

China Clinical Trial Application and Consultation System – an Industry Aspect

S. Wen Chang, Ph.D.

**RDPAC Representative
APEC LSIF RHSC, Industry Representative
VP, N. Asia Strategy and China Regulatory Sciences,
Global Regulatory Sciences
Bristol-Meyers Squibb**

The Second China - Japan Symposium

Disclosures

- I am currently an employee of Bristol-Myers Squibb. I am VP, N. Asia Strategy and China Regulatory Sciences, Global Regulatory Sciences. I am APEC LSIF RHSC, Industry Representative. I am also the member of RDPAC and PhRMA AP KIT.
- The following are my views and not necessarily the views of the Bristol-Meyers Squibb or APEC LSIF RHSC or RDPAC or PhRMA
- My contact information: wen.chang@bms.com

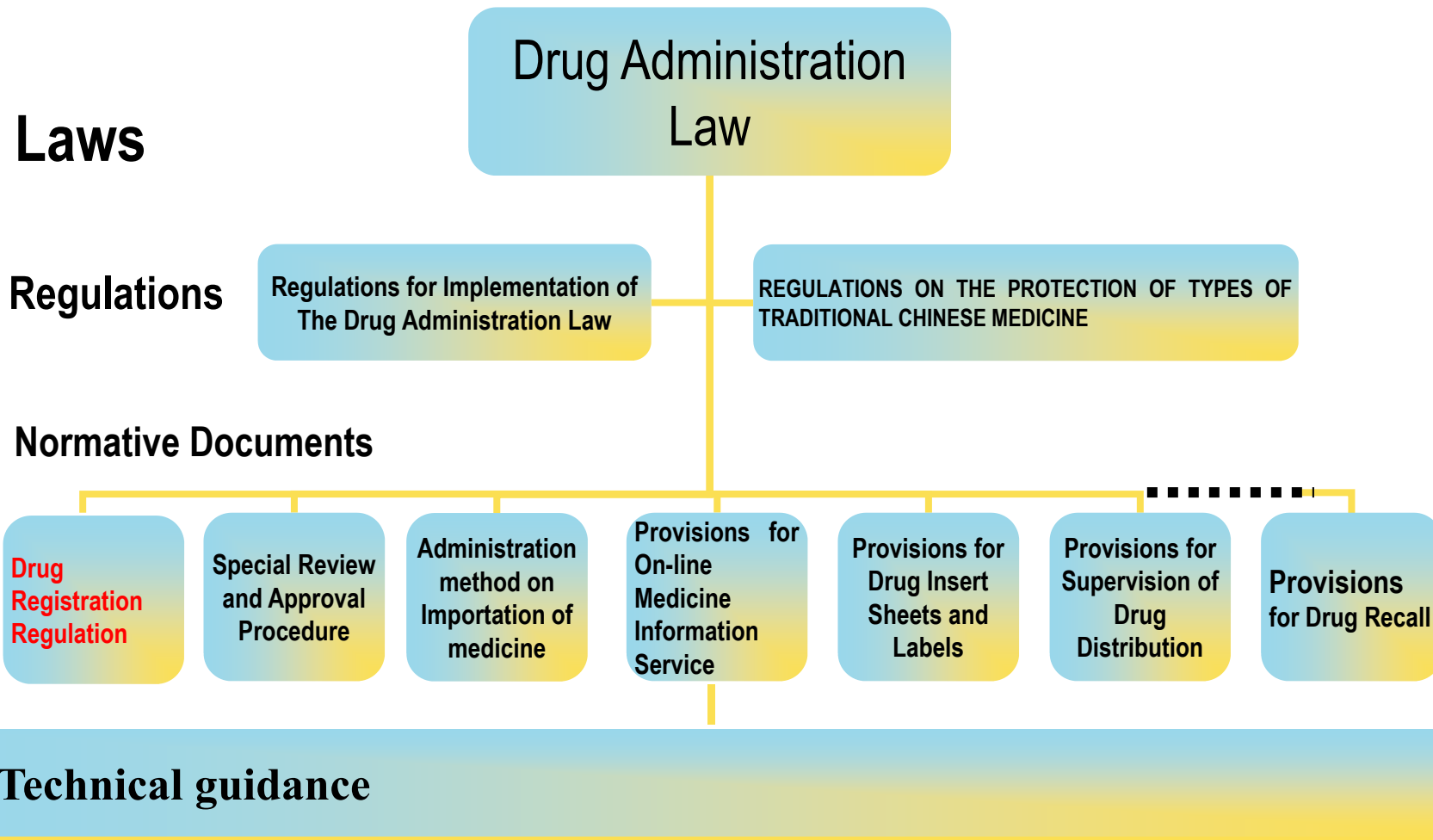
Agenda

- **The regulation requirements for clinical trial application**
- **Consultation mechanism through out the process**
- **Effective consultation with Health Authority**

Agenda

- **The regulation requirements for clinical trial application**
- Consultation mechanism through out the process
- Effective consultation with Authority

The regulation system



The chapter of Drug Registration Regulation

Chapter

- General Provisions
- Application for Drug Registration
- **Drug Clinical Trials**
- **Application and Approval of New Drugs**
- Application and Approval of Generic Drugs
- **Application and Approval of Import Drugs**
- Application of Non-Prescription Drugs
- Supplemental Application and approval
- Drug Re-Registration
- Testing for Drug Registration
- Drug Registration Specifications and Insert Sheet
- Timeline
- Second Review
- Legal Liabilities
- Supplementary Provisions

Annex (registration category and Application Dossier Requirements):

- **Annex 1: for Traditional Chinese Medicines and Natural Medicinal Products**
- **Annex 2: for Chemical drug**
- **Annex 3: for Biological product**
- **Annex 4: for Supplementary Application**
- **Annex 5: for Drug Re-Registration**

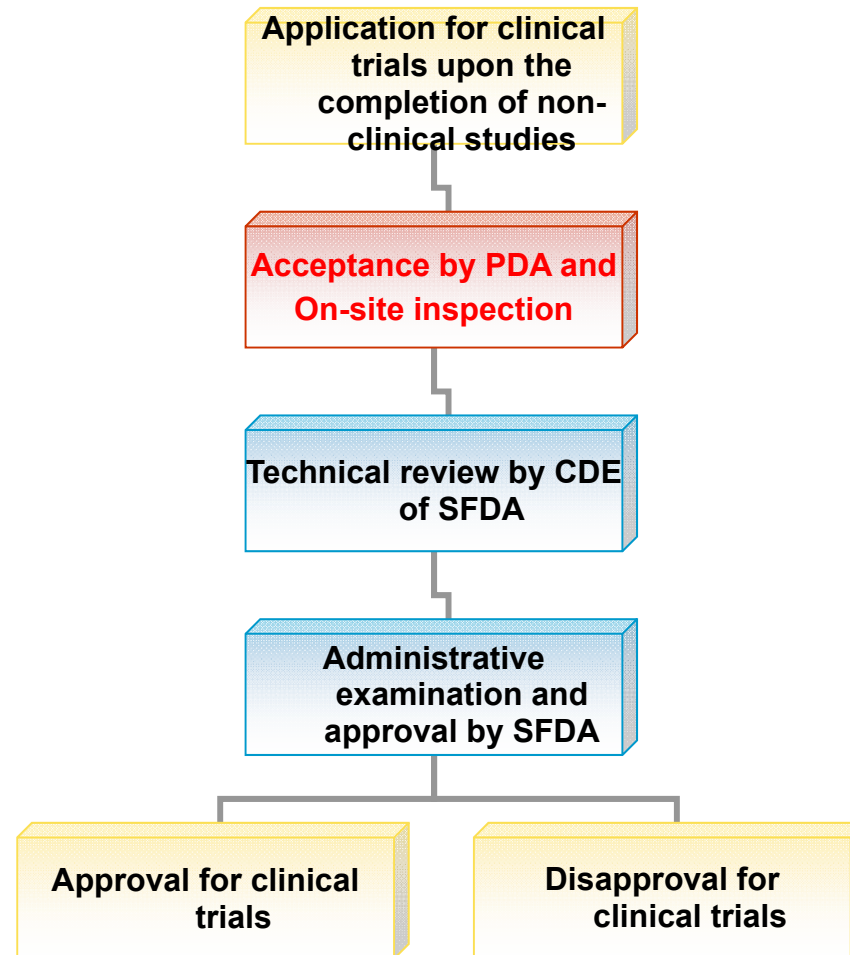
Application Dossier including:

- **General information**
- **Files of pharmaceutical research**
- **Files of pharmacological & toxicological research**
- **Files of clinical research**

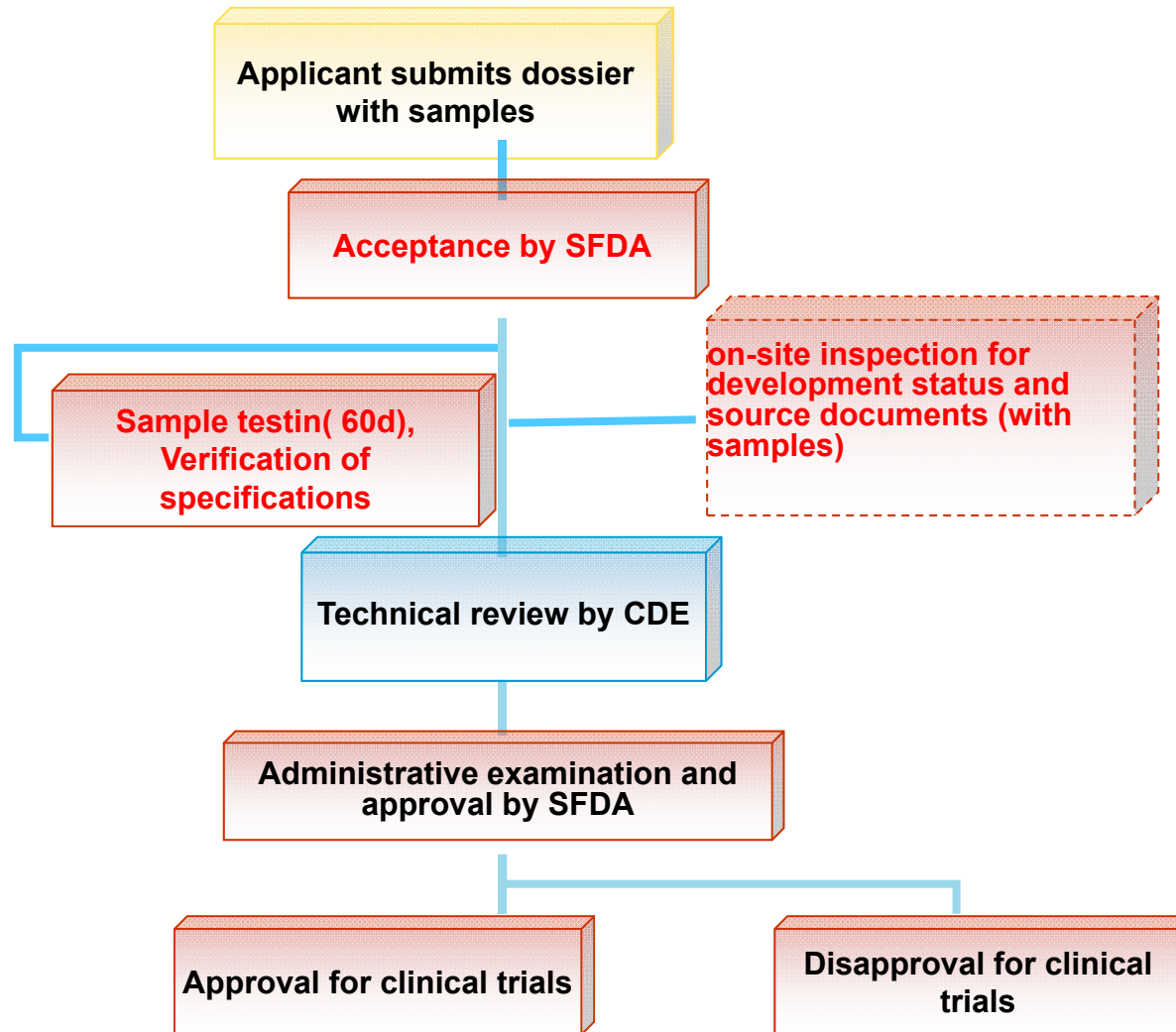
The Categories of Application and Approval for clinical trials

- **New drug registration with two applications and two approvals**
 - Application for clinical trial and application for manufacture (or marketing)
 - System of approval was conducted for clinical trial application
- **Circumstances for submitting clinical trial application**
 - New drug registration application
 - Import drug registration applications
 - International multi-center clinical trial application (data used or not used for registration)

Application for Clinical Trials for New Drugs



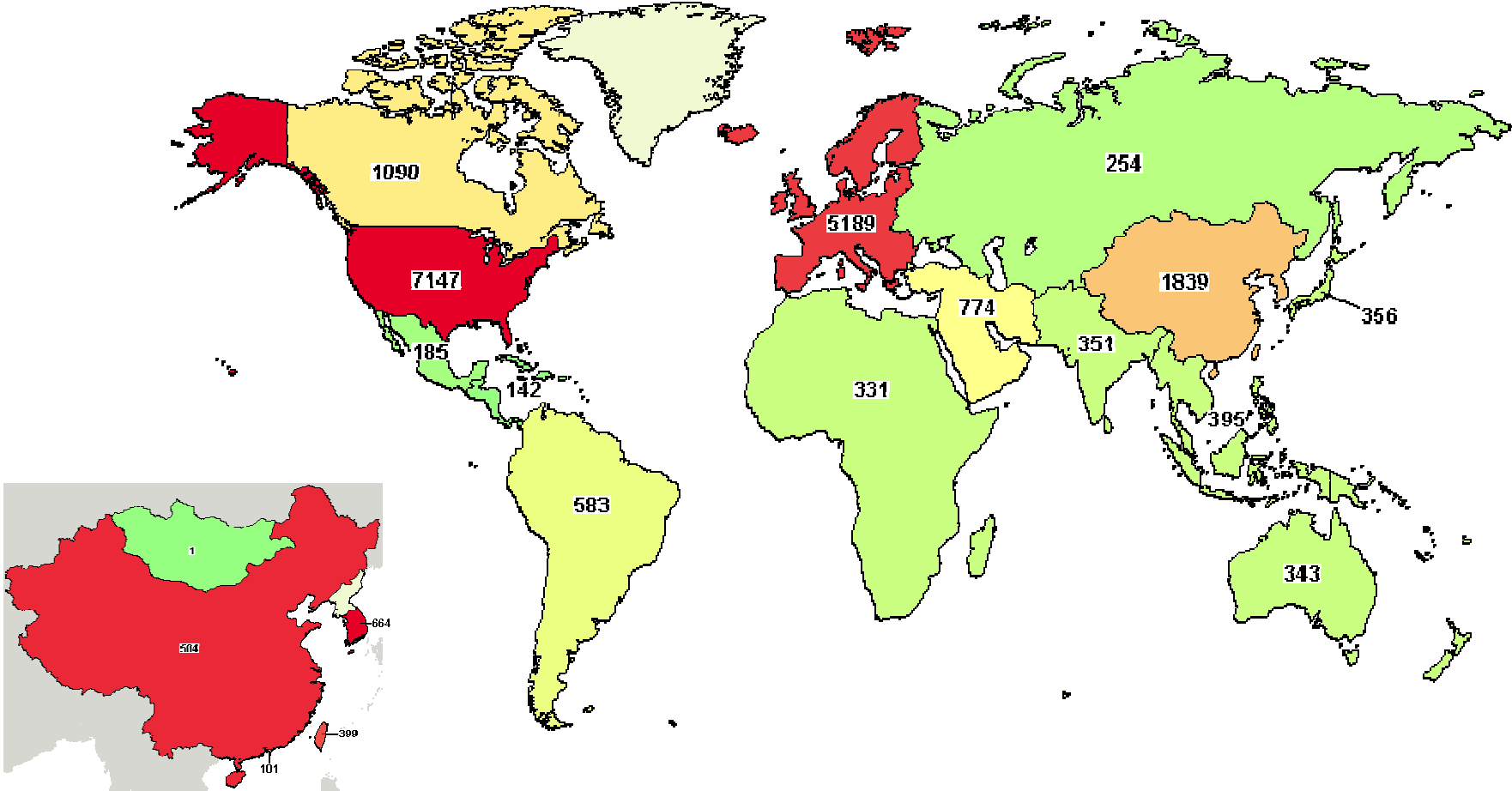
Application for Clinical Trials for Import product



International Multicenter Clinical Trial (IMCT)

- The drugs shall be already approved or in phase II or III clinical trial overseas
- SFDA does not accept trial application for any preventive vaccine not being approved overseas yet
- While approving to conduct an international multi-center clinical trial, the SFDA may require to conduct phase I clinical trial first in China
- The data obtained from an IMCT for drug registration application in China shall include complete report of IMCT

Distributions of Clinical Trials in the World in 2010 (Clinical Trials Registered in www.clinicaltrials.gov)

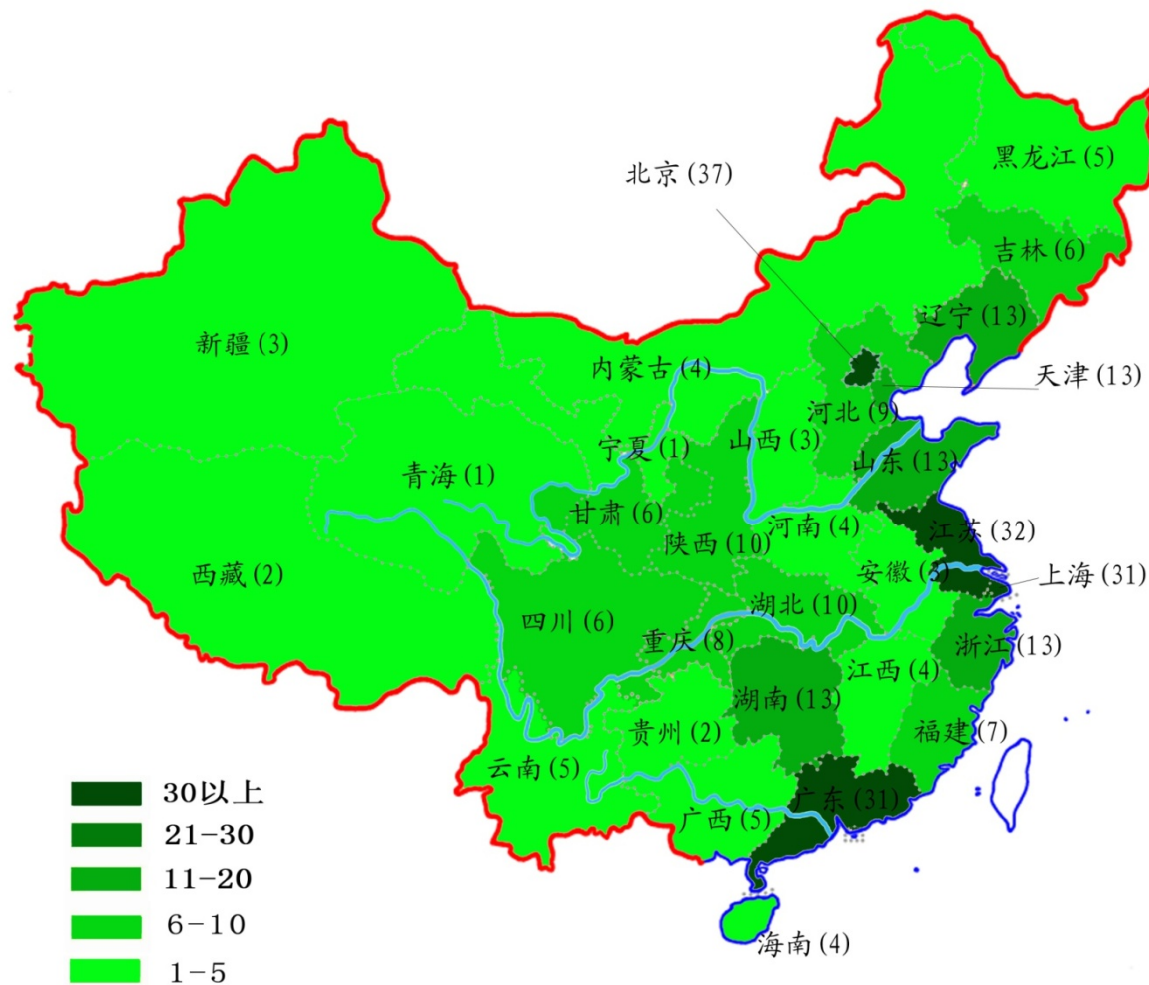


Distributions of Clinical Trials in the World

Region Name	Study number in different year		
	2008	2009	2010
World	17067	17181	17406
Africa	322	331	331
Central America	189	188	142
East Asia	1275	1523	1839
Japan	332	344	356
China	359 (2.1%)	447 (2.6%)	504 (2.9%)
Korea	387	521	664
Taiwan	363	359	399
Hangkong	87	105	101
Europe	4443	4866	5189
Middle East	689	705	774
North America	9256	8613	7951
Canada	1296	1206	1090
Mexico	233	213	185
United States	8457	7765	7147
North Asia	352	313	254
Pacifica	457	416	343
South America	635	638	583
South Asia	336	327	351

Clinical trial has to be conducted in Clinical Sites Certified by SFDA

By Feb 2011, SFDA has totally released 25 issues of Public announcement of certificated clinical trial institutions for drugs:
Total 307 institutions (including 3 in HK)
 (www.sfda.gov.cn)



General framework for the supervision of drug clinical trials

■ Before the trial:

- Verify the qualifications of clinical trial institutions for drugs
- Ethics Committee registration
- Record of the clinical trials before conducting

■ During the trial:

- inspection and monitoring
- Supervision of the conduct of clinical trials (safety data monitoring)

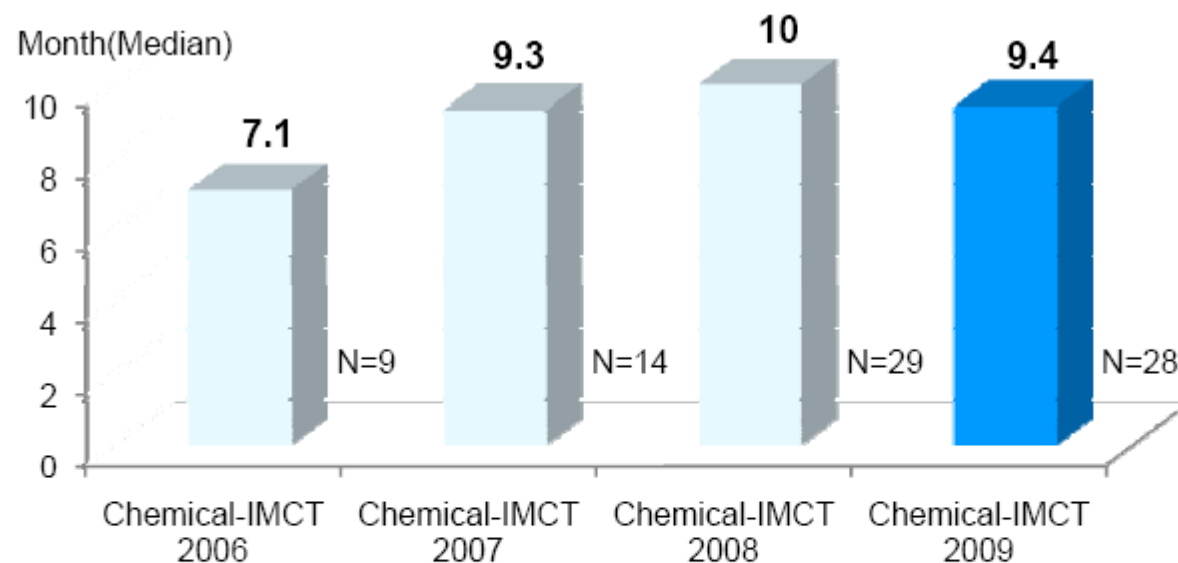
■ After the trial:

- On-site inspection of clinical trial registration prior to scientific review (routine)
- Caused inspection in the process of review (based on the requirements for review)

Policy and timeline for approval of clinical trials in different countries

Country	USA	Japan	EU	India	China
Defined time	30 days	30 days	60 days	40 days	145 days
Policy of approval	System of registration	System of registration	System of review and approval	System of review and approval	System of review and approval
No. of reviewers (2008)	2632	521	530		120

Findings of total timeline from submission to approval - Chemical IMCT (Category 1.1)



Notes: Data supplementation included in the total timeline

Agenda

- The regulation requirements for clinical trial application
- **Consultation mechanism through out the process**
- Effective consultation with Authority

Communication channel between applicants and administrative/technical review - 1

SFDA

- Regulatory consultation arranged every month (2 or 3 times per month for every division)
- Consultation on special topic accepted after application
- Telephone consultation

Acceptance and Service Center

- Face to face consultation
- Telephone consultation
- Request for suggestion and opinion with applicator and industry periodically

Communication channel between applicants and administrative/technical review - 2

CDE

- Panel meeting
- Consulting day weekly
- Open day and communication meetings
- Symposium and training hosted by CDE
- Fax, Phone, video, e-mail communication are possible
- “New “ Technical Review Principle and Procedure published on March 23, 2010
 - Publish target review progress, reviewers, review conclusions
 - Comments to review management, process, and review results can be submitted through web, paper or FTF
 - Defined “lead review department” for CTA, responsible for communication with Sponsor
 - Submit request for communication on critical technical issues and development strategy is possible during new drug development process

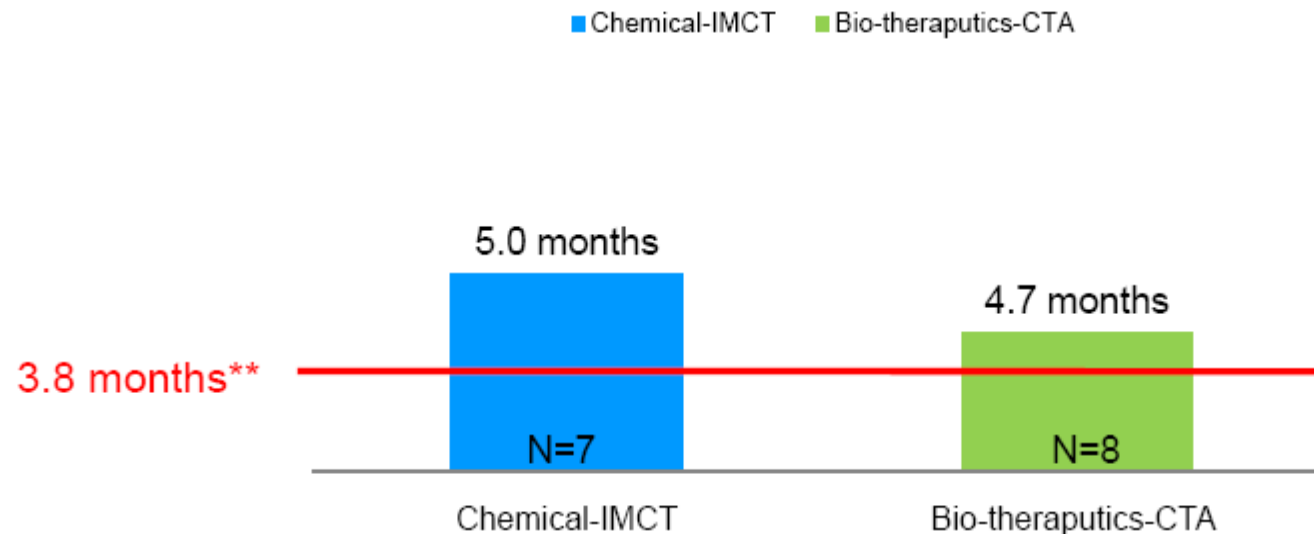
Communication channel between applicants and administrative/technical review - 3

CDE

- **Formal Consultation based on Special Review and Approval Procedure for Drug Registration**
 - Early consultation
 - Time: Before the application of clinical trial
 - Contents: Application for Special Review and Approval Procedure and important technical matters
 - Independent topic consultation
 - Time: During technical review and clinical trial implementation
 - Contents: Major safety concerns, amendments of clinical trial protocol, major variations of indications or qualification, summary and evaluation of the results of clinical trial for finished phase

Findings - SRP Application

Timeline of technical review in CDE*



Notes:

- * Time frame is from technical review starting to completing in CDE
- ** CDE technical review within 80 wd(3.8 months) for SRP clinical trial applications (DRR)

Agenda

- The regulation requirements for clinical trial application
- Consultation mechanism through out the process
- **Effective consultation with Authority**

Fundamental values of communication, for HA and Sponsor

- Quality
- Efficiency
- Clarity
- Transparency
- Consistency



Sponsor's role in the communication

- **Who has primary responsibility for good review?**
 - Interaction in development phase are (primarily) the responsibility of the sponsor
 - Execution of the review process is (primarily the) the responsibility of Health Authority

Purpose of effective HA meeting

- Obtain clear messages from Review Agency, even if suggestion/advice is not positive for sponsor
- Recognition of developing product
- Concerns for feedback/advice for development strategy
- Ascertain the Agency's views on the applicable statutory requirements well in advance of submission of a marketing application
- Issue/concerns for global development strategy or global study design are discussed with different health authorities simultaneously and feedback from those HA are reflected to the strategy or the study design

Key element for Quality Decision Making – works both ways for industry and HA

- Key quality documentation (SOP, assessment templates, policies)
- Professional development/retaining of staffs
- Built-in quality controls
- Structured, integrated peer reviews, advisory committees
- Benchmarking and key performance indicators
- Continual improvement activities
- An established setup and process that allows regular contact between HA and industry
- Transparent system for public information and sharing HA comments

Summary

- Define regulation requirements, application and approval procedures for application of clinical trials
- Discuss multiple channel consultation mechanism
- Complex procedure and time required for clinical trials approval is a barrier for participating global clinical trials. **It may also slow down innovation for local industry from a global point of view.**
- Require guideline for protocol amendments or risk controls during the clinical trials
- Looking forward to fully execution of the new Technical Review Principle and Procedure, and its publication of implementation guidelines

Thank you!