

# Latest Progression of Chinese Drug Registration Management

Zhang Wei, Department of Drug  
Registration



I. Revision and update progression of Drug Registration  
Laws and Regulations

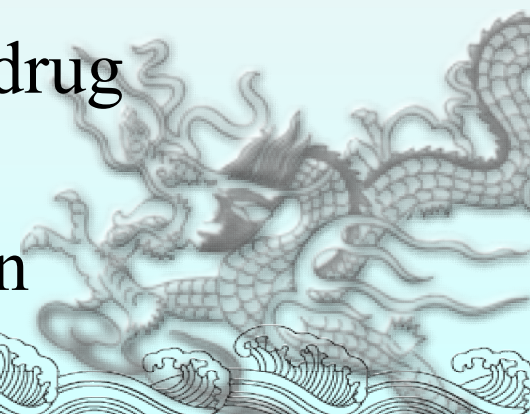
II. About drug registration approval

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IV. Progression of drug research supervision and  
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# Revision and Update Progression of Drug Registration Laws and Regulations



# Further Improvement in Construction of Drug Registration Legal System



1. Study and formulate “Measures for Drug Research Supervision and Management”

2. Complete the formulation of “Rules for Drug Standard Management”

3. Formulate and release “Management Rules for Registration and Filing of Pharmaceutical Raw and Auxiliary Materials” and its related supporting documents

# Revision and Update Progression of Drug Registration Laws and Regulations

- ◆ DMF——Management Rules for Registration and Filing of Pharmaceutical Raw and Auxiliary Materials
- ◆ Rules for Drug Standard Management
- ◆ Technical Guideline of Natural Drug Registration
- ◆ Measures for Drug Research Supervision and Management and serial supporting normative documents
- ◆ GRP
- ◆ Electronic Submission and Common Technical Documentation (CTD)





# Goals of Establishing Chinese DMF System

## Serve the Technical Review

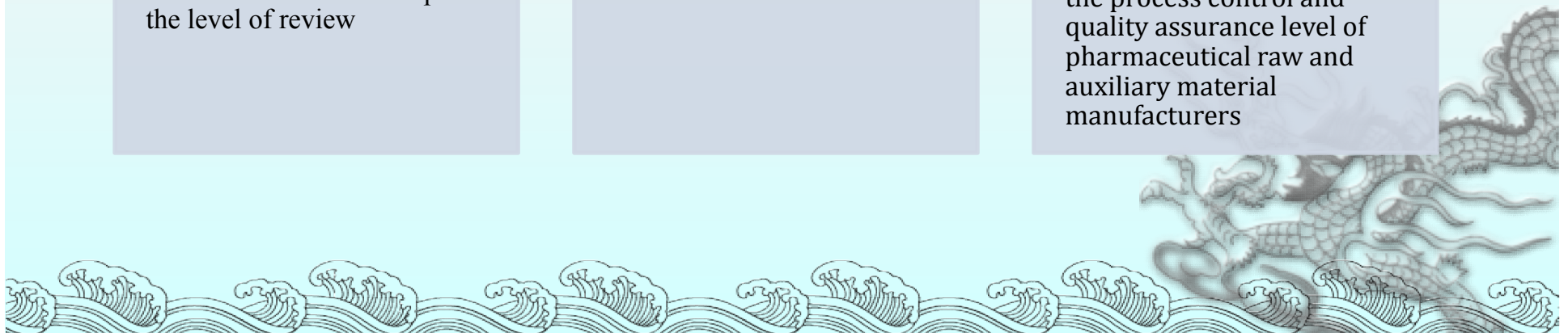
- Benefit the enterprises' application of real technical documents, and improve the reliability of review
- Directly cite DMF in the preparation technical documents to improve the efficacy of review
- The application of the electronic documents with CTD format promotes the electronic review and improve the level of review

## Serve the Dynamic Audit and Inspection

- Provide technical data for site inspection
- Provide technical data for dynamic GMP inspection
- Improve the category-centered inspection level
- Improve the controllability of production process and the traceability of supply chains

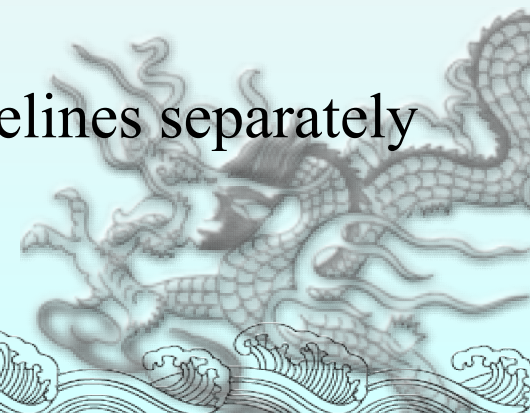
## Sever the Preparation Enterprises

- Improve the applicability of raw and auxiliary materials used in the scientific research of preparation enterprises depending on their decisions
- Implement the preparation enterprises to be the first person in charge, and improve the auditing of supply chains
- Clear responsibility, improve the process control and quality assurance level of pharmaceutical raw and auxiliary material manufacturers



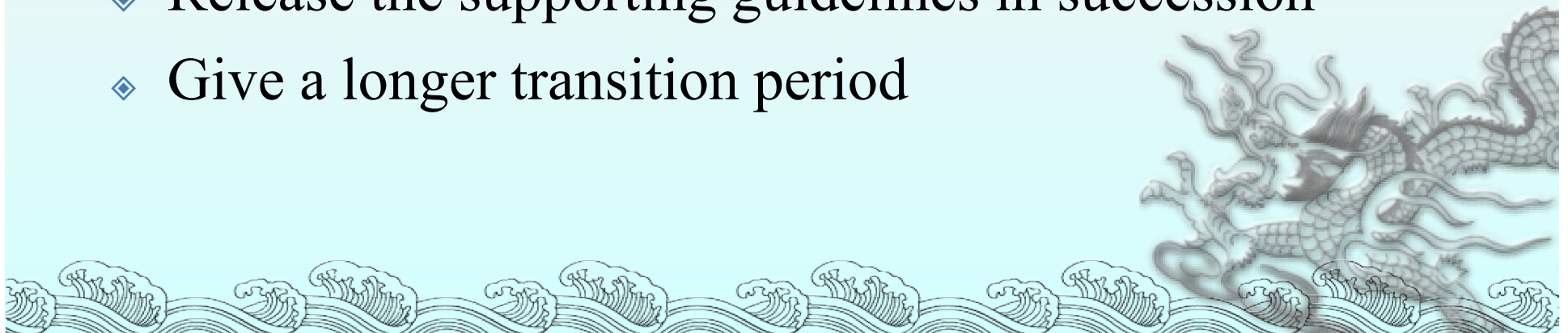
# Features of Chinese DMF System

- ◆ Chinese DMF mainly promotes the implementation of the first responsible person of drug manufacturers, which benefits the trace of supply chains, and the improvement of supervision and management efficacy and review efficacy
- ◆ The coexisting ways of implementation of registration and filing for some pharmaceutical raw and auxiliary materials of Chinese DMF
- ◆ Filing information system management of pharmaceutical raw and auxiliary materials; synchronous implementation of the application of electronic technical documents with CTD format
- ◆ Release the text and the filing application guidelines separately



# Progression of Chinese DMF

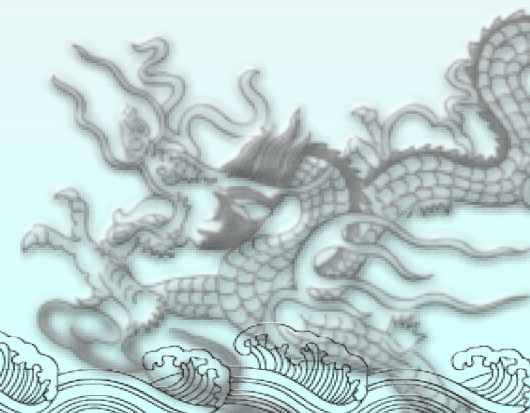
- ◆ “Notice of Suggestions on Filing Management Provisions for Pharmaceutical Raw and Auxiliary Materials (Draft for Comment)” (SFDA [2010] No. 183) begins to seek for views
- ◆ Text of management provisions to be released recently
- ◆ Release the supporting guidelines in succession
- ◆ Give a longer transition period





# Rules for Drug Standard Management

- ◆ Draft for Comment of “Measures for Drug Standard Management”
- ◆ 65 articles in 7 chapters in total
- ◆ Standardize the work responsibility and division, formulation and release, revision and abolishment, management and publication, implementation and supervision of pharmacopeia standards and registration standard management



# Study and Formulate the Policies for Promoting the Development of Traditional Chinese Ethnic Drugs

Study and formulate “Technical Guidelines for Natural Drug Research”

Study and draft the opinions on strengthening the management of the traditional Chinese ethnic drugs

Complete the related management work on the category protection of Chinese medicines



# Rules for Drug Research Supervision and Management and Serial Supporting Normative Documents

## 1. Formulate the Measures for Drug Research Supervision and Management

- Clarify the legal responsibilities of various participating parties in the clinical trials of drugs
- Strengthen the management of sponsor, study institutions and ethics committees on clinical trials
- Enhance the supervision and inspection of the drug supervision and management departments on the clinical trial institutions and processes of drugs

## 2. Explore the compulsory liability insurance and other relevant remedy systems, independent ethics committee systems and informed consent systems, strengthen the subject protection.

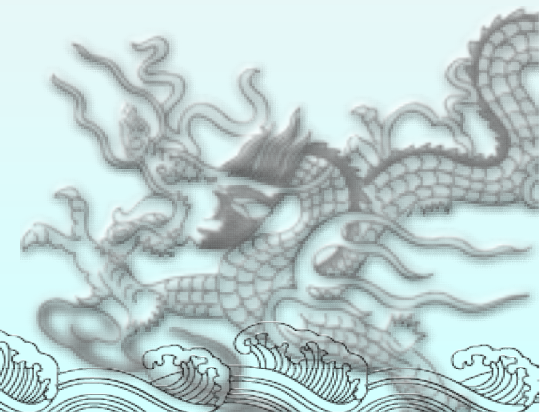
## 3. Formulate and issue the normative documents to guide the development of clinical trials of drugs

- Formulate the supervision and inspection guideline to guide the supervision



# GRP of China

- ◆ Organize the translation of FDA and EU's GRP
- ◆ Set a special GRP research group
- ◆ Preliminarily establish the basic principles of Chinese GRP: Principles of science, transparency, conformity, and efficacy
- ◆ Establish the basic framework of Chinese GRP: Good Registration Practice for Pharmaceuticals + Standard Operation Manuals for each department



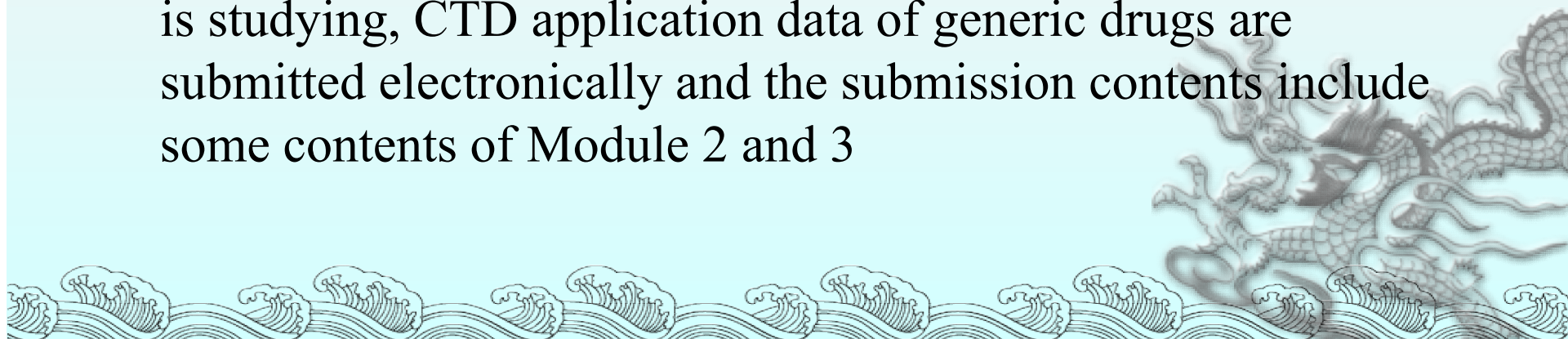
# Basic Information of Electronic Submission and Approval of Chinese Drug Registration

- \* On-going:

Electronic Instruction Label Submission System, will connect to the review system in the future, and realize the disclosure of the approved instruction label information

Electronic Drug Standard Submission and Approval System, in the future, the drug executive standard can be opened to the specific groups according to the different limits of authority

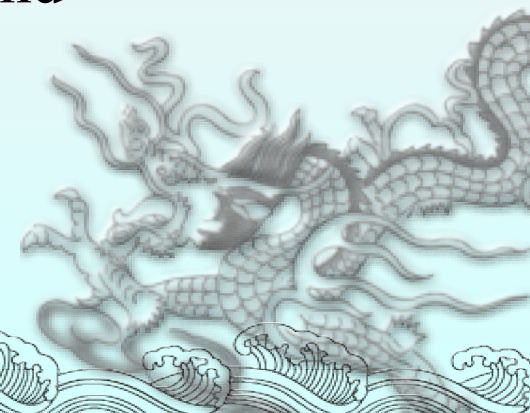
Electronic Submission of Application Data with CTD Format is studying, CTD application data of generic drugs are submitted electronically and the submission contents include some contents of Module 2 and 3





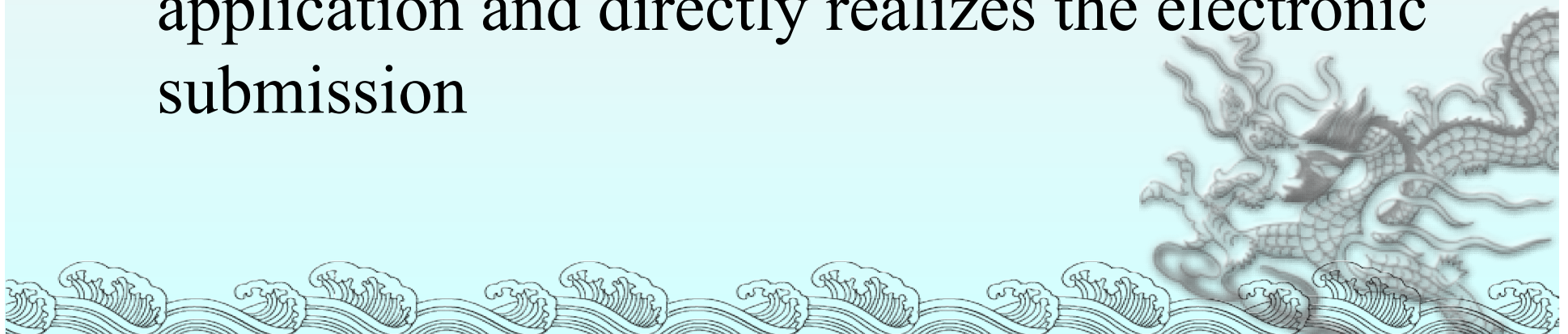
# Progression in Common Technical Documentation for Chinese Drug Registration

- ◆ On May 5<sup>th</sup> , 2010, “Letter of Opinions on Declared Data with CTD Format” was released (SFDA [2010]86)
- ◆ Propose the specific requirements for the CTD application data of generic drugs
- ◆ Including the requirements for application data with CTD format (Pharmacy part and Bioequivalence part)
- ◆ Summary of main study data (Pharmacy part and Bioequivalence part)



## Progression in Common Technical Documentation for Chinese Drug Registration

- ◆ The relevant work team starting to participate since July 2010 is responsible for translation and arrangement work of EU and FDA's guidelines on electronic submission
- ◆ The CTD format after seeking for suggestions is used firstly during the generic drug category application and directly realizes the electronic submission



# Significance of Promoting CTD Electronic Submission on Chinese Drug Registration

## Higher technical requirements

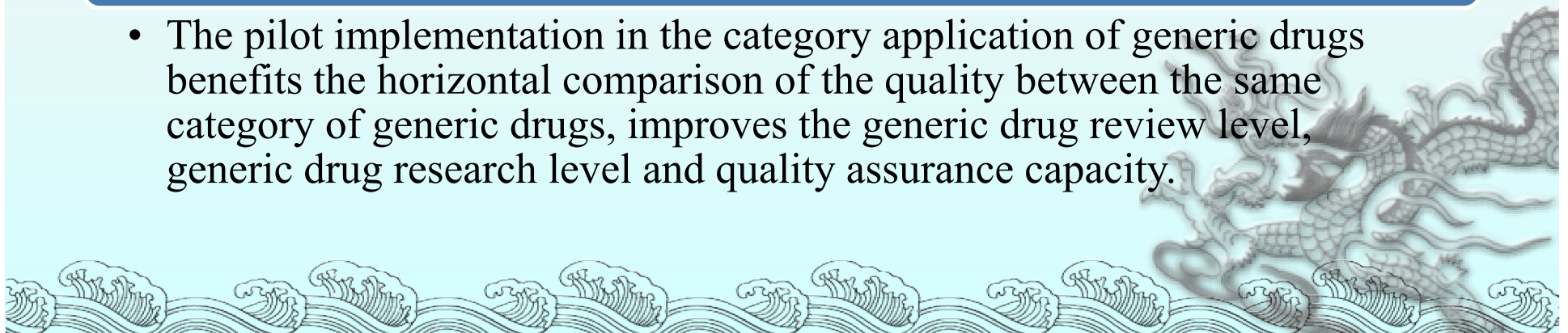
- --CTD is not only a simple requirement for document format, but also a higher technical requirement for study contents and level in general

## Higher review quality and efficacy

- The electronization of CTD application will greatly accelerate the electronic review work strength and resolve the conflict that the review strength mismatches the application strength

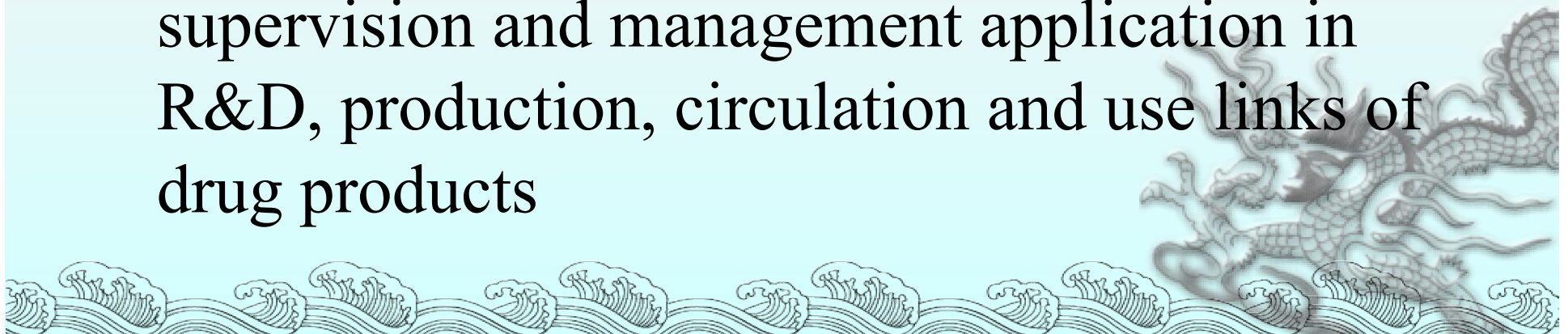
## Practice significance of generic drug review

- The pilot implementation in the category application of generic drugs benefits the horizontal comparison of the quality between the same category of generic drugs, improves the generic drug review level, generic drug research level and quality assurance capacity.



# Future Development Direction in China

- ◆ CTD submission and electronic submission of registration materials
- ◆ Electronization of all drug registration materials including CTD
- ◆ High-end application of electronic materials, including the full-field and multi-department supervision and management application in R&D, production, circulation and use links of drug products





# About Drug Registration Approval





# Analysis of Drug Registration Work Data

## Reception situation of drug registration

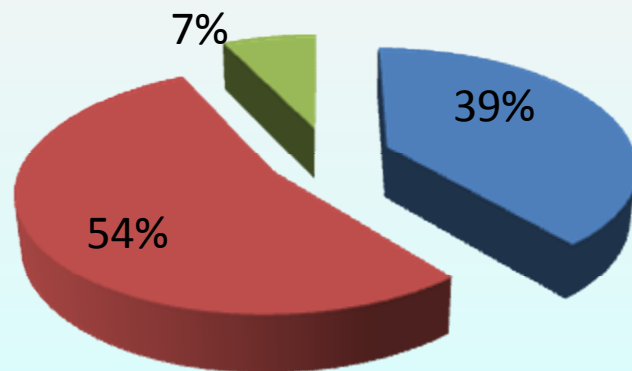
	Domestic application reception				Foreign application reception
	Chemical drug	Chinese medicine	Biologic	Supplemental application	
Quantity	1528	105	69	2433	599
Sum	4135			2433	599
Total	4734				

# Analysis of Drug Registration Work Data

## Reception situation of drug registration

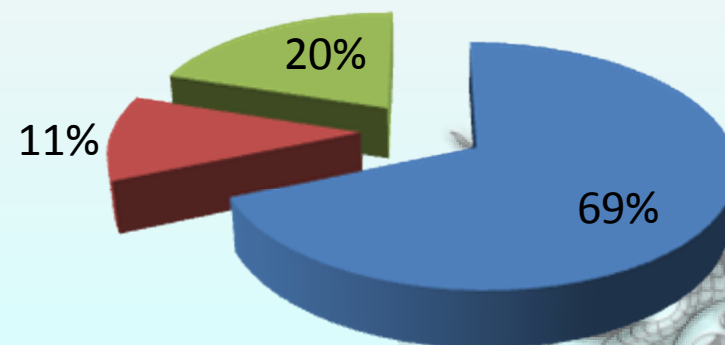
Reception amount of various chemical drugs

■ New drugs ■ Generic drugs ■ Changed drugs



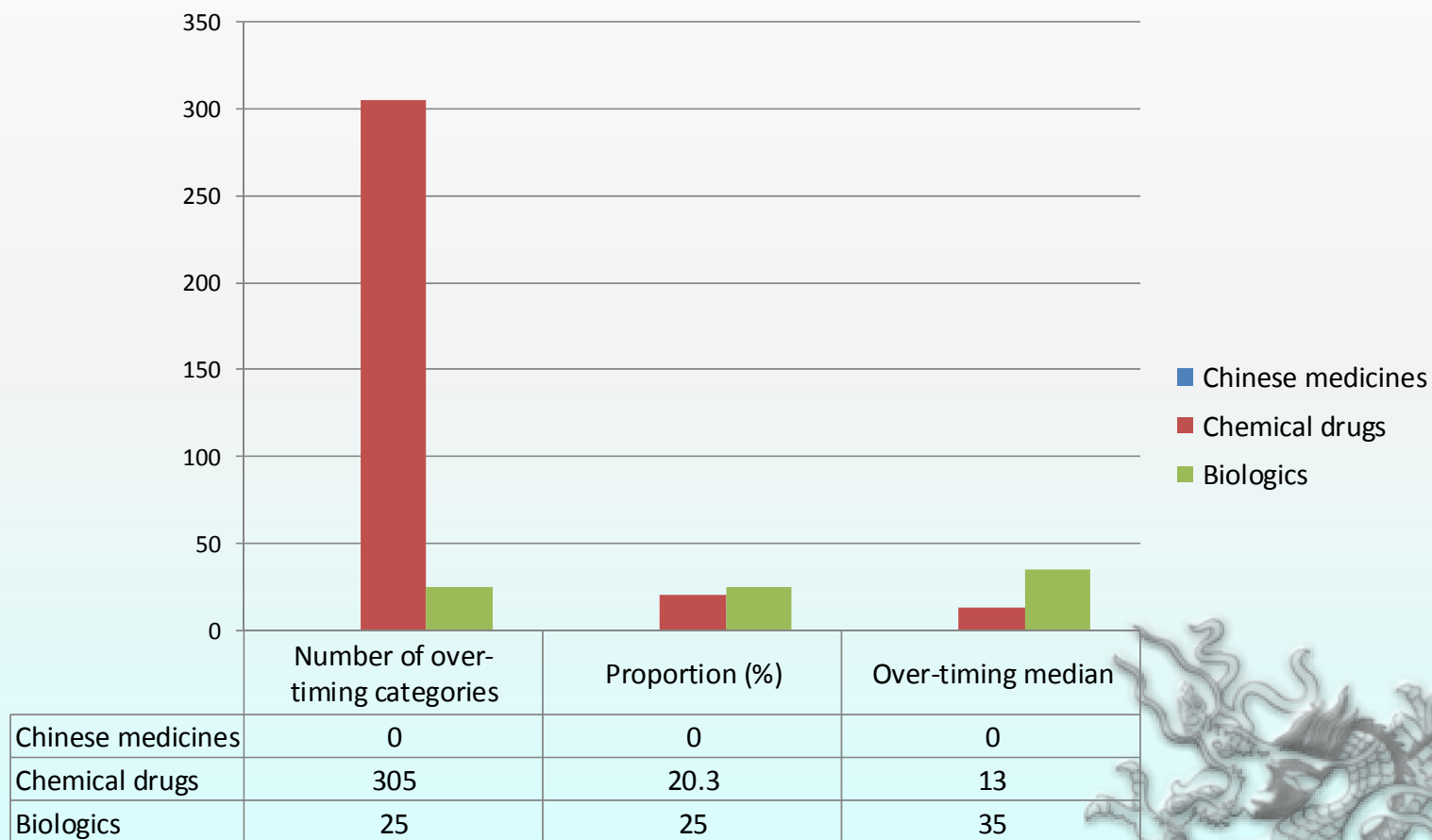
Registration reception of various Chinese medicines

■ New drugs ■ Generic drugs ■ Changed drugs



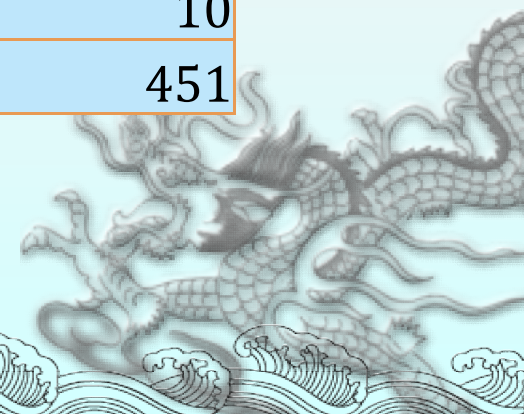
# Analysis of Drug Registration Work Data

Review Timing Analysis



# Analysis of Drug Registration Work Data

Data of Approved Drugs in 2010		
Category	Quantity (calculated by the reception number)	Number of involved drug categories
Chemical drugs	794	369
Chinese medicines	80	72
Biologics	12	10
Total	886	451



# Analysis of Drug Registration Work Data

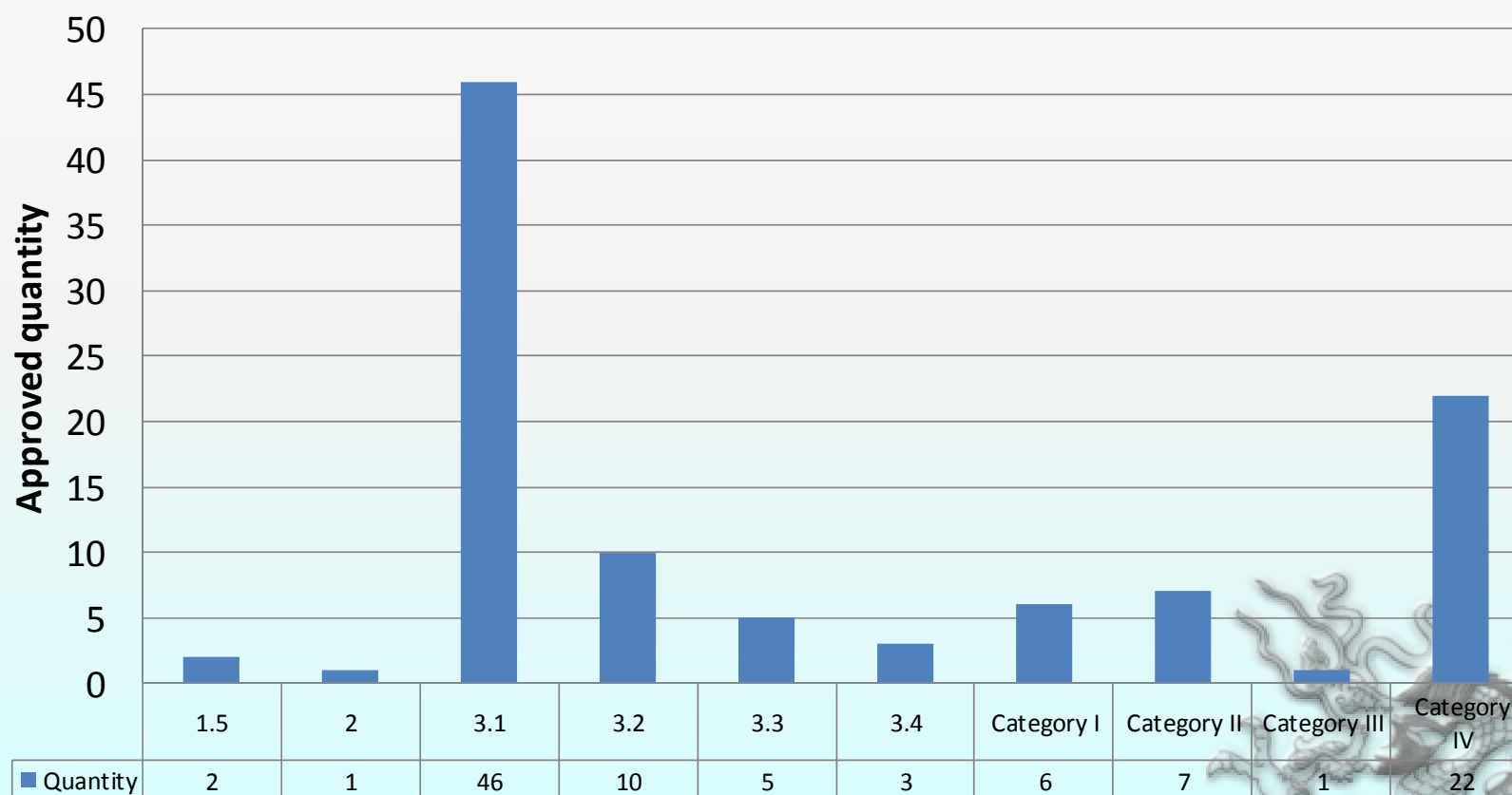
Data of Approved Drugs in 2010								
Chemical drugs			Chinese medicines			Biologics		
New drug	Form-changed drug	Generic drug	New drug	Form-changed drug	Generic drug	New drug	Form-changed drug	Generic drug
103	51	640	12	59	9	9	1	2
794			80			12		
886								

Data of Approved Drugs in 2010								
Chemical drugs			Chinese medicines			Biologics		
New drug	Form-changed drug	Generic drug	New drug	Form-changed drug	Generic drug	New drug	Form-changed drug	Generic drug
103	51	640	12	59	9	9	1	2
794			80			12		
886								



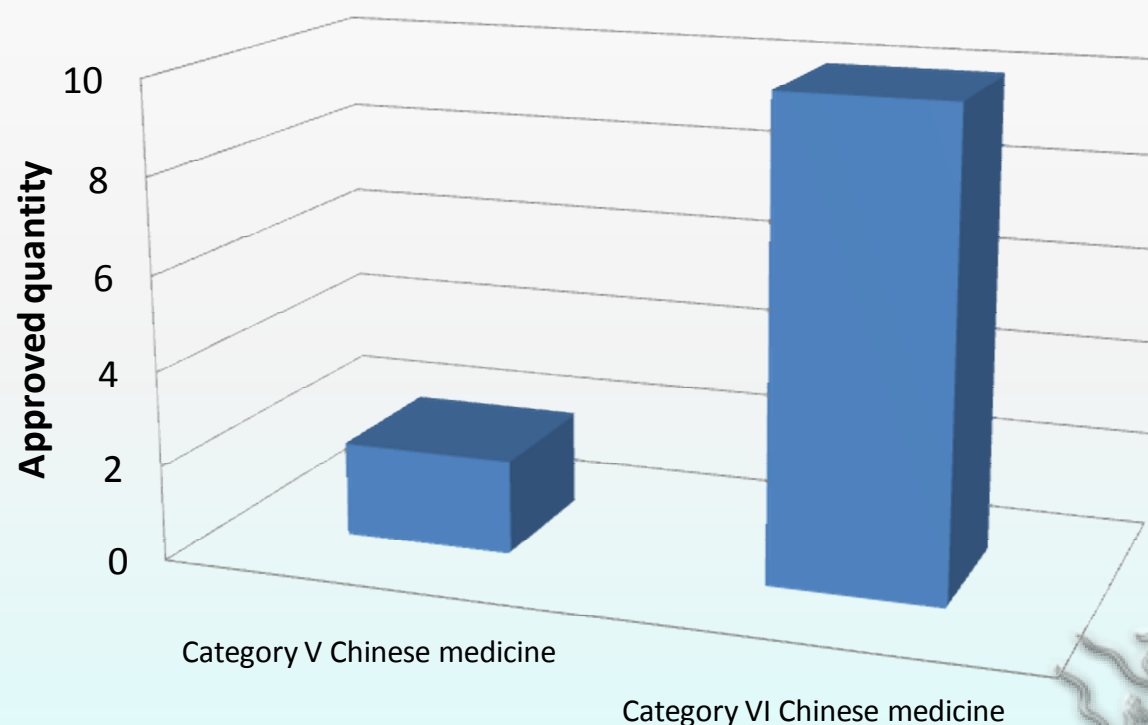
# Analysis of Drug Registration Work Data

Comparison of Approved Quantity between Different Registered Categories of Chemical Drugs in 2010



# Analysis of Drug Registration Work Data

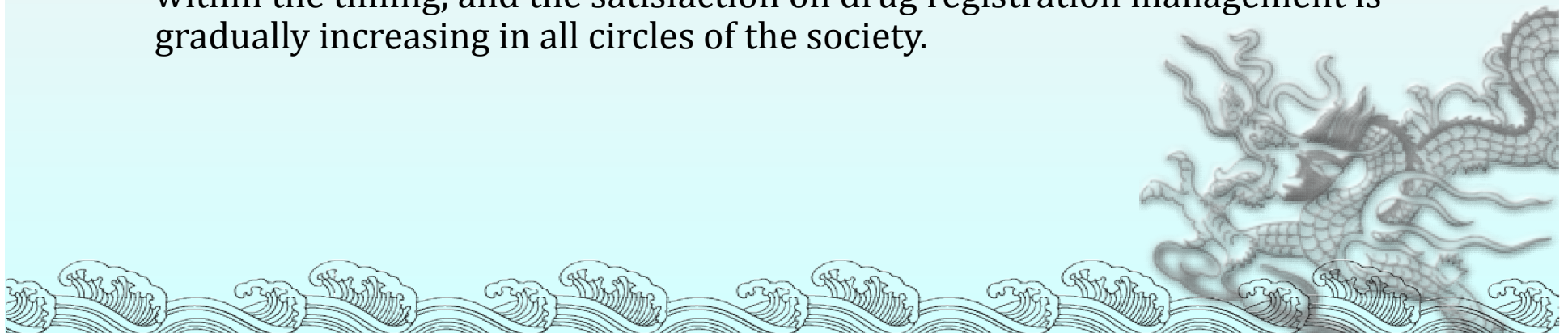
Comparison of Approved Quantity between Different Registered Categories of Chinese Medicines in 2010



	Category V Chinese medicine	Category VI Chinese medicine
Quantity	2	10

# Data Change——Analysis on Overall Tendency of Drug Registration Work

- ◆ The increasing proportion of new drug application suggests the legislation idea of encouraging innovation and promoting generic drugs is practiced
- ◆ By continuously completing the drug review and approval systems, enhancing the site inspection of drug registration and strictly implementing the drug review and approval standards, the falsification phenomenon has been restricted effectively, which purifies the drug registration environment to a certain degree.
- ◆ The number and structure of drug registration applications gradually return back to the normal state, the review and approval are basically completed within the timing, and the satisfaction on drug registration management is gradually increasing in all circles of the society.



# Approval Situation of Clinical Trials

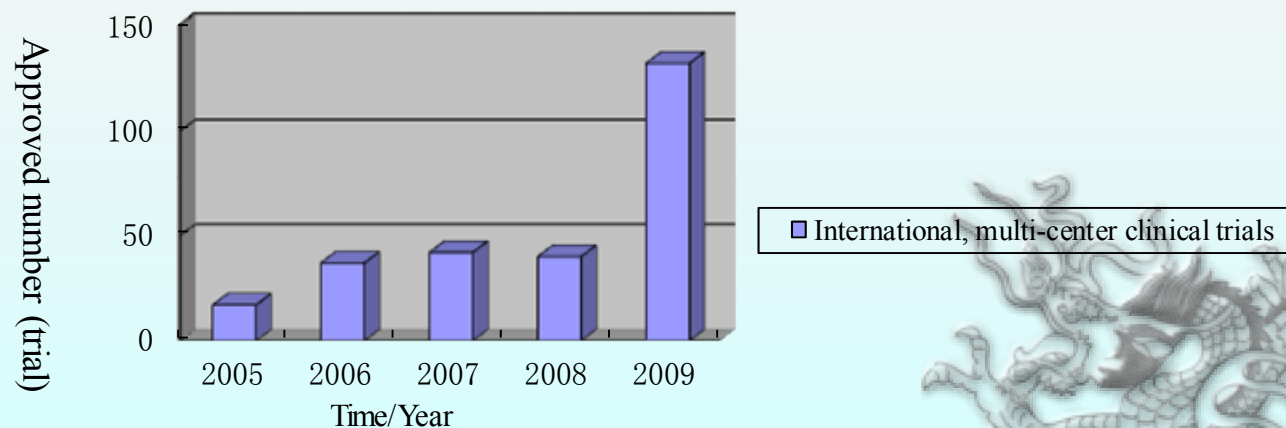
The summary of drugs approved to enter the clinical study in 2009 is shown in the table below:

Registration category	Domestic application			Foreign application
	Chemical drug	Chinese medicine	Biologic	
Reception No.	658 (20 of class1.1)	101	26	320 (132 international multi-center clinical study)
Compound or prescription	267	91	/	171
Total (Reception No.)	1105			

# About International, Multi-center Clinical Trials

- The participation degree of China in the synchronic research of global new drug research and development is increasing year by year.
- In 320 clinical trials from foreign applicants that was approved in 2009, 132 are the international, multi-center clinical trials, significantly increasing compared with the last years. The approval summary of the application for international, multi-center clinical trials in the past 5 years is seen in Fig. 1

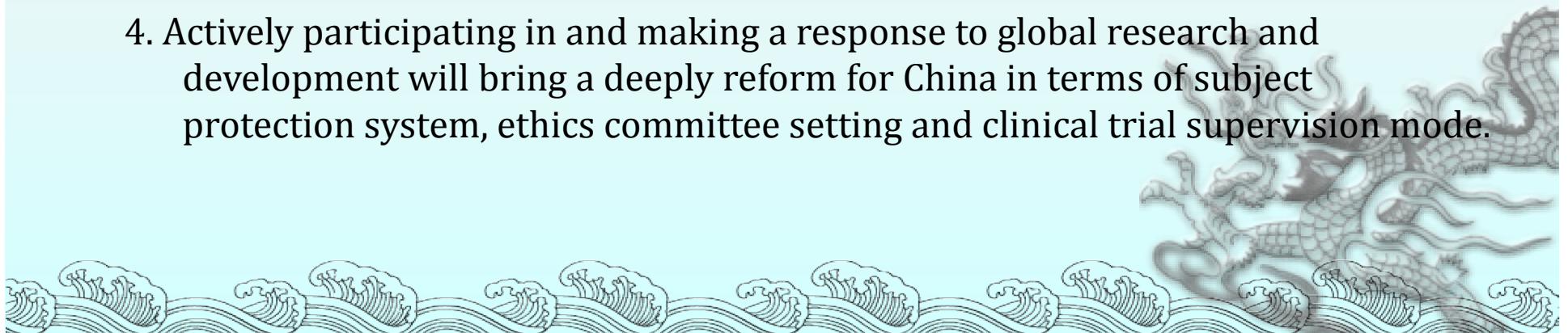
Fig. 1 Number of International, Multi-center Clinical Trials Approved during 2005-2009





# Application and Review of International, Multi-center Clinical Trials in China

1. As there is rapid social and economic development in China, the distribution of disease types is wide, the clinical resources are rich, and the R&D costs are relatively cheap, China becomes one of optional important countries for global research and development.
2. China is continuously completing and improving the construction of legal system, approval system and supervision capacity with the objective of gradually catching up the international standards and specifications and the mutual coordination.
3. Facing the main tendency of globally synchronic research and development, China shall be brave to handle the challenges, grasp the opportunities, further optimize the allocation of review resources, and further improve the review capacity, quality and efficacy.
4. Actively participating in and making a response to global research and development will bring a deeply reform for China in terms of subject protection system, ethics committee setting and clinical trial supervision mode.



# Progression of Drug Registration Management System Mechanism Reform



# Reform of Review and Approval Systems Mechanism

Several considerations on accelerating the reform promotion of drug review and approval systems

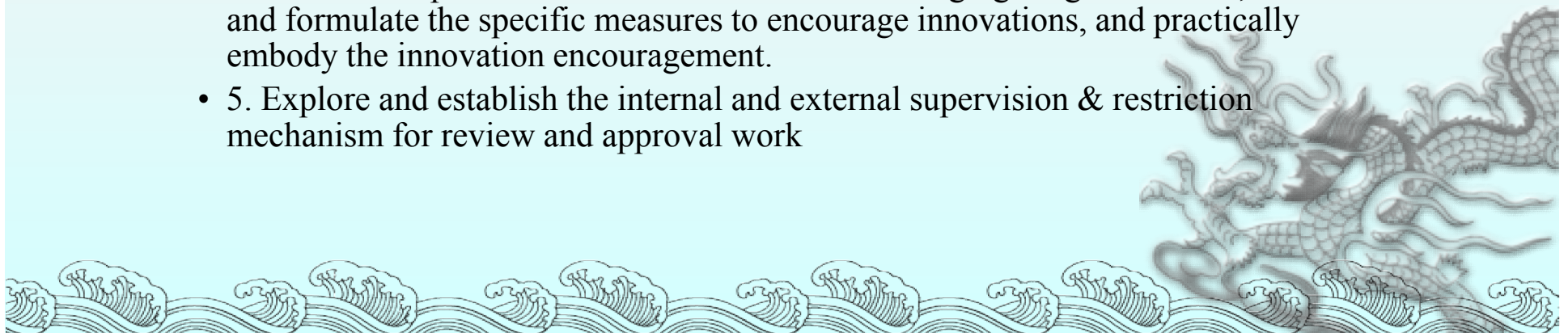
- Targeting to reduce the unnecessary procedures and improve the efficacy, actively explore the scientific division of technical review and administrative approval rights
- Targeting to enhance the risk management and control and improve the predictability of review and approval processes, actively explore the reform of clinical review and production review management modes and the adjustment of the management strategies
- Targeting to establish an uniform, efficient, coordinated and flexible review and approval systems, further optimize the allocation of drug registration review and approval resources (central and local, inside SFDA, management of experts)
- Enhance the running investigation of drug registration system, and timely find out the indicated issues and the difficulties during the implementation of regulations and policies to make an active response and resolve as early as possible



# Reform of Review and Approval Systems Mechanism

## Several works to optimize the drug review and approval mechanisms

- 1. Explore and establish the drug registration work quality & efficacy assessment mechanism and the administrative performance assessment mechanism
- 2. Accelerate and promote the formulation and implementation of Good Registration Practice for Pharmaceuticals and Good Review Practice for Pharmaceuticals (GRP), and the draft of Chinese GRP has been made primarily
- 3. Explore and establish the drug registration management expert consultation committee
- 4. Further complete the work mechanism of encouraging drug innovation, research and formulate the specific measures to encourage innovations, and practically embody the innovation encouragement.
- 5. Explore and establish the internal and external supervision & restriction mechanism for review and approval work

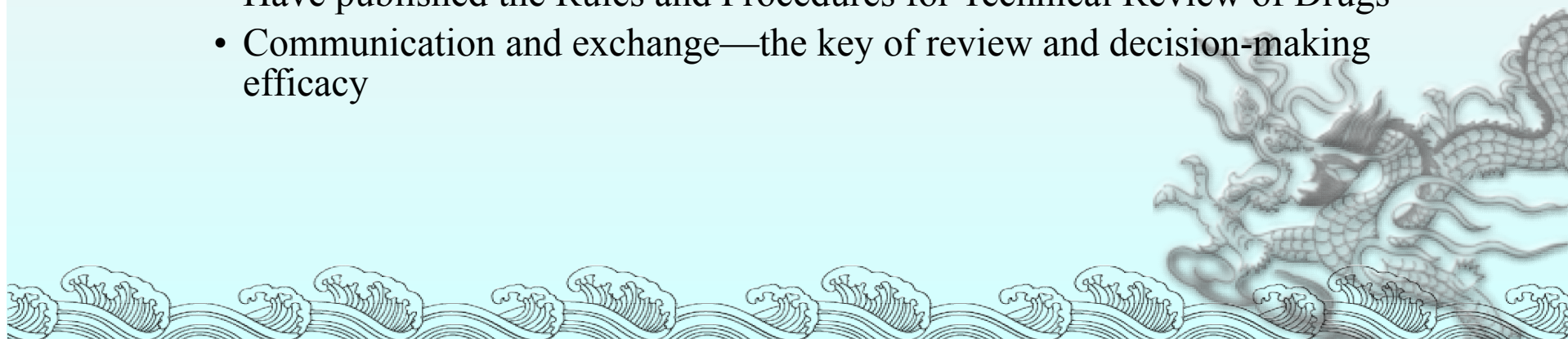




# Reform of Review and Approval Systems Mechanism

## Institutional reform of drug review and evaluation centers

- Conduct surrounding the work mechanism, review quality and review efficacy
- Establish the review correction, academic supervision and quality evaluation mechanisms
- Occupational and professional review duty system
- Have published the Rules and Procedures for Technical Review of Drugs
- Communication and exchange—the key of review and decision-making efficacy





# Institutional reform of CDE



# Progression of Drug Research Supervision and Management



- ◆ Establishment of the research supervision and management legal system
- ◆ Establishment of the research supervision, management and inspection system
- ◆ About the primary practice of electronic supervision and management



# Establishment of the Research Supervision and Management Legal System

## Formulate the Measures for Drug Research Supervision and Management

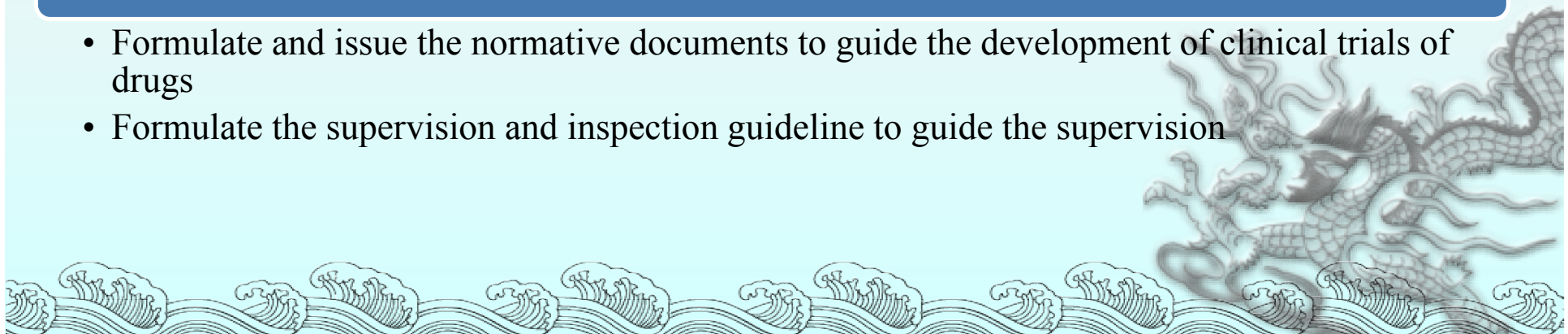
- Clarify the legal responsibilities of various participating parties in the clinical trials of drugs
- Strengthen the management of sponsor, study institutions and ethics committees on clinical trials
- Enhance the supervision and inspection of the drug supervision and management departments on the clinical trial institutions and processes of drugs

## Strengthen the subject protection

- Explore the compulsory liability insurance and other relevant remedy systems, independent ethics committee systems and informed consent systems

## Standardize and enhance the supervision and inspection

- Formulate and issue the normative documents to guide the development of clinical trials of drugs
- Formulate the supervision and inspection guideline to guide the supervision



# Establishment of the Research Supervision, Management and Inspection System

## Establish an inspector team within the drug supervision and management system

- Complete the selection, assignment, evaluation and management of inspectors and complete the management of the expert team

## Site inspection work mechanism and clinical trial supervision & inspection

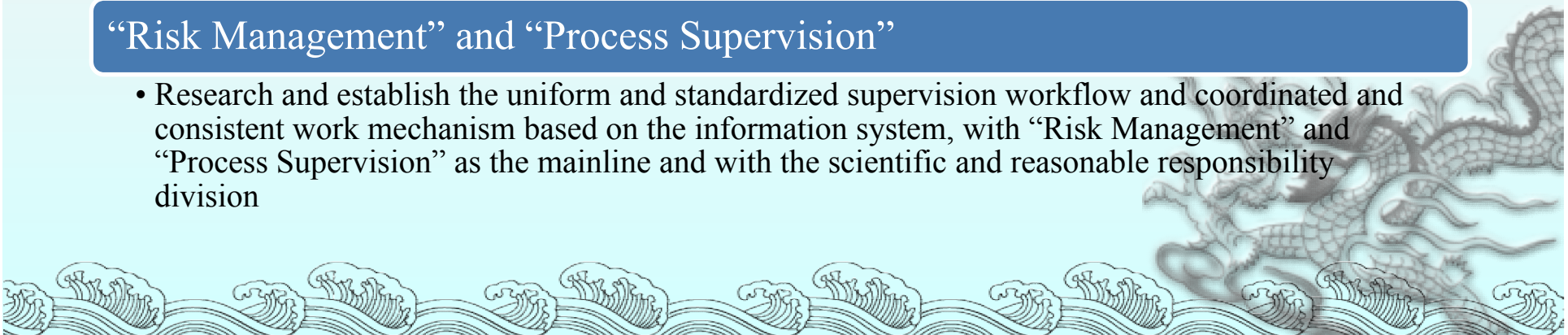
- Research and establish the scientific clinical trial registration site inspection work mechanism and clinical trial supervision & inspection system with technical review as the core and site inspection as the support

## Supervision and inspection requirements and standards

- Detail and complete the supervision and inspection requirements and standards for clinical trials, standardize the site inspection of clinical trials, and enhance the guidance for organization, implementation and management of clinical trial site inspections in various provinces.

## “Risk Management” and “Process Supervision”

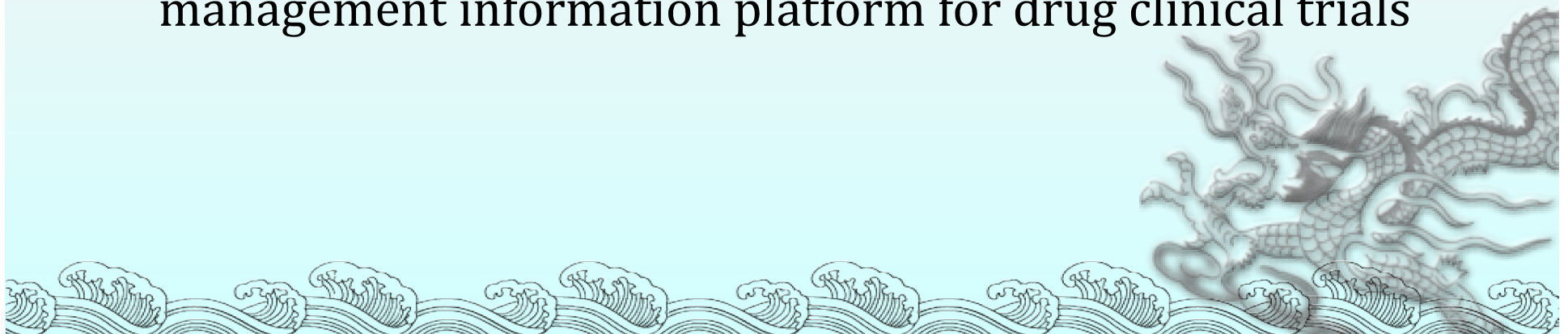
- Research and establish the uniform and standardized supervision workflow and coordinated and consistent work mechanism based on the information system, with “Risk Management” and “Process Supervision” as the mainline and with the scientific and reasonable responsibility division





# About the Primary Practice of Electronic Supervision and Management

- ◆ The electronic supervision and management has been realized primarily in Tianjin, and the primary experience has been accumulated.
- ◆ Formulate and publish the uniform information construction data standards and management specifications
- ◆ Objective: To establish a national, uniform supervision and management information platform for drug clinical trials



# Thinking of the “12th Five-year Plan” for Drug Registration Management



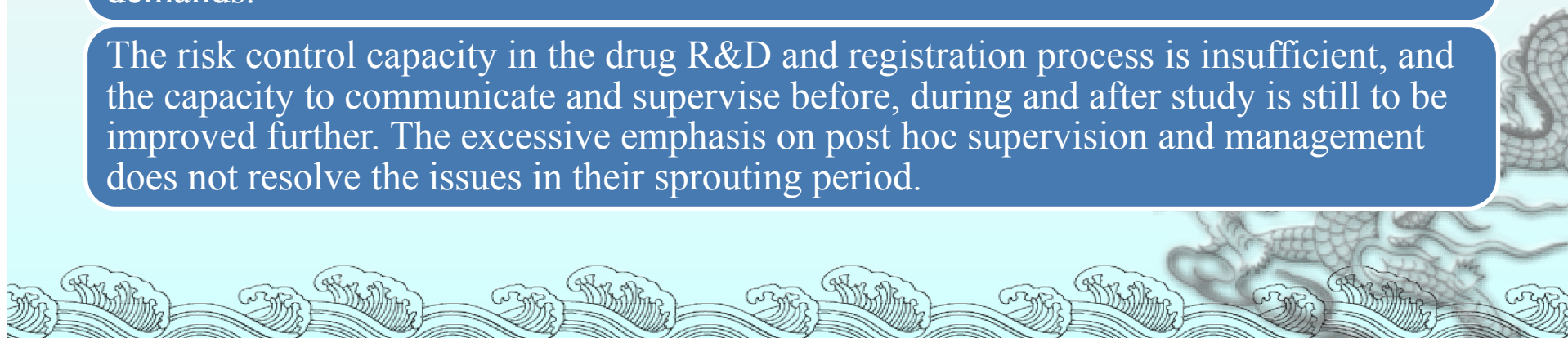
# Issues and Challenges of Drug Registration Management

The system institution and legislation construction of drug registration management can not be fully adaptable to the demand of the new drug innovative production and industrial development changes in China

The relevant management regulations in the drug R&D field (especially the clinical trial link) are still to be completed, and the complete system still needs to be constructed for technical guidance principles.

The whole-process supervision and inspection system of drug registration is not complete, and there is lack of professional and full-time inspection teams, shortage of administrative resources while continuous increase of supervision and management demands.

The risk control capacity in the drug R&D and registration process is insufficient, and the capacity to communicate and supervise before, during and after study is still to be improved further. The excessive emphasis on post hoc supervision and management does not resolve the issues in their sprouting period.



# Specific Issues Faced by Drug Registration Management

Process of drug registration

Study

Submit

Review and  
Approval

Supervision

1. The relevant management regulations are still to be completed, and the complete system still needs to be constructed for technical guidance principles.
2. The supervision and inspection system is not complete.
3. The excessive emphasis on post hoc supervision and management does not resolve the issues in their sprouting period.

1. The current materials submission requirements can not meet the review requirements increasingly.
2. Lack of electronic submission specifications and systems.
3. Lack of the channels to communicate with the applicants before submission and the process control

1. Lack of GRP
2. Lack of knowledge management systems required by review
3. The electronic review system is still to be improved further
4. Lack of investigation on the standardization of application data
5. Lack of the third party's validation, re-validation from validity to science
6. The review and approval capacities for innovative drugs still need to be further improved.

1. The supervision and inspection mechanism is not flexible, and fails to combine the construction of the integrity mechanism.
2. The post hoc supervision and management is emphasized too much and there is no advanced communication and process control capacity.

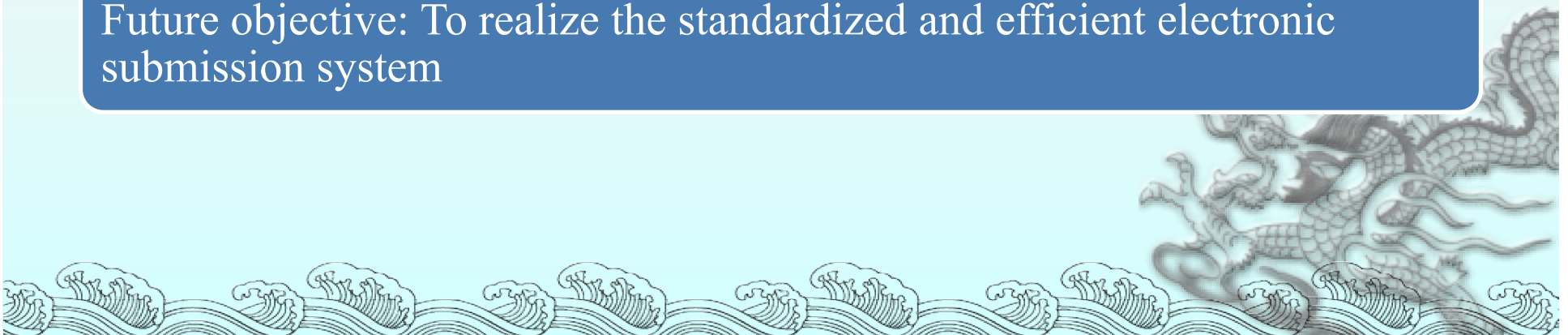


# Strategies and Thinking

## Registration submission links

- With the common technical documentation (CTD) of drug registration as the starting point, pay importance to the introduction of international specifications for application materials, improve the science of application materials and promote the increase of the research level.
- Actively explore the electronic submission of CTD application materials, pay importance to the science of materials and improve the submission efficacy, and introduce the energy-saving and environment-friendly work modes at the same time.
- Establish the whole-process (beforehand, in-process and post hoc) communication mechanism for supervisors and applicants, and assist with the corresponding supervision and management process control measures, so as to resolve the issues in their sprouting period.

Future objective: To realize the standardized and efficient electronic submission system



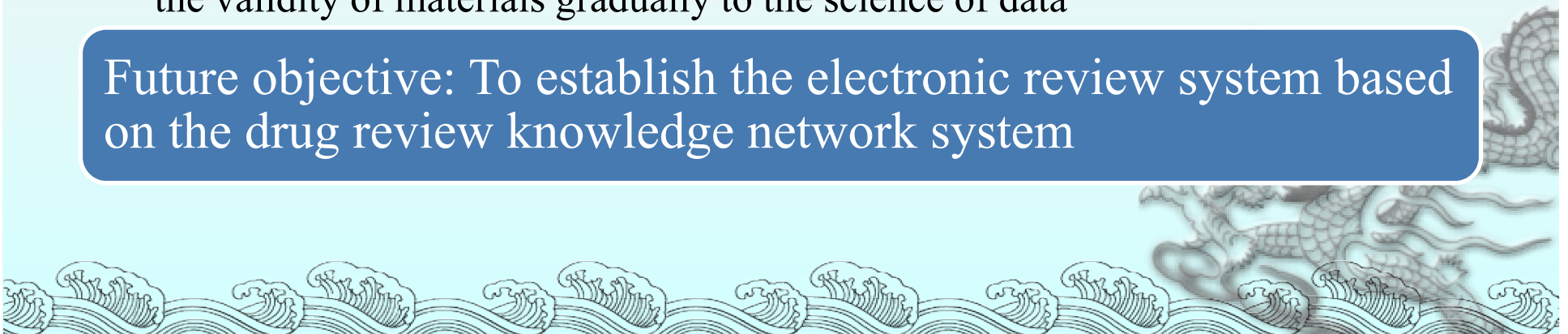


# Strategies and Thinking

## Review and approval links

- Improve the standardization investigation of application data by combining the promotion of CTD application format
- Promote the formulation and implementation of Good Registration Practice for Pharmaceuticals and Good Review Practice for Pharmaceuticals (GRP)
- Gradually establish the knowledge management system required by high-efficient review while completing the electronic review system
- Further enhance the third party validation methods, validation from improving the validity of materials gradually to the science of data

Future objective: To establish the electronic review system based on the drug review knowledge network system



# Strategies and Thinking

## Supervision and management links

- Establish the regulations: Formulate the Measures for Drug Research Supervision and Management and its relevant supporting regulations.
- Establish the systems: Research and establish the scientific registration management systems with technical review as the key and audit, inspection, testing and verification as the support.
- Establish the teams: Establish the internationalized, professional and full-time inspector teams.
- Establish the mechanisms: Establish the uniformed, coordinated, flexible, and efficient dynamic audit & inspection mechanisms, and focus on the combination of the audit and inspection with the honesty system.
- Establish the institution: Research, explore and establish the grading and classification management institutions for drug R&D units, drug clinical trial institutions, contracted study organizations, drug registration applicants and their registration commissioners.
- Establish the platforms: Establish the drug research supervision and management information platforms.

Future objective: To establish the scientific, complete electronic registration supervision and management systems

# International Exchange and Cooperation



# International Exchange and Cooperation

## Sino-US

- FDA exchange
- Generic Drug Forum
- Conference under JCCT framework
- BIO Chinese Annual Meeting

## Sino-Japan and Korea

- Seoul Conference

## Sino-Japan



# International Exchange and Cooperation

## ICH

- APEC
- ICH Chinese Study Team

## WHO Vaccine Pre-authentication

- Vaccine pre-authentication
- System authentication

## IRCH FHH





# About the Work of ICH Chinese Study Team

- ◆ Formulated work specifications
- ◆ Regular work meetings
- ◆ Positive advancements:

Publication of the translated version of ICH guidelines

Expanded study team members

Completed logo design of ICH Chinese Study Team

Established research achievement online disc

2010 Annual Report



