Considerations on Ethnic Difference in Clinical Review

Dr. ZhiMin YANG

Center for Drug Evaluation,
State Food & Drug Administration

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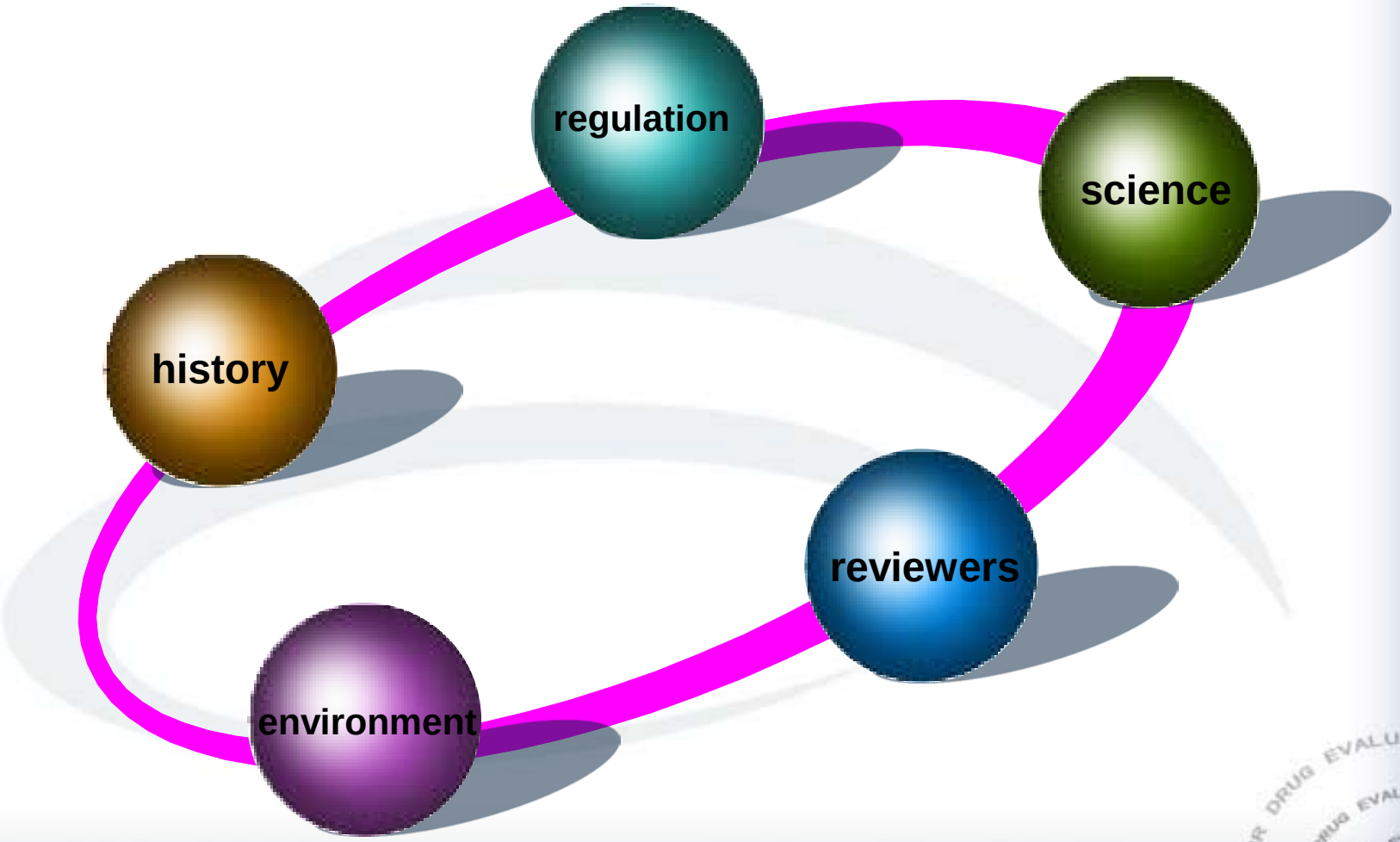
- Background
- Registration applications from Japanese Enterprises
- Considerations on ethnic difference in clinical review
- Challenges
- Our viewpoint


regulation
science
history
reviewers
environment

Considerations on ethnic difference in clinical review

- Regulatory viewpoint
- Scientific viewpoint

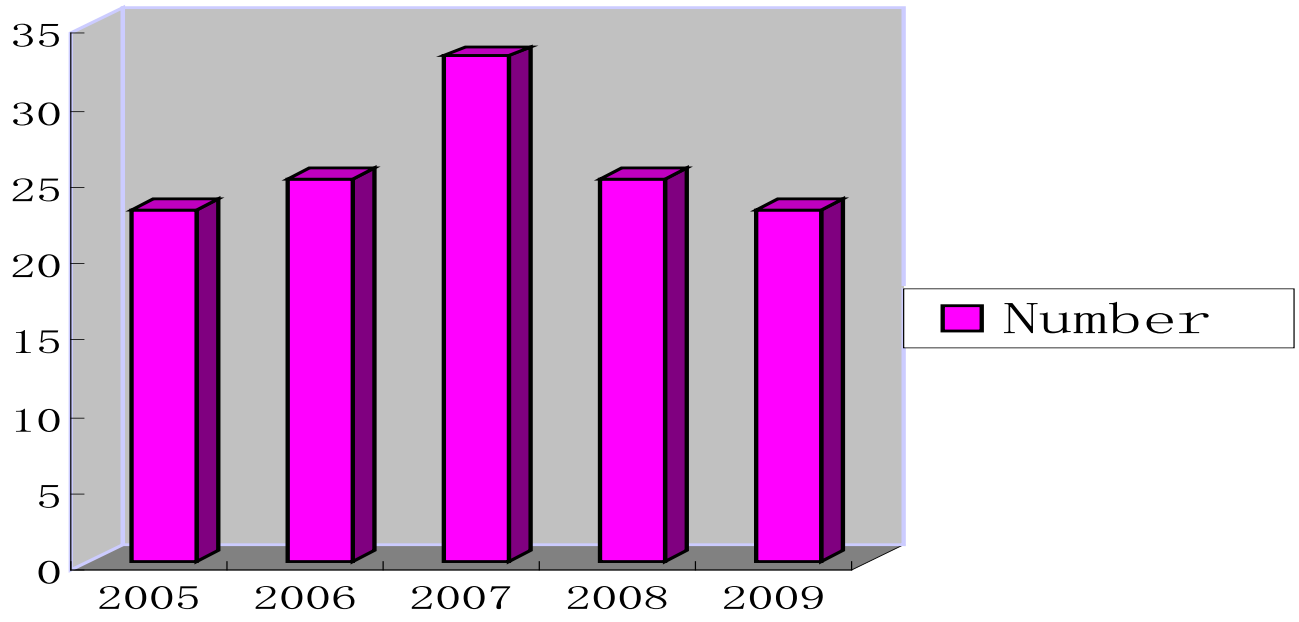
Background

Evolving process to understand the ethnic difference in Japan

Time	1980's	1990	1998	Now
Background	Cautious to join global simultaneous development	Co-sponsored ICH	E5 Promulgated	
Technical requirement	Must repeat clinical trial in Japan	Pay attention on ethnic difference	Actively join global development, in particular early phase study Expect China's participation in late phase study to accelerate the development Constitute International Affairs, Establish IND pathway	
Implication	Lengthy lag of new drug approval		Issues need to be addressed: 1) 科学管理; 2) mutual recognition on clinical data	

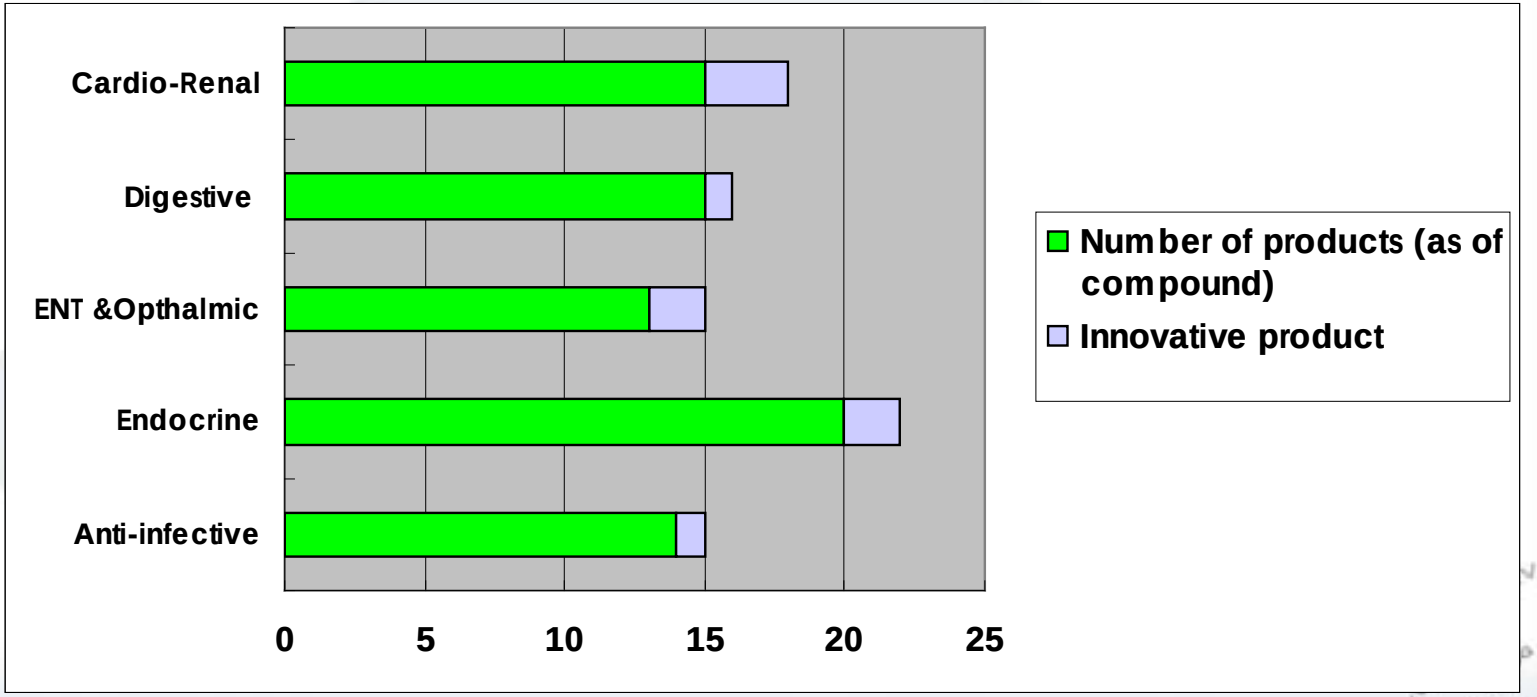
Registration applications from Japanese Enterprises

- **By number of products (as of compound)**



Registration applications from Japanese enterprises

- **By indication**



Registration applications from Japanese Enterprises

- **Products & Applicants**

Product：　129 compound

Applicants:　more than 50

Average：　2.58 product per applicant

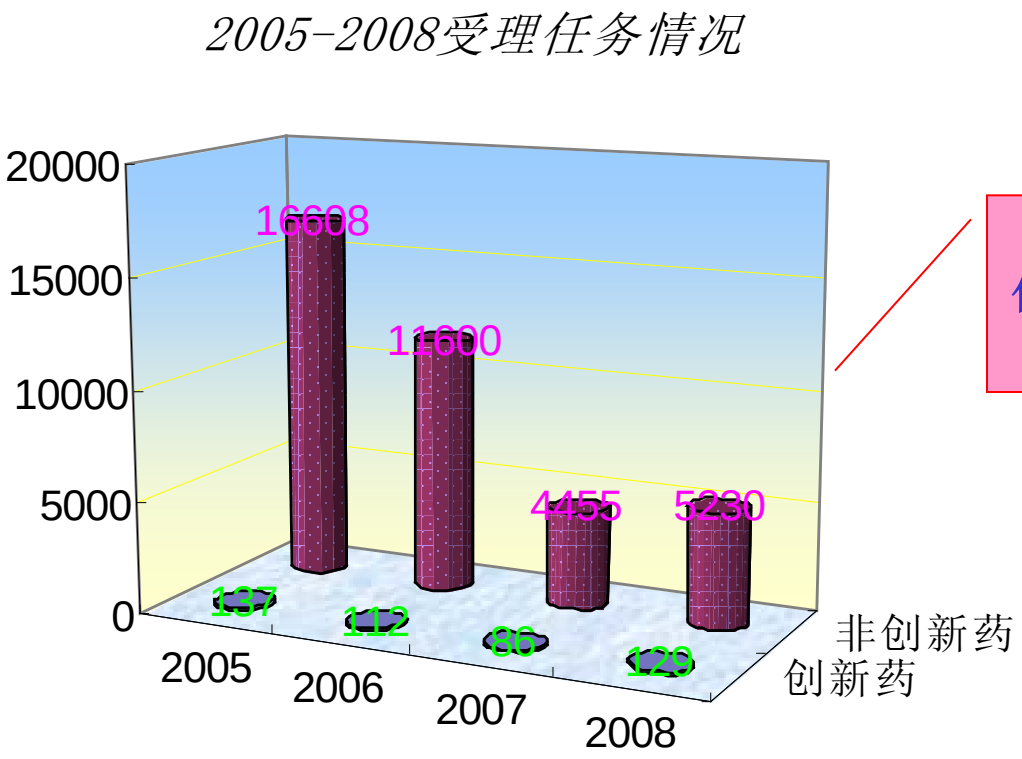
Amendment on Drug Registration Regulation

Time	1985	1998	2002	2005	2007
Law, Rules	Drug Administrative Law & its implementing rule		Drug Administrative Law & its implementing rule		
DRR*	1st edition	2nd edition	3rd edition	4th edition	5th edition
Background	Central government / provincial	SFDA	Join WTO	Administrative Licensing Law	Innovation
Norms		GCP	GLP	GMP	
Guidance			Gradually established		

open

*DRR: drug registration regulation

Registration applications from Chinese enterprises (2005-2008)



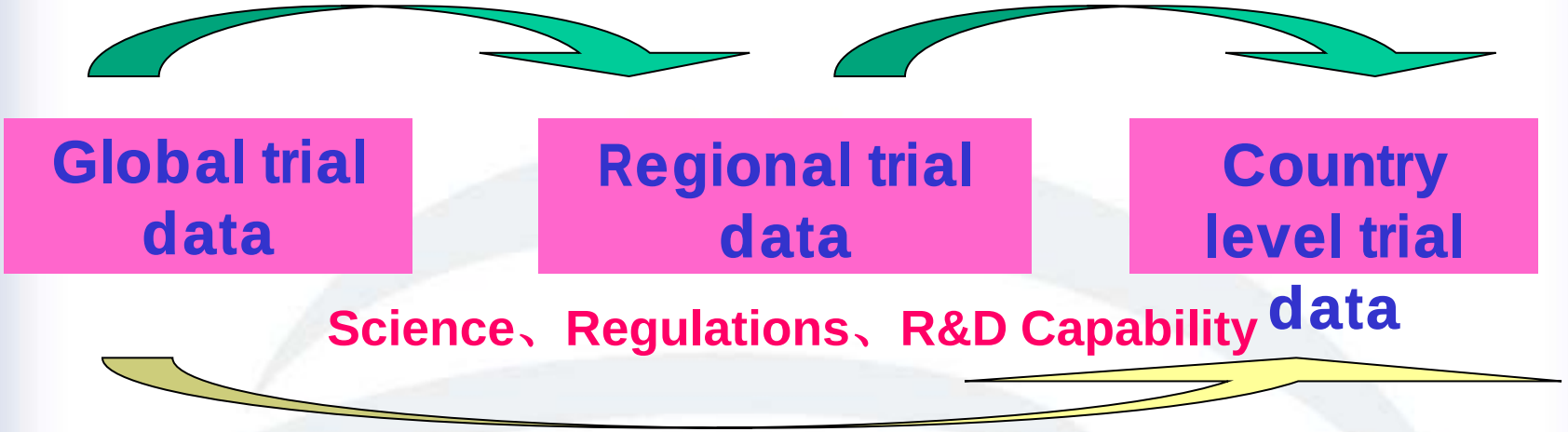
The basis of Japan-China exchanges

- ✓ It is gradually developing in a stable condition
- ✓ It still has some gaps comparing to multinational companies from Europe & US
- ✓ Hope a breakthrough in drug innovation & development
- ✓ Find out more chance of communication & cooperation, and internationalization
- ✓ Improve efficiency of R & D and save resource

Considerations on ethnic difference in clinical review

- Regulatory viewpoint
- Scientific viewpoint

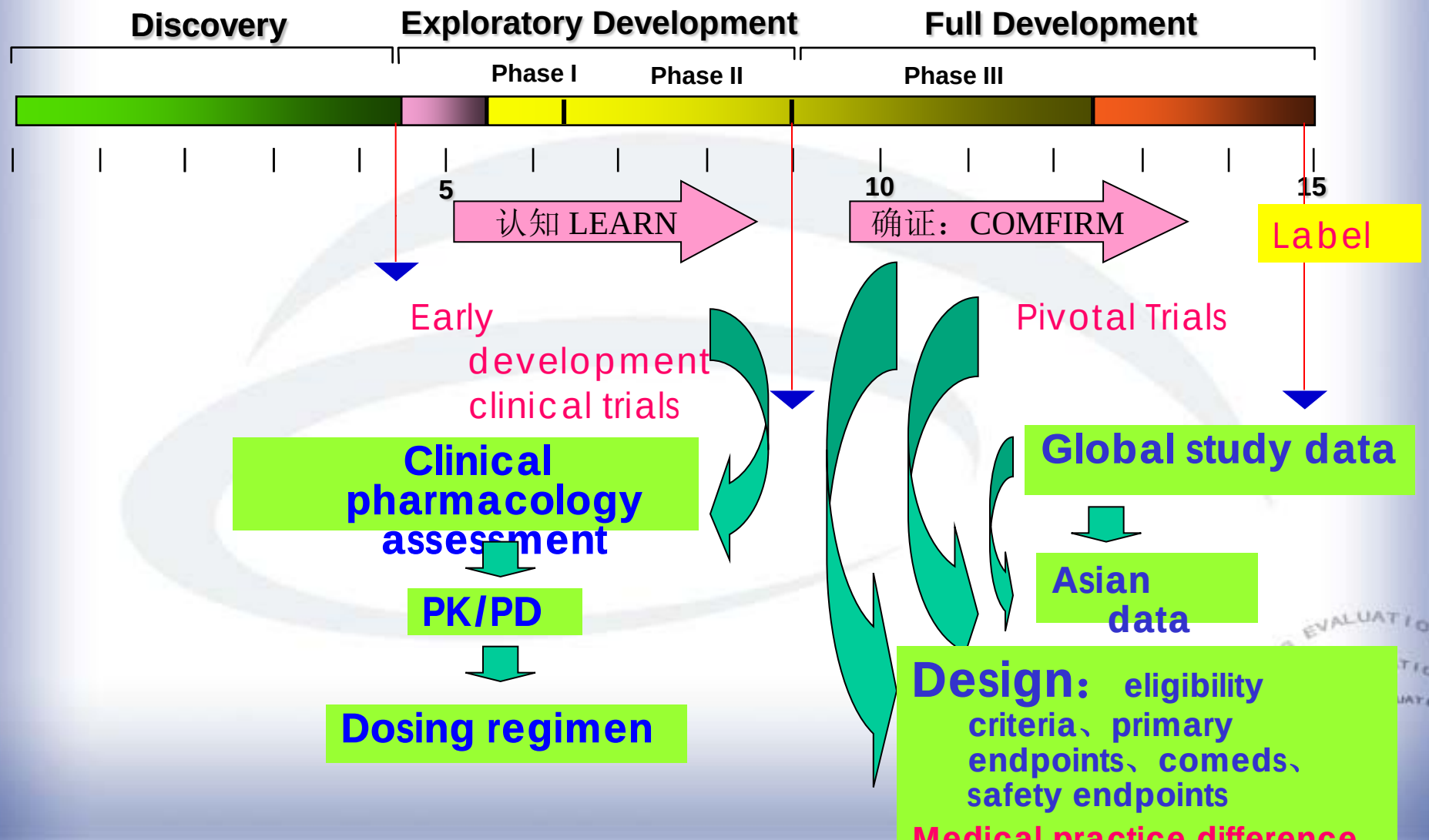
Evaluation of Foreign Trial Data



Core of Evaluation：

---- Does the drug's safety and efficacy profile provide adequate risk/benefit to the treated patient population?

Evaluation of Foreign Trial Data (Cont'd)



Evaluation of Foreign Trial Data (Cont'd)

- Global trial data
- Asian data
- Clinical pharmacology difference
- Medical practice difference, when compared to China

Evaluation of Foreign Trial Data (Cont'd)

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Result of global study

- ✓ Early launched to market
- ✓ Mainly based on clinical observation
- ✓ Lack of standardized & systematic clinical data
- ✓ Indication is very broad
- ✓ The dosage is different with that approved by Europe & US

? **Accurate indication, appropriate dosage, safety and efficacy data**

For example： Anti-allergic drug

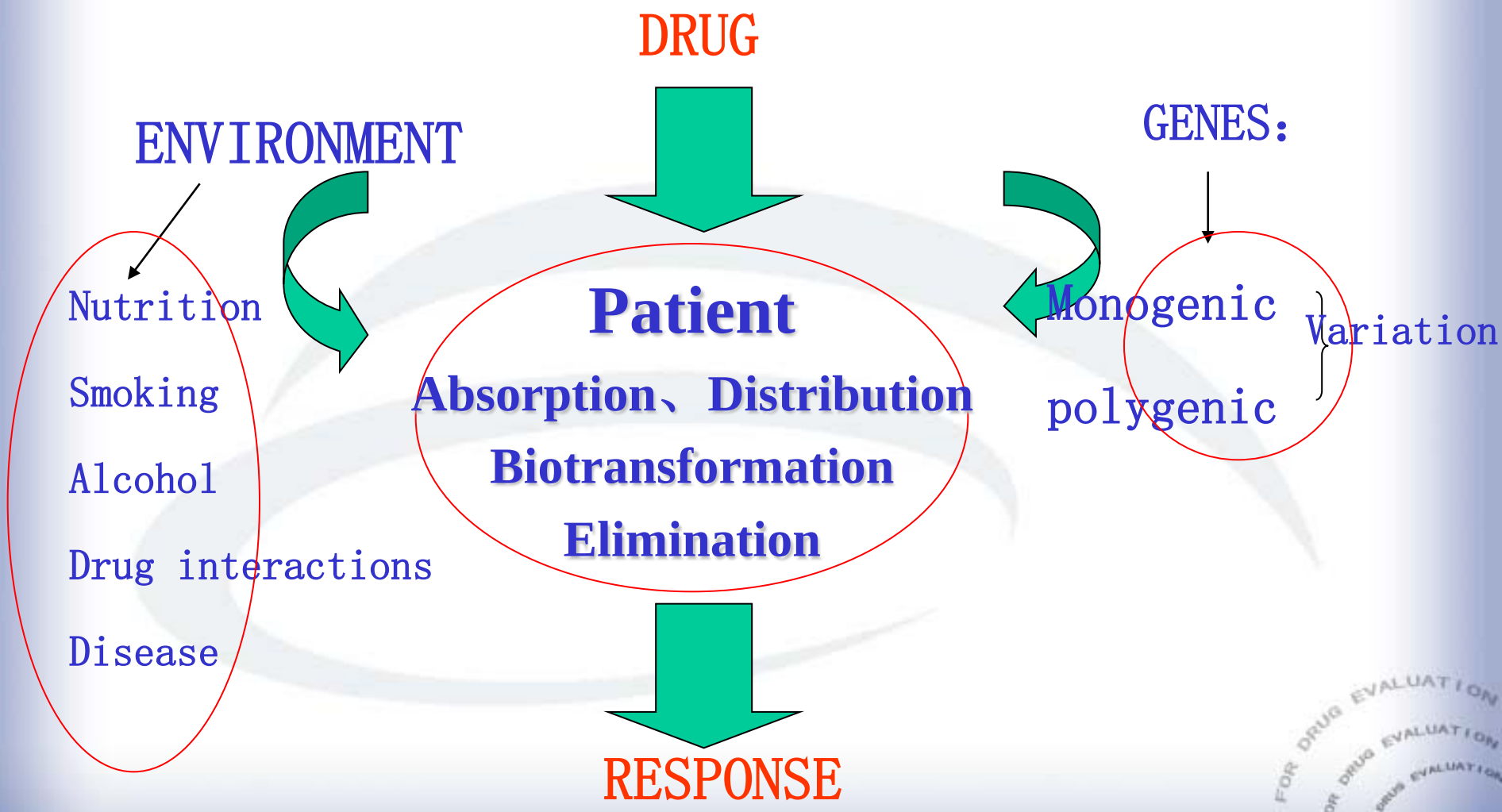
- ✓ Indication： allergic rhinitis
- ✓ Dosage: 10mg Q.D.
- ✓ It was launched in ## in 1983

Data：

1. The drug's half life is 5 hours and its metabolites is inactive
2. Several clinical studies： positive control, the half life of positive controls is 18 hours and 20 hours, and administration for positive control is once daily.
3. To observe efficacy after 2 weeks treatment
4. The sample size is more than 70 pairs in each randomized & control study
5. There are some observational studies which the total case is 500.

Effectiveness?

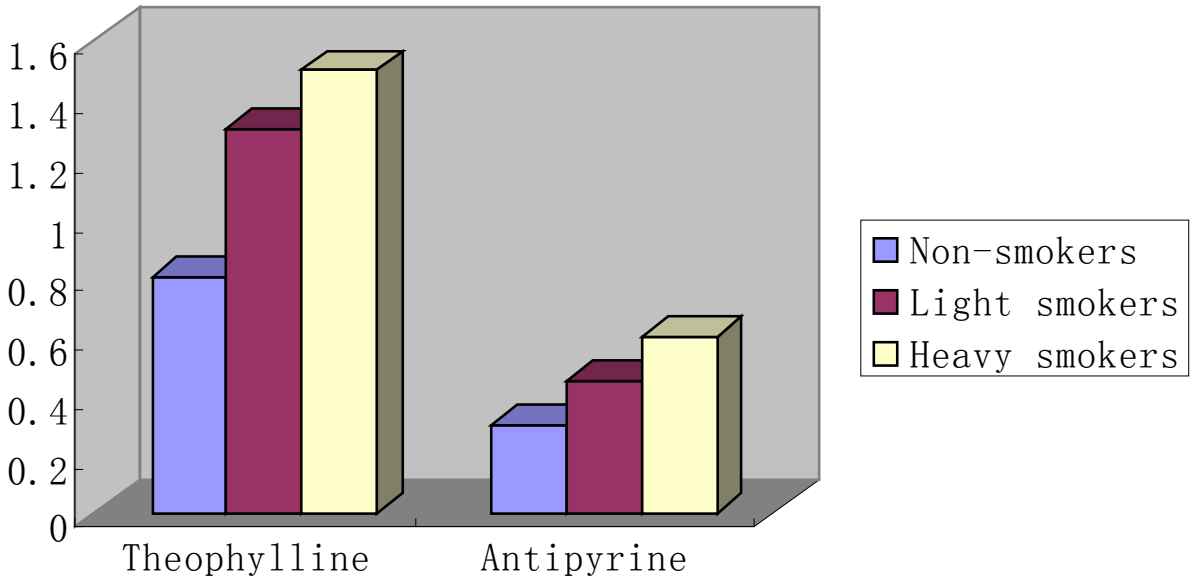
Clinical pharmacology difference



LIFESTYLE OPTIONS

Smoking:polycyclic hydrocarbons induce enzymes

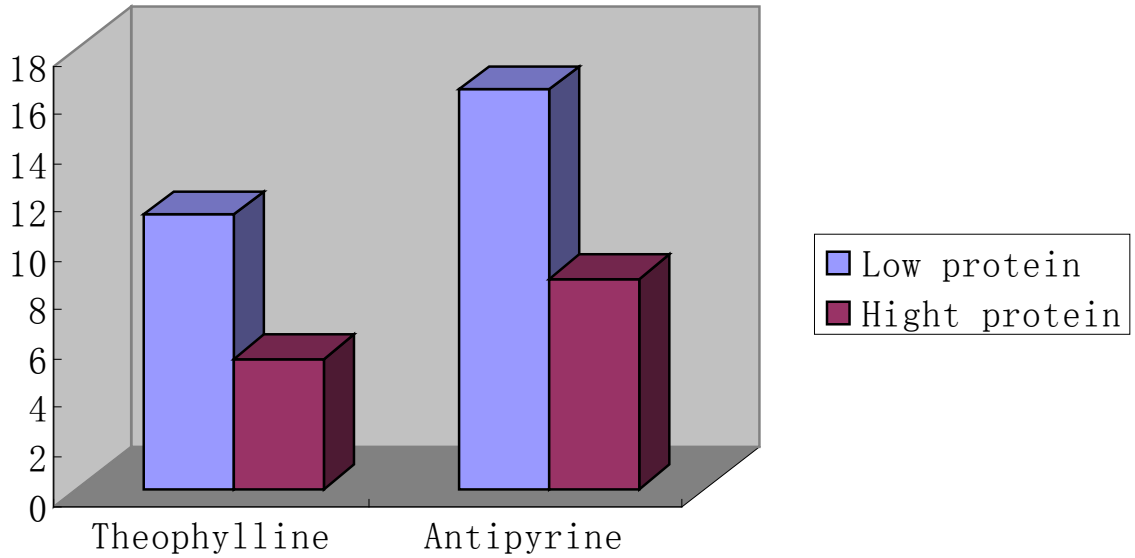
Clearance Ml/min/kg



NUTRITIONAL STATUS/DIET

Protein rich diet: stimulates enzyme synthesis

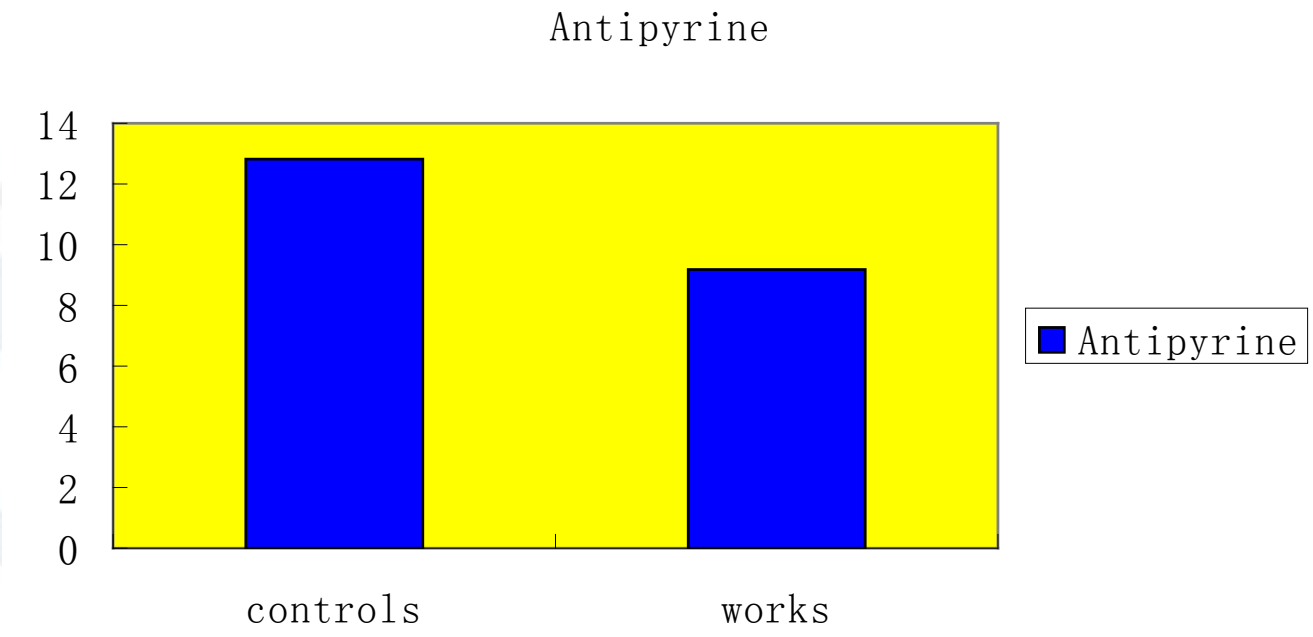
Half-life hours



ENVIRONMENTAL FACTORS

Pesticides

Half-life hours



Difference from medical practice in China

- **Disease definition**：differences in epidemiology of the same disease in China vs. foreign countries
- **Patient population**：influence of food、life style, and culture on the drug treatment
- **Disease diagnosis/treatment**：diagnostic method, SOC, comeds, compliance, experience with the drug of individual doctors
- 。。。。。。

Difference from medical practice in China

Impact on efficacy

For example：epidemiology、diagnostic methods、comeds

Impact on safety

For example：food, culture, comeds

Challenges

- **IND pathway not yet established**
- **Regulatory system and competence to be improved in accommodating to the requirement for developing innovative drug**

  role & responsibility of IRB/EC*

  electronic data management of clinical trial

  risk management & liability system during clinical trial

  ……

IRB/EC: institutional review board / ethnical committee

Our viewpoint

- Collaboration with open and scientific attitude
- Mainly focus on early phase study and accumulate the experience
- Advance the establishment of IND pathway
- Led by government, establish the mechanism to promote the direct cooperation between labs. Select the appropriate probe compound to be studied, evaluated and sum-up under the harmonized condition.

Our suggestions

- Better understand the technical requirement of Drug Registration Regulation
- Improve the quality of applications
- Promote the effective communication
- Accumulate experience and improve competence

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Thanks!