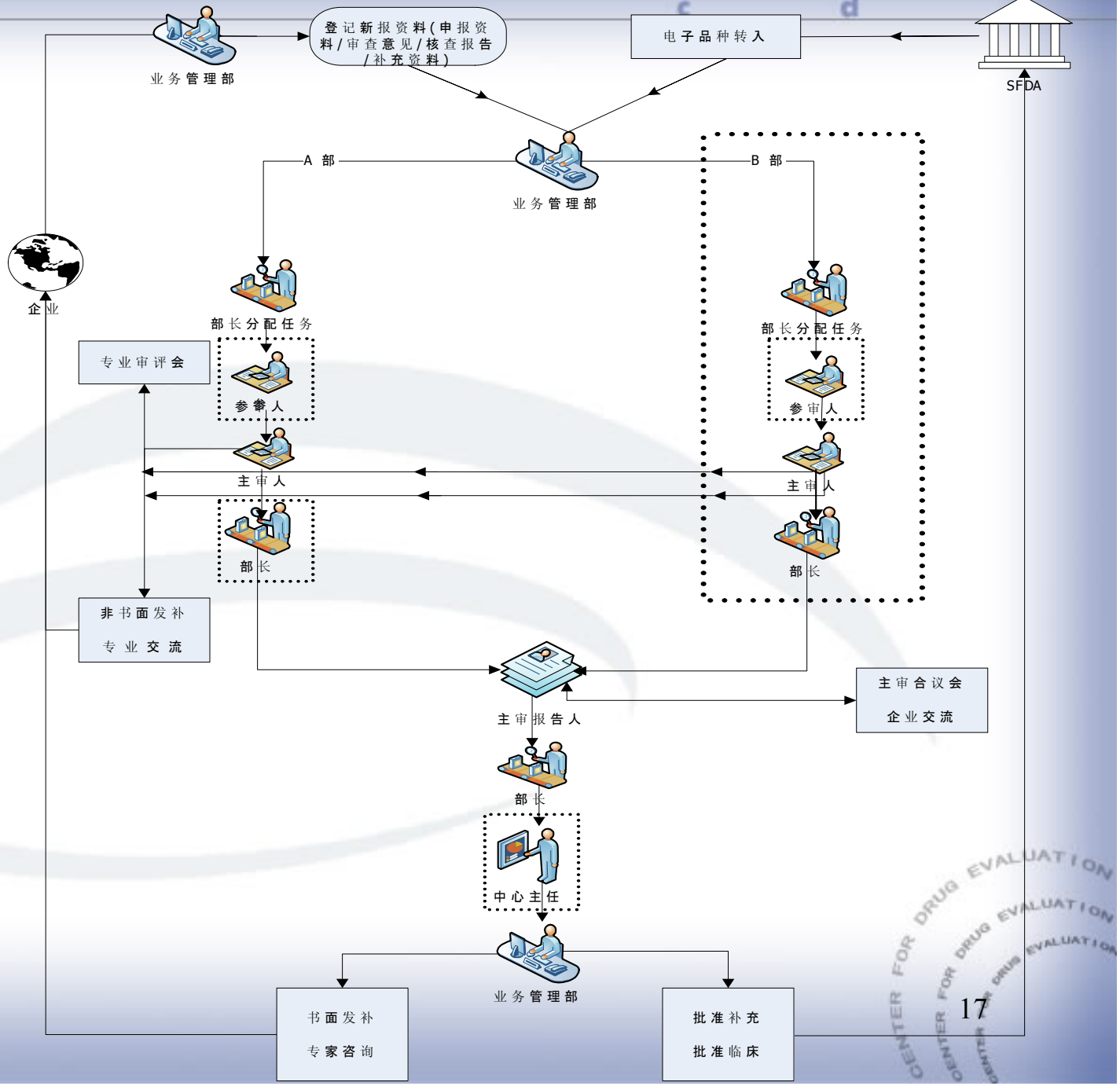
•Review process –single discipline



•Review process -sequential



•Review Process -Simplified

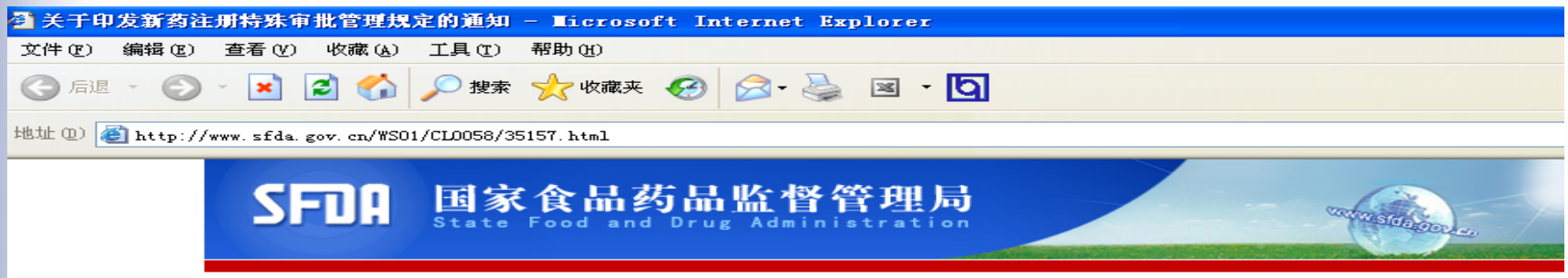


Review Timeline

Type of application	Department / Working days	Reception Center	CDE(IND /NDA)	DDR/SFDA
New dossier	New drug appl.	30	90/150	20#
	Special review procedure	30	80/120	20#
	Generic drug appl.	30	160	20#
	supplemental appl.	30	40	20#
Supplementary dossier	New drug appl.	0	30/50	20#
	Special review procedure	0	20/30	20#
	Generic drug appl.	0	53	20#
	supplemental appl.	0	13	20#

Extra 10 days by approval of commissioner for special cases
Another 10 days to delivery the decision

Special review procedure (issued in Jan.2009)



关于印发新药注册特殊审批管理规定的通知

国食药监注[2009]17号

2009年01月07日 发布

各省、自治区、直辖市食品药品监督管理局（药品监督管理局），总后卫生部药品监督管理局：

为鼓励研究创制新药，有效控制风险，根据《药品注册管理办法》，国家局组织制定了《新药注册特殊审批管理规定》，现予印发，请遵照执行。

国家食品药品监督管理局

第二条 根据《药品注册管理办法》第四十五条的规定，国家食品药品监督管理局对符合下列情形的新药注册申请实行特殊审批：

（一）未在国内上市销售的从植物、动物、矿物等物质中提取的有效成份及其制剂，新发现的药材及其制剂；

（二）未在国内外获准上市的化学原料药及其制剂、生物制品；

（三）治疗艾滋病、恶性肿瘤、罕见病等疾病且具有明显临床治疗优势的新药；

（四）治疗尚无有效治疗手段的疾病的新药。

➢What qualifies for special review procedure

•Small molecules or biologics that have not been approved in China or ROW;

•Applicable to both abroad and domestic applications;

•**New drugs for treating HIV/AIDS, malignant tumors, rare diseases with significant clinical efficacy**

➢Main characteristics:

•• Shortened review and approval period (80 working days)

••May submit pre - IND meeting requests prior to application

••Under certain circumstances may submit supplementary documents during review process

Purpose:

- Explore and establish a suitable IND review a nd approval process that fit the Chinese envir onment
- Establish a responsive communication chann el and system
- Establish a comprehensive and transparent s ystem for new drug review process

How to communicate with CDE?

1.Regular review meeting (Usually monthly)

- ✓ Submitted by reviewer in process
- ✓ Including sponsor,reviewer and external expert

2.Dialogue meeting between CDE and sponsor (as needed) *

- ✓ Pre-IND，Pre-NDA, or in review process;
- ✓ Submitted by either reviewer or sponsor;
- ✓ Face to face ,Telephone or Video conference；

3.Face to face discussions(each Wednesday-consulting day)

4.Telephone(after 3:30pm every day)

5.Openning day

6.Information feeback via CDE internet (www.cde.org.cn)

7.Internal technical journal or article of CDE

8.others:training course,seminar

*The guidance development is ongoing.

Summary of Major Changes

1. More flat organization

5 Review Offices
11 review division
3 Disciplines

9 Review Offices
4 Disciplines

2. Review office from TA-based to discipline-based

3. Two new offices set up

internal QA

Internal Statistics

Summary of Major Changes

4. Improved flexibility

5. Improved transparency :

- ✓ **Opening review plan monthly**
- ✓ **Opening review timeline, status and reviewer**
- ✓ **Opening review report of the first NDA**
- ✓ **Encouraging communication and consulting**
- ✓ **…**

Challenges for CDE

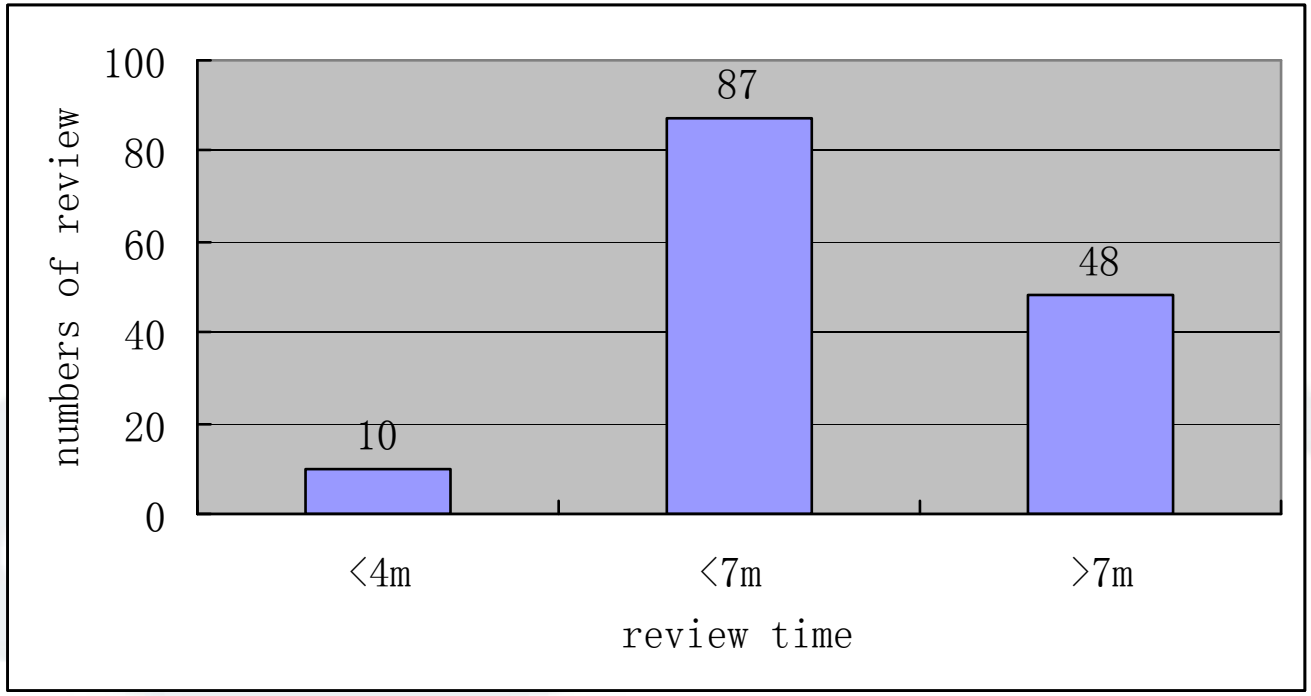
➢**For IND**

- ***Review time too long to participate simultaneous global development***

➢**For NDA**

- ***"Drug lag": Many drugs are available in China 3-4 years after its initial approval in the US and Europe***

Review Time for Multinational Clinical Trials



Increasing workload & limited resource

Chinese SFDA vs. US FDA - Review Capacity and Resource (2005)

	US FDA	Chinese SFDA
Drug Review Responsibility	CDER (Center for Drug Evaluation and Research)	CDE (Center for Drug Evaluation)
New Drugs	20	1,113
Generic Drugs	344	8,075
Number of Employees	1,800	120

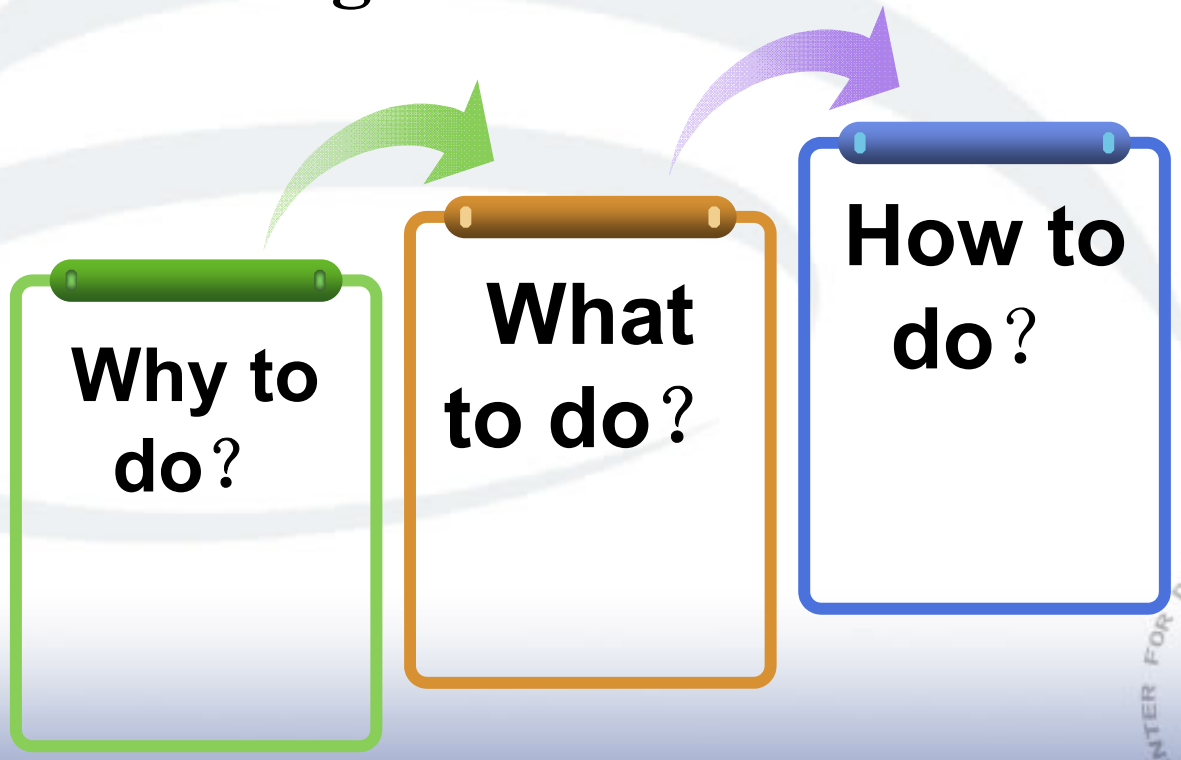
Source Data: Dr. Zili LI, Merck & Co, Inc at CMR Conference, December 4, 2007

Potential ethnic difference evaluation

The regulatory authority always prefer to have local clinical data from their own population .

Feasibility ,necessity and availability of duplication of clinical trial in each region.

- **How to make use of foreign data, reduce unnecessary clinical trial, establish regulatory requirement reasonably，expedite the new medical product registration in local ?**

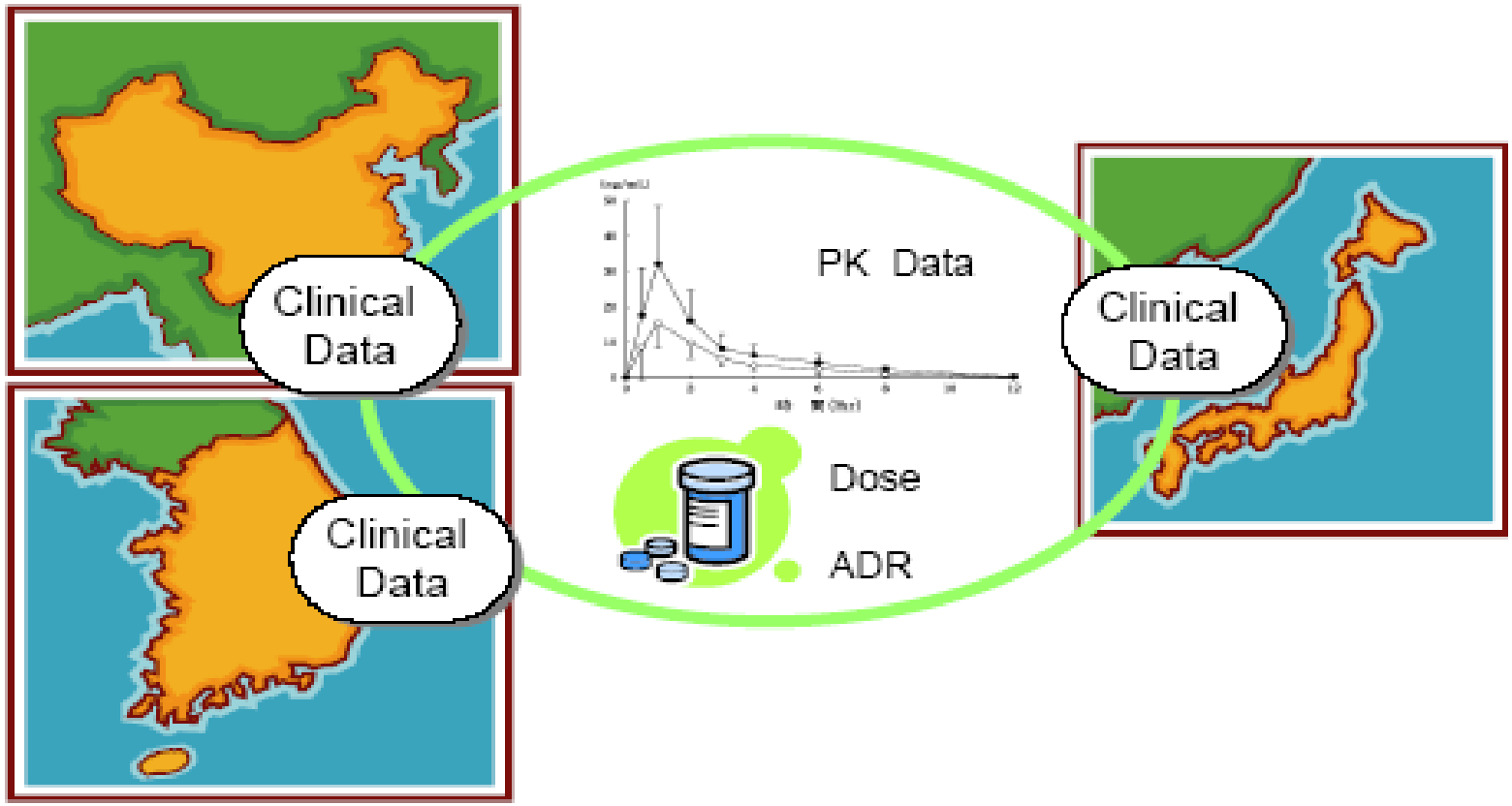


How to share experience and resource in Asian Region

- ✓Limited human resource and capability have been a dilemma for many other regulatory agencies in Asia.
- ✓Possibility of cooperation in Asian region

Health Ministers' Joint Statement among China, Korea & Japan (April 8, 2007)

China/Korea/Japan Joint Research Project on Ethnic Factors in Clinical Data



conclusion

- The goal of regulatory agencies is providing efficient and rapid access to new therapies whilst protecting patient safety
- Making great efforts to exploring appropriate review and approval model under current regulatory system in China
- Global drug development brought us more communication and cooperation opportunity
- Exploring appropriate to share experience and resource in Asian Region

•Thank you for your attention!

Website: www//CDE.ORG.CN

History of China Drug Registration Regulation

1. New Drug Registration Regulation

   (*SDA, 1st May 1999, Chemical Drug, TCM)*

2. Bio-Product Registration Regulation

   (*SDA, 1st May 1999)*

3. Import Drug Registration Regulation

   (*SDA, 1st May 1999, Chemical Drug, TCM)*

4. Generics Product Registration Regulation

   (*SDA, 1st May 1999)*

5. Drug Registration Regulation

   (*SDA, interim, 1st Dec.2002)*

6. Drug Registration Regulation

   (SF*DA, amendment, 1st May 2005)*

7. Drug Registration Regulation

   (SFDA, amendment, 1st Oct. 2007)