Recent Trend of Pharmaceutical Regulations in Taiwan

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Outline

- Organization and Responsibility of TFDA
- Recent Trend of IND Regulations in Taiwan
- Recent Trend of NDA Regulations in Taiwan
- Recent Trend of Post-Marketing Management in Taiwan
- Future Prospects

Organization and Responsibility of TFDA

Establishment of Taiwan FDA, DoH

- Taiwan FDA (TFDA) was inaugurated on Jan. 1st, 2010
  - Four Bureaus of Department of Health was integrated

Food Safety
食品處

Pharmaceutical Affairs
藥政處

FDA

Food & Drug Analysis
藥物食品檢驗局

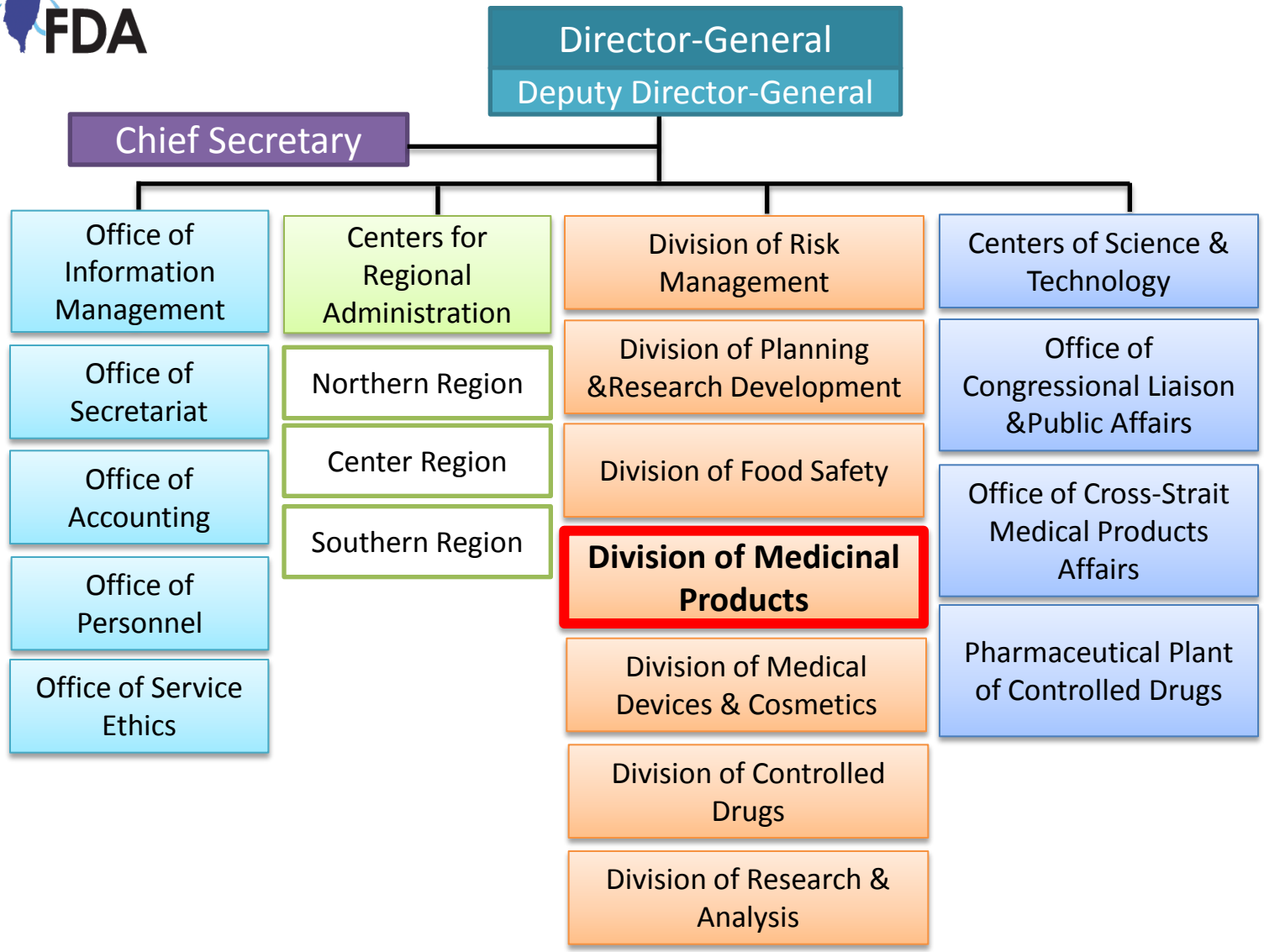
Controlled Drugs
管制藥品管理局

Reorganization of Taiwan TFDA, MOHW

- The Ministry of Health and Welfare (MOHW)
  - Formed on July 23rd, 2013 from the Department of Health
  - Following the restructuration of the Executive Yuan

To Promote The Health And Well-being Of All Citizens.

TFDA Organization Chart



Our Vision and Mission

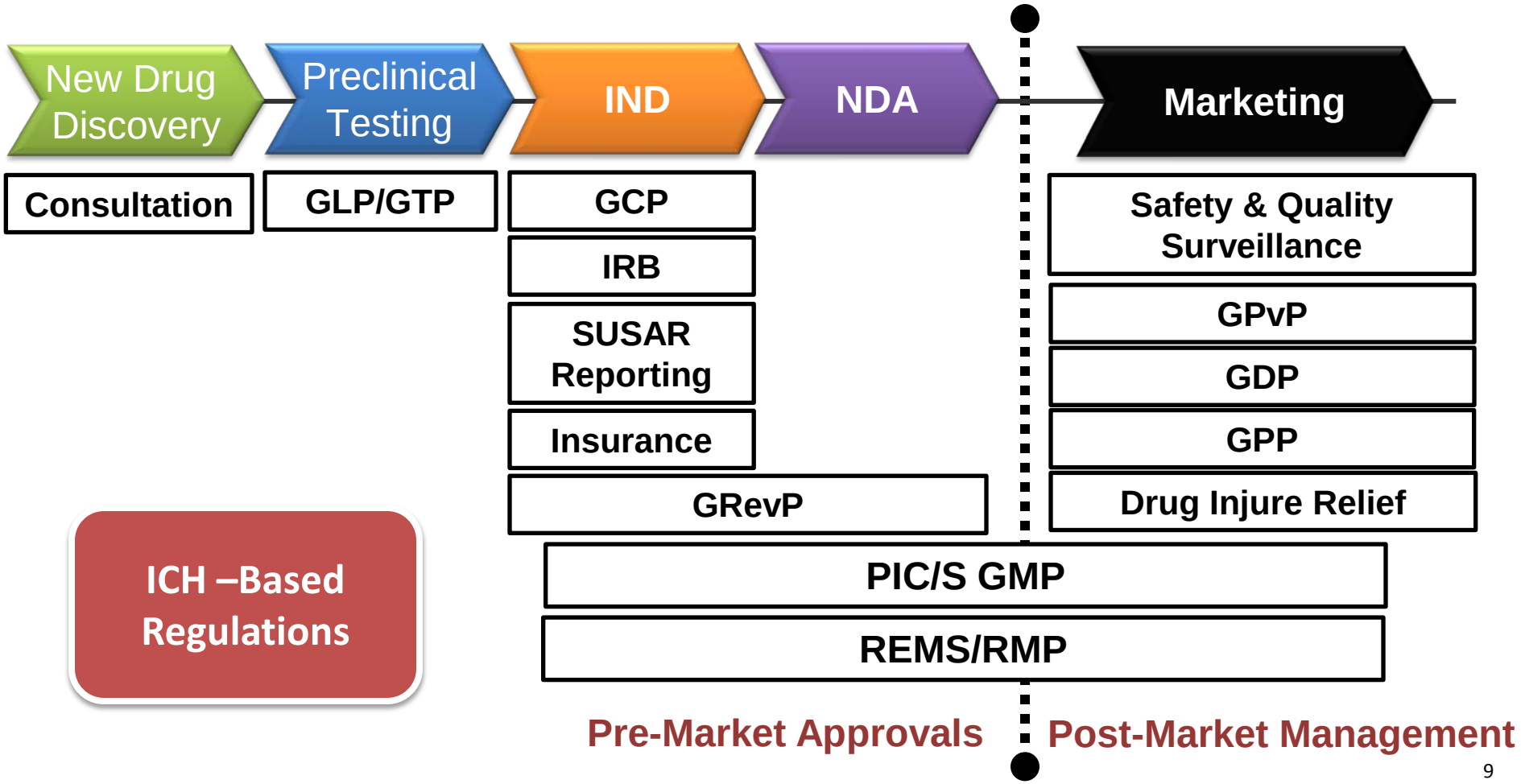
- Vision
  - To Safeguard National Health and Lead the Nation to a New Era of Food and Drug Management
- Mission
  - To Safeguard Food and Drug Safety
  - To Begin a New Technology Era
  - To Create a Safe Consumer Environment

Assure QUALITY, SAFETY, EFFICACY of Medicinal Products

Help to Speed the Development of Innovative Medicine

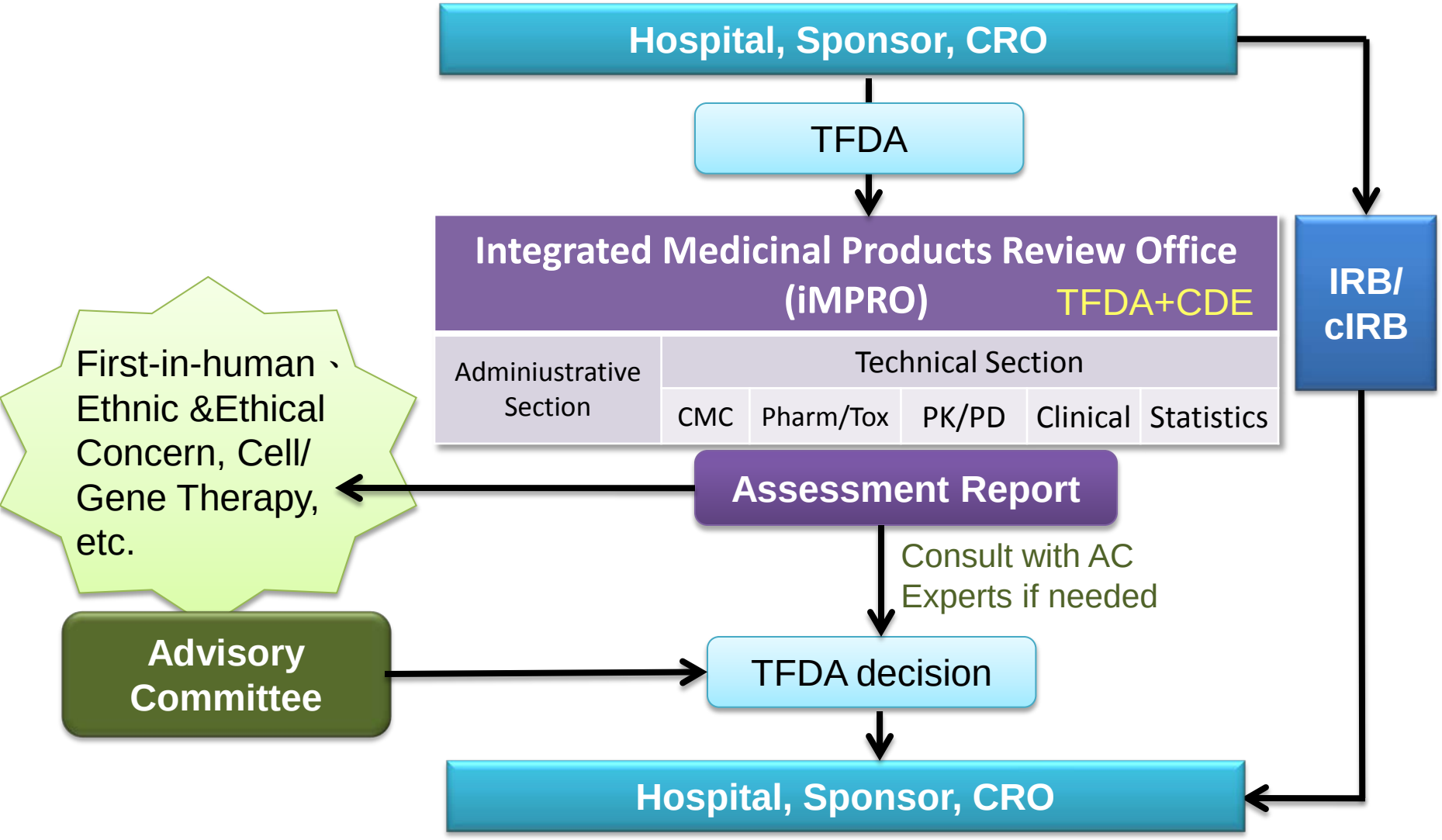
Pharmaceutical Regulation in Taiwan

- Life cycle management of medicinal products



Recent Trend of IND Regulations in Taiwan

Review Process for IND Applications



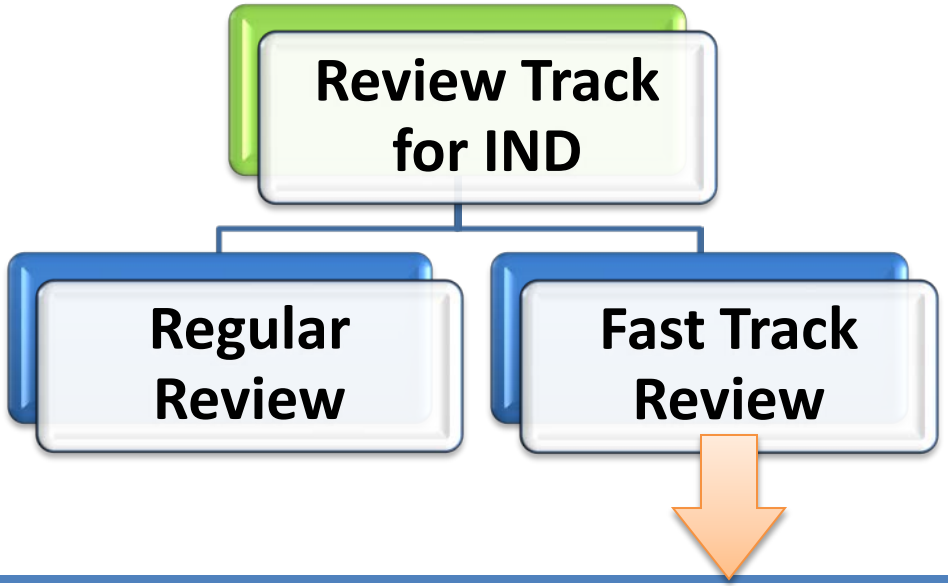
Establishment of Modern Clinical Trial Infrastructure in Taiwan

- Goal
  - Establish infrastructures for clinical trial conduction to meet international standard
  - Strengthen quality of clinical trials and enhance IND review efficiency
  - Introduce early-phase multi-national, multi-center trials, concurrently with global drug development

Establishment of Modern Clinical Trial Environment in Taiwan

- Enhance IND Review Efficiency
- GCP Inspection
- Training for Clinical Trial Professionals
- Government Funding Research Centers & Qualified Clinical Trial Sites for IND
- Enhance IRB Quality and Review Efficiency

Review Track for IND



Applicable for:

1. IND with the Same **US FDA-Approved** IND Number (July, 2004)
2. Multinational multicenter trials **simultaneously conducted in one of the medically advanced countries**; Taiwan's medical center hospital also involved (Aug, 2010)

GCP Inspection in Taiwan

- Routine inspection
  - Clinical trials for registration

ICH-GCP

- For-cause inspection
  - Clinical trial with SAE occurred
  - Clinical trial with GCP violation and safety concern
    - Protocol violation, mismanagement of investigational drug (IVRS error, Error packaging), or wrong delivery of study drug (human error)
- GCP Inspector Training

Training for Clinical Trial Professionals

- Regulation of Good Clinical Practice
  - Article 14
    - All staff involved in clinical trial should be qualified by education, training, and experience to perform his or her respective tasks
- Pharmaceutical Affairs Act
  - Article 41 (Jan, 2013)
    - The central competent health authority shall entrust professional medical groups to conduct educational training programs to cultivate talents in skills of clinical trial every year.
- Regulation of Human Trials
  - Article 4
    - A trial conductor should be a licensed physician, dentist, or traditional Chinese medicine physician with **5 or more years of experience in clinical treatment**.
    - The trial conductors are required to **receive human trial related training of more than 30 hours, and medical ethic related courses for more than 9 hours within past 6 years**

Government Funding Research Centers & Qualified Clinical Trial Sites for IND

- Chung Gung Medical Hospital*#
- National Health Research Institute#
- China Medical University Hospital *#
- Taichung Veterans General Hospital+
- Chung Shan Medical University Hospital+
- Changhua Christian Hospital+
- Jainan Mental Hospital, DOH+
- National Cheng Kung University Hospital*#
- Chi Mei Medical Center+
- Kaohsiung Medical University Hospital#+
- Kaohsiung Municipal Kai-Syuan Psychiatric Hospital+
- National Taiwan University Hospital*#
- Wanfang Hospital*
- Taipei Veterans General Hospital#
- Taipei Medical University Hospital#+
- Mackay Memorial Hospital+
- Koo Foundation Sun Yat-Sen Cancer Center+
- Bali Psychiatric Center, DOH+
- Yuli Hospital+

●Qualified Clinical Trial Sites for IND: 134 Teaching Hospitals

Type of Clinical Research Centers	No.
Excellent Center*	5
Excellent Center of Oncology#	8
General Clinical Research Center+	12

Conformation to International Regulation on Protection of Human Subjects

- Declaration of Helsinki and ICH-GCP
- IRB inspection and Certification
- SCIDER/ FERCAP Recognition Program 2005-2012

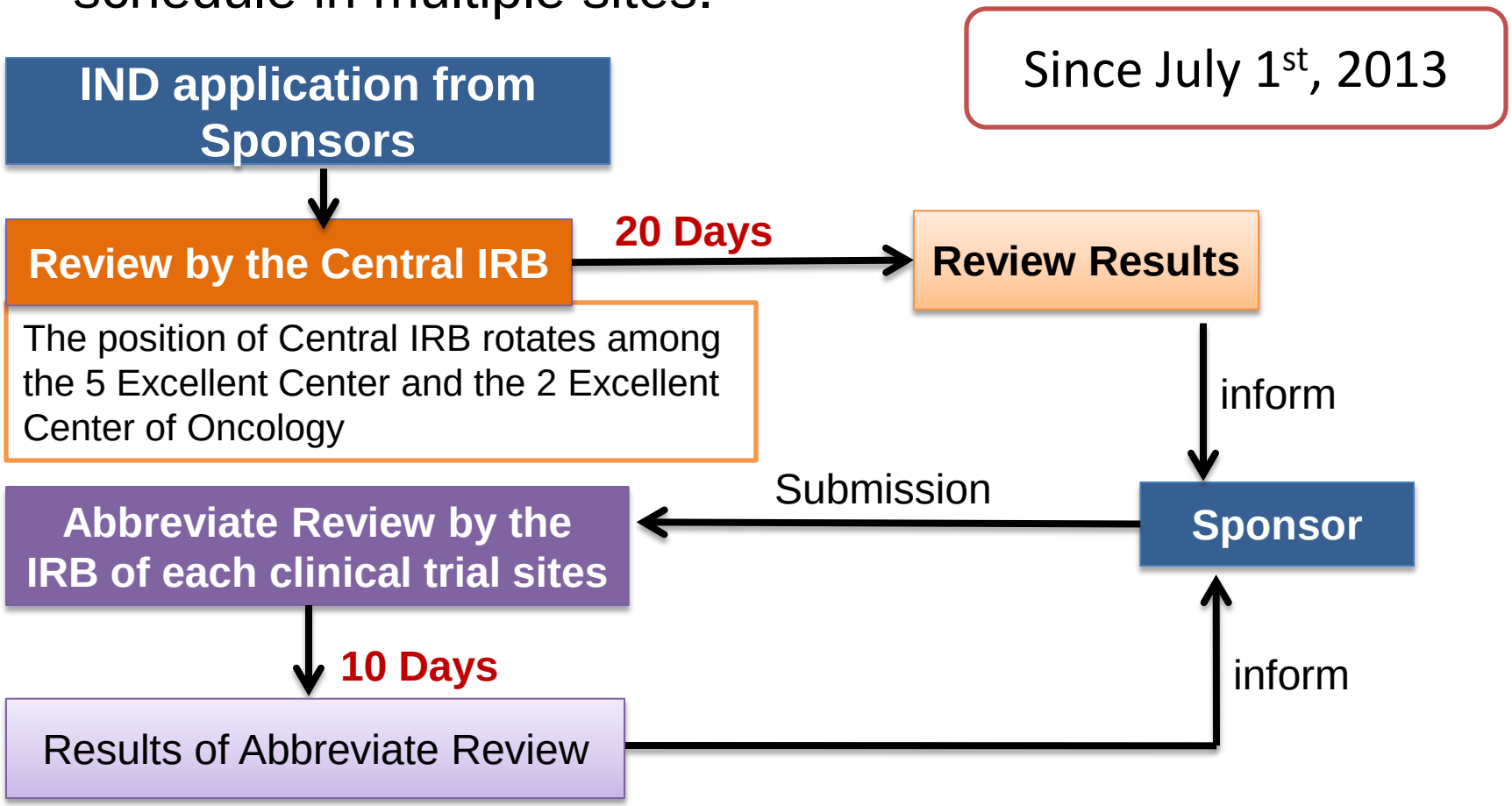
Country	China	South Korea	Taiwan	Thailand	Others	Total
No.	31	26	**23**	12	16	108

- AAHRPP Accreditation

Country	USA	South Korea	India	Canada	Taiwan	China	Singapore	Total
No.	166	4	3	3	**1**	1	1	179

Central IRB System

- To control IRB review time and synchronize the trial schedule in multiple sites.



Simultaneous Global Clinical Trials

- MOU between Taiwan Center of Excellence and International Pharmaceutical Company

Taipei Veterans General Hospital

- 2009 Sanofi Aventis
- 2010 GSK
- 2011 Norvatis

National Taiwan University Hospital

- 2007 GSK
- 2009 Norvatis, Boehringer Ingelheim
- 2012 Pfizer, Bayer, MSD

China Medical University Hospital

- 2010 Norvatis

Chung Gung Medical Hospital

- 2010 Norvatis
- 2012 GSK
- 2013 MSD

Chung Gung Medical Hospital

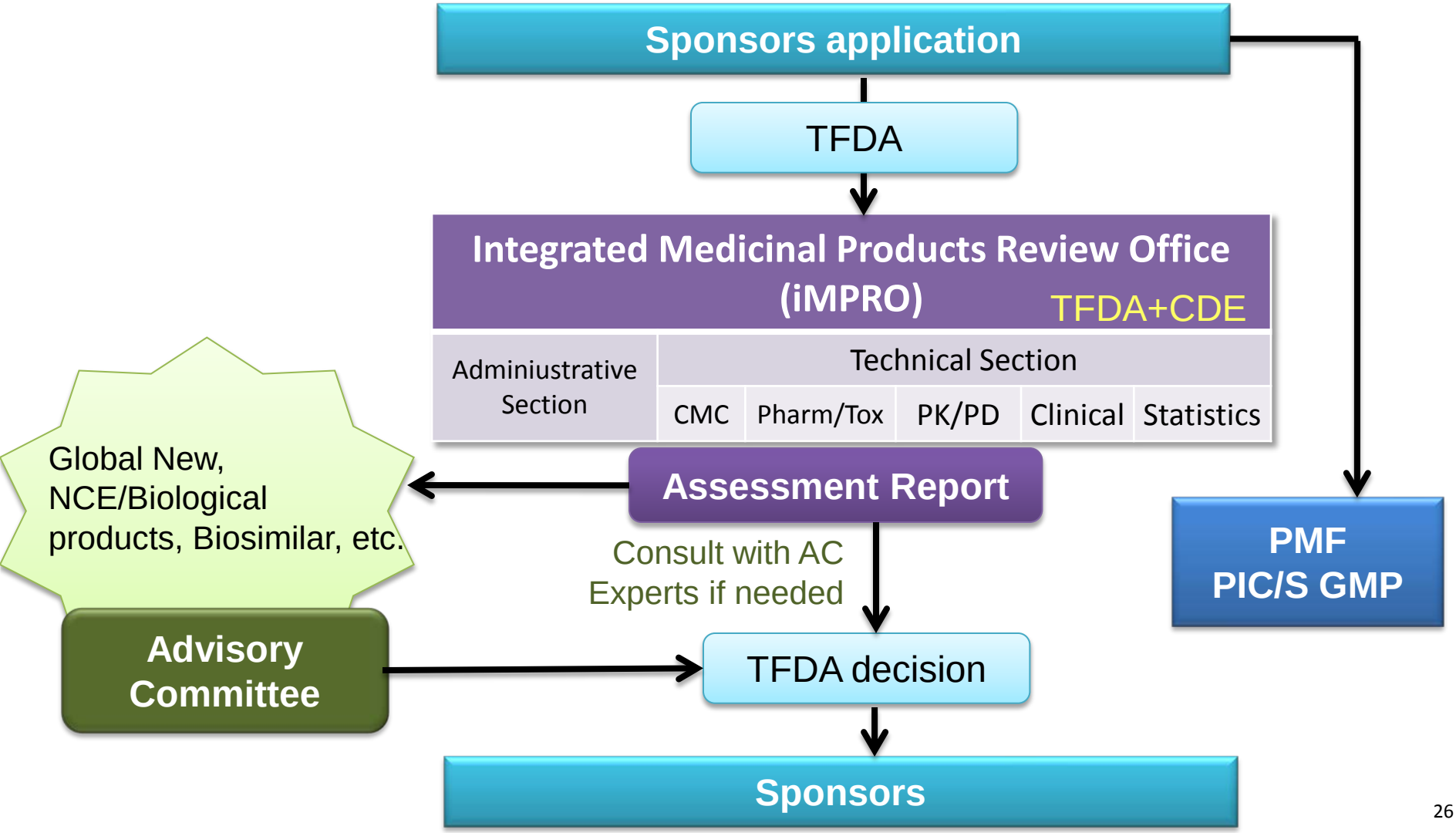
- 2010 Norvatis, MSD
- 2011 Norvatis

Case Sharing– Afatinib

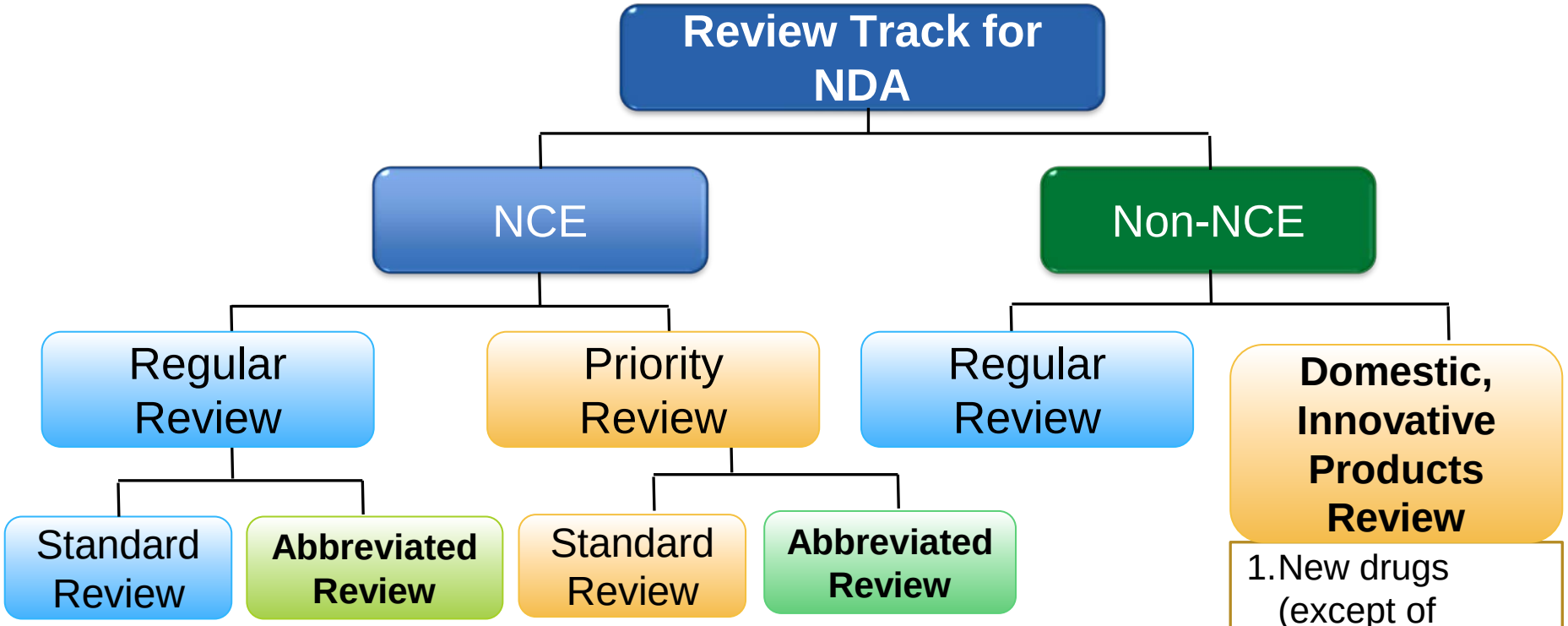
- New Chemical Entity
- Indication: Target therapy drug for advanced non-small cell lung cancer
  - a selective, irreversible ErbB family blocker for the treatment of patients with locally advanced or metastatic NSCLC with EGFR mutation
- **First approved in the world (2013)**
- **Multinational Trial lead by Taiwan Principle Investigator**

Recent Trend of NDA Regulations in Taiwan

Review Process for NDA Applications



Review Track for NDA



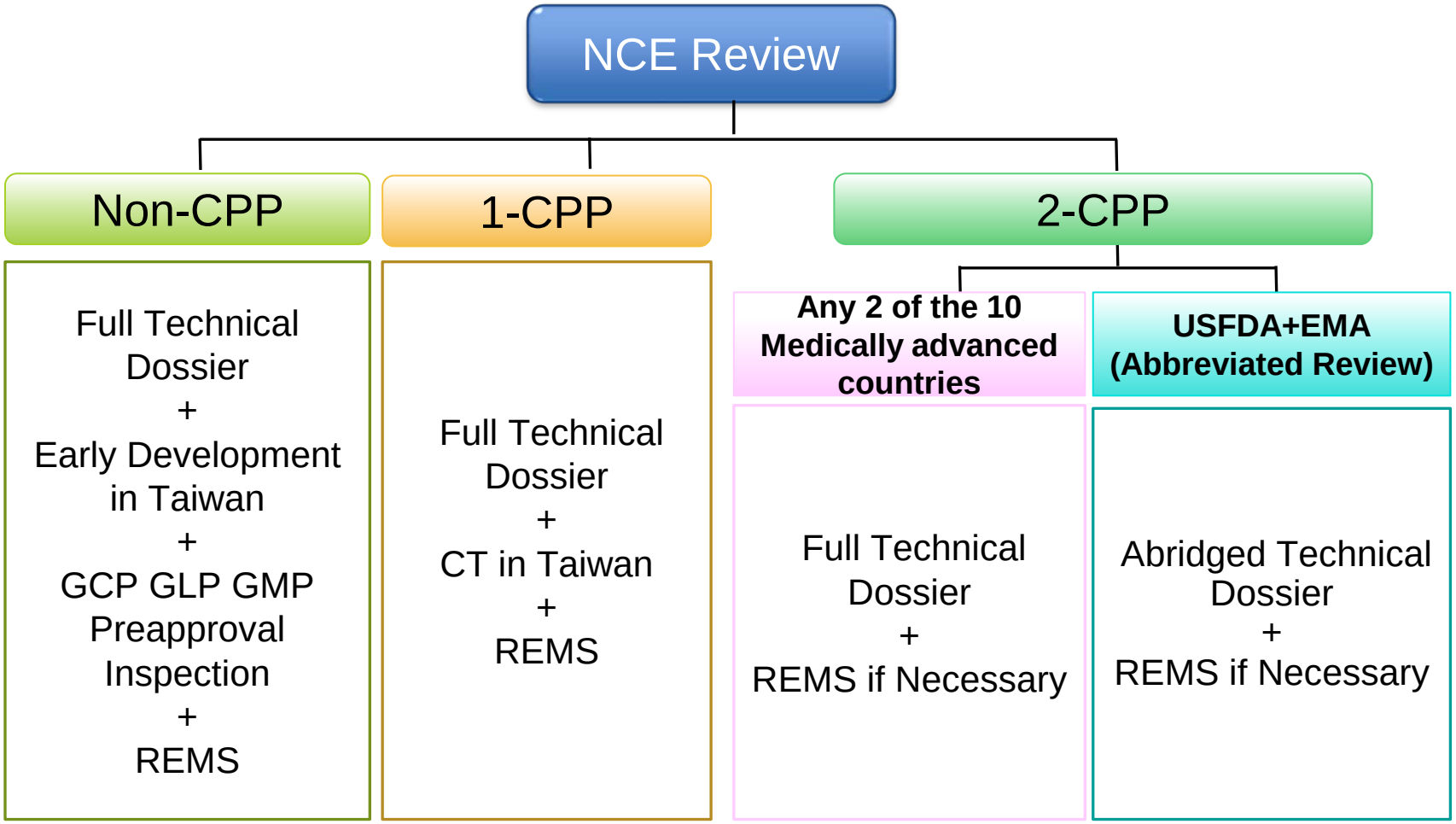
- **Priority Review：**
  NCE+ Serious Disease+ Unmet Medical Needs
- **Abbreviated Review：**
  NCE+US FDA & EMA Approved
  + No Ethnics Difference & Same Indication

1. New drugs (except of NCE/NME, Biologics, Botanicals)
   +
2. Domestic Manufactured Products; fulfill PIC/S GMP regulation

Recent Regulations for NDA

- Publish Assessment Report for NCE/NME (Aug. 2010)
- Points to Consider for Review and Approval of NCE/NME (Nov. 2012)
- Risk Evaluation and Mitigation Strategy (REMS) or Risk Management Plan (RMP) (April, 2012)
- Implementation of Common Technical Documents (CTD) Format (Nov. 2012)
- Implementation of eCTD (Oct. 2012)
- NCE-2 (April, 2013)
  - The review principle for the pharmaceutical drugs that has been marketed in the ten advanced countries for 10yrs, but is a NCE in Taiwan (except for biological products)
- Relaxation of CPP Requirements (May 2012)
- Accelerated Approval (Aug, 2013)

Relaxation of CPP Requirements



CPP: Certification of Pharmaceutical Products

Case Sharing– Afatinib

- New Chemical Entity
- Indication: Target therapy drug for advanced non-small cell lung cancer
  - a selective, irreversible ErbB family blocker for the treatment of patients with locally advanced or metastatic NSCLC with EGFR mutation
- **First approved in the world (2013)**
- **Review Track: Non-CPP**

Accelerated Approval

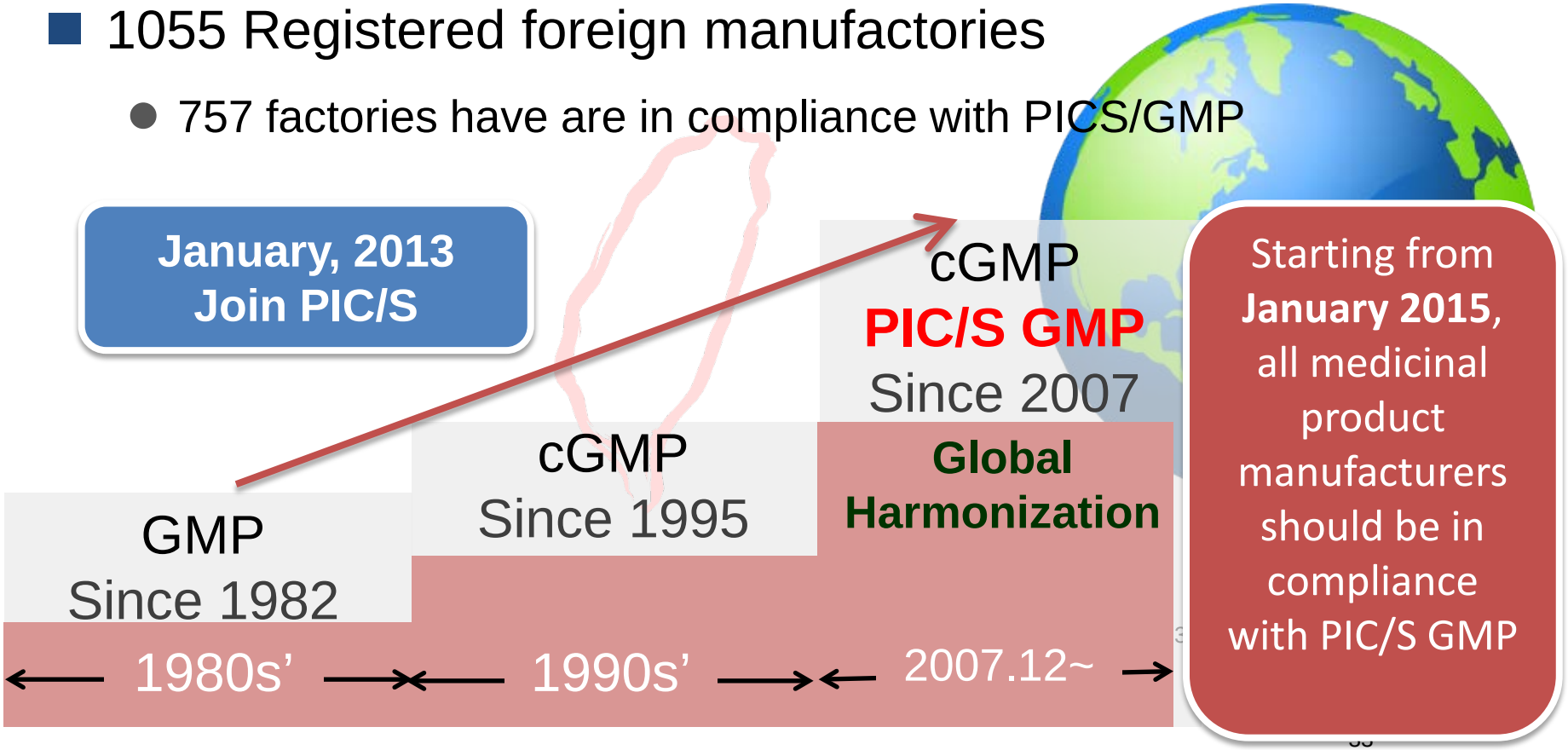
- Accelerating approval for drugs for serious conditions that fill an unmet medical need
  - Base on a surrogate endpoint
    - A laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit
  - Studies that demonstrate a drug's effect on a surrogate endpoint must be "adequate and well controlled"
- Post-marketing (Phase IV) confirmatory trials are generally required to verify clinical efficacy
    - REMS/RMPs could be required.

Recent Regulations for NDA:
For Special Categories of New Drugs

- Botanical Products
  - Guideline for Review and Approval of Botanical Products (Apr. 2013)
- Biologics:
  - Biosimilar
    - Guideline for Review and Approval of Biosimilar Products (2008)
    - Points to Consider for Review and Approval of Biosimilar Products (2010)
    - Guideline for Review and Approval of Biosimilar Monoclonal Antibodies (Sep. 2013)
  - Vaccines
    - Guideline for Review and Approval of Pandemic influenza vaccines (Oct. 2010)
  - Cell and gene therapy products
    - Guidance on investigational human cell/ gene therapy products
    - Content and format of investigational new drug (IND) applications for human cell and gene therapy products (Draft, Feb. 2011)

Quality Assurance for Drug Manufacturing

- 158 GMP Pharmaceutical manufactories in Taiwan
  - 44 factories are in compliance with PIC/S GMP
- 1055 Registered foreign manufactories
  - 757 factories have are in compliance with PICS/GMP



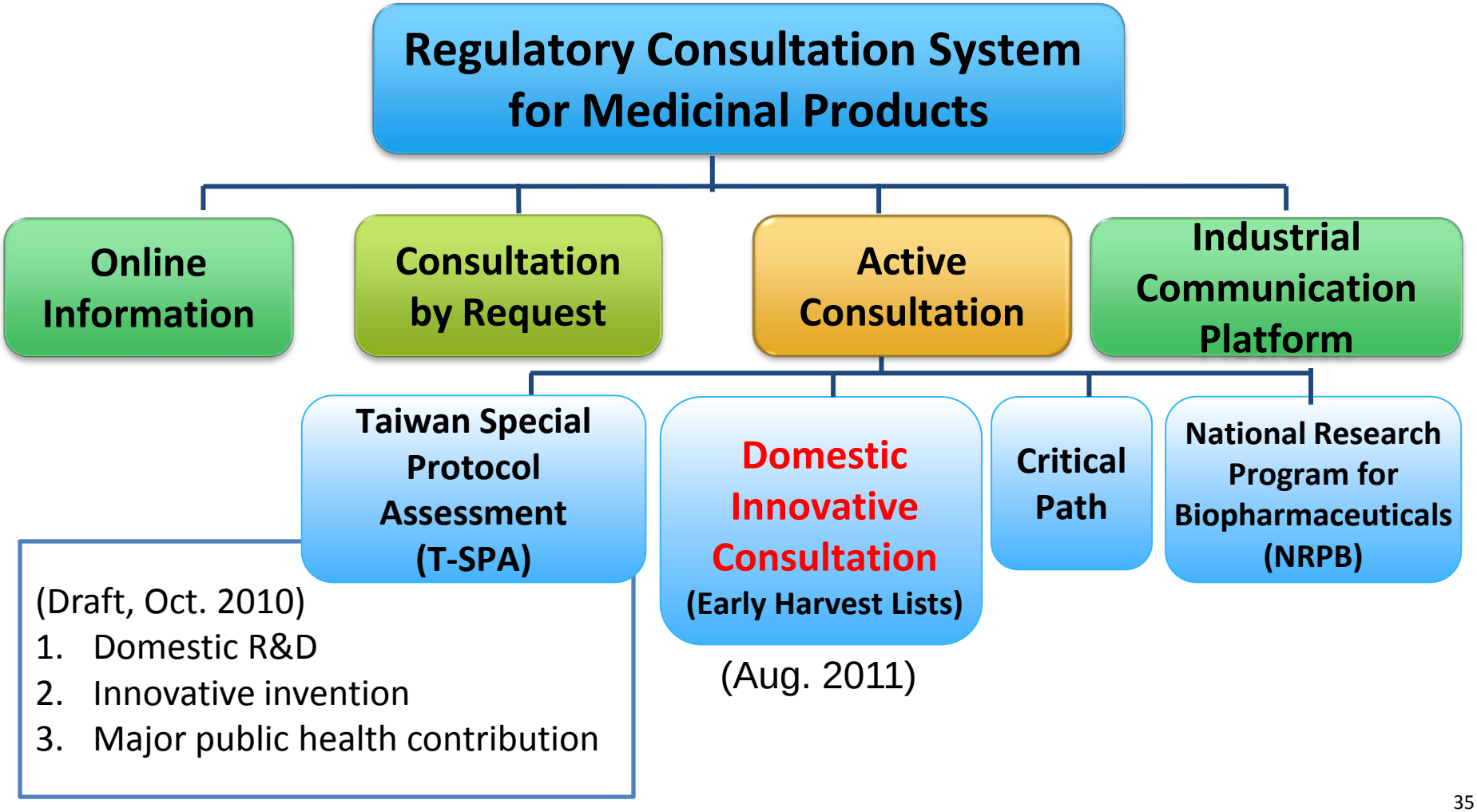
Regulatory Consultation System

Assure QUALITY, SAFETY, EFFICACY of Medicinal Products

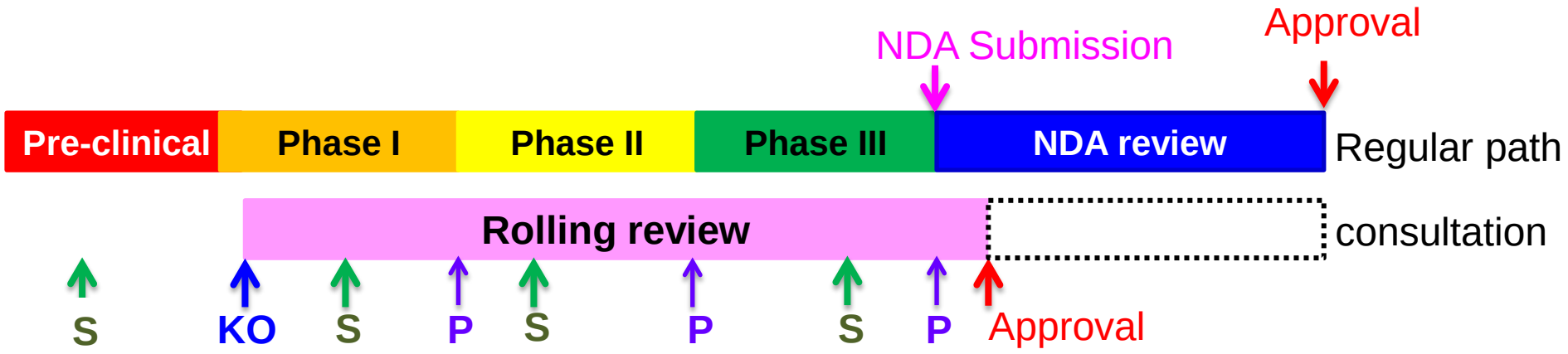
Help to Speed the Development of Innovative Medicine

- Mission:
  - To promote the public health by encouraging innovation and access to new drugs

Regulatory Consultation System



Domestic Innovative Consultation

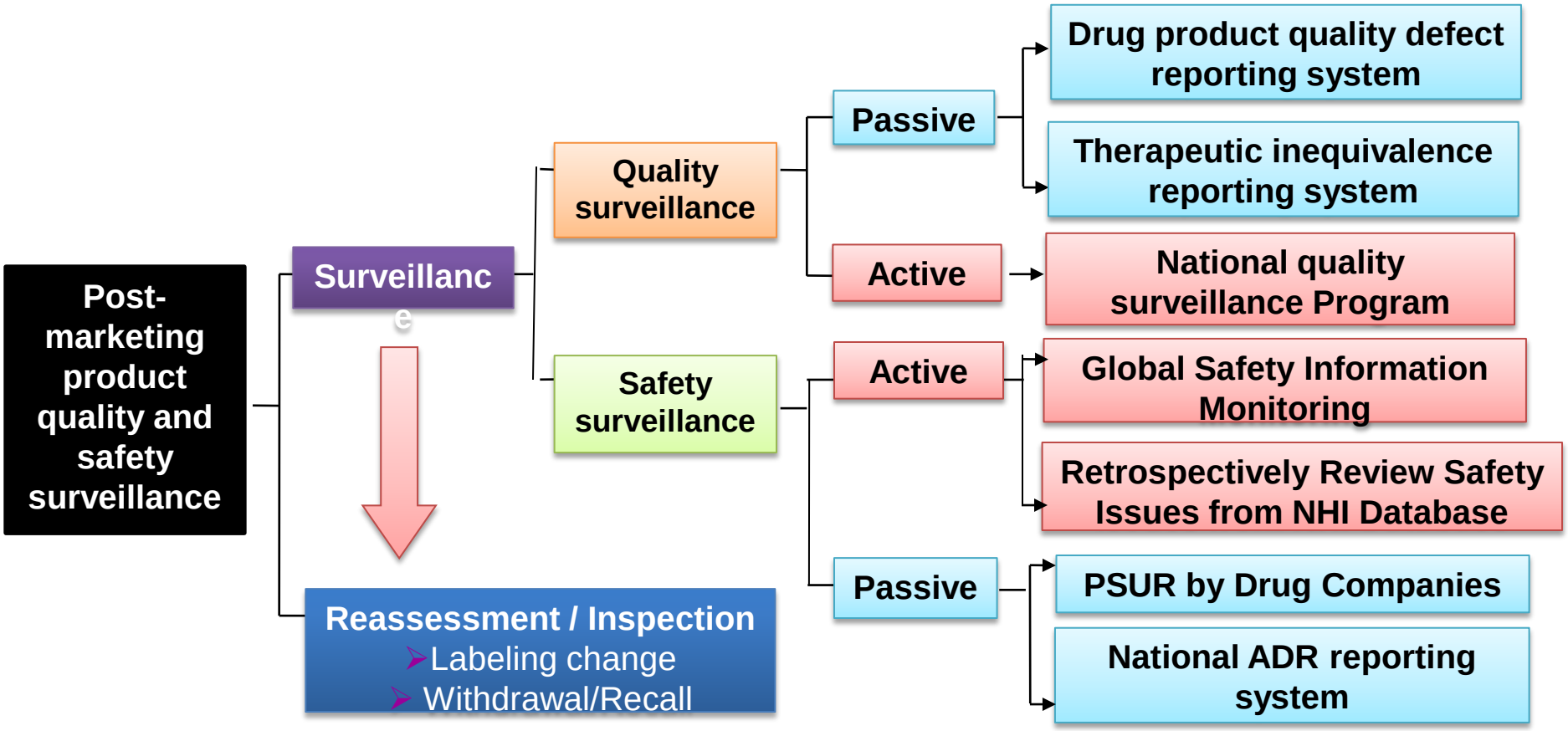


S: Sponsor meeting KO: Kick-off meeting P: Pre-filing meeting

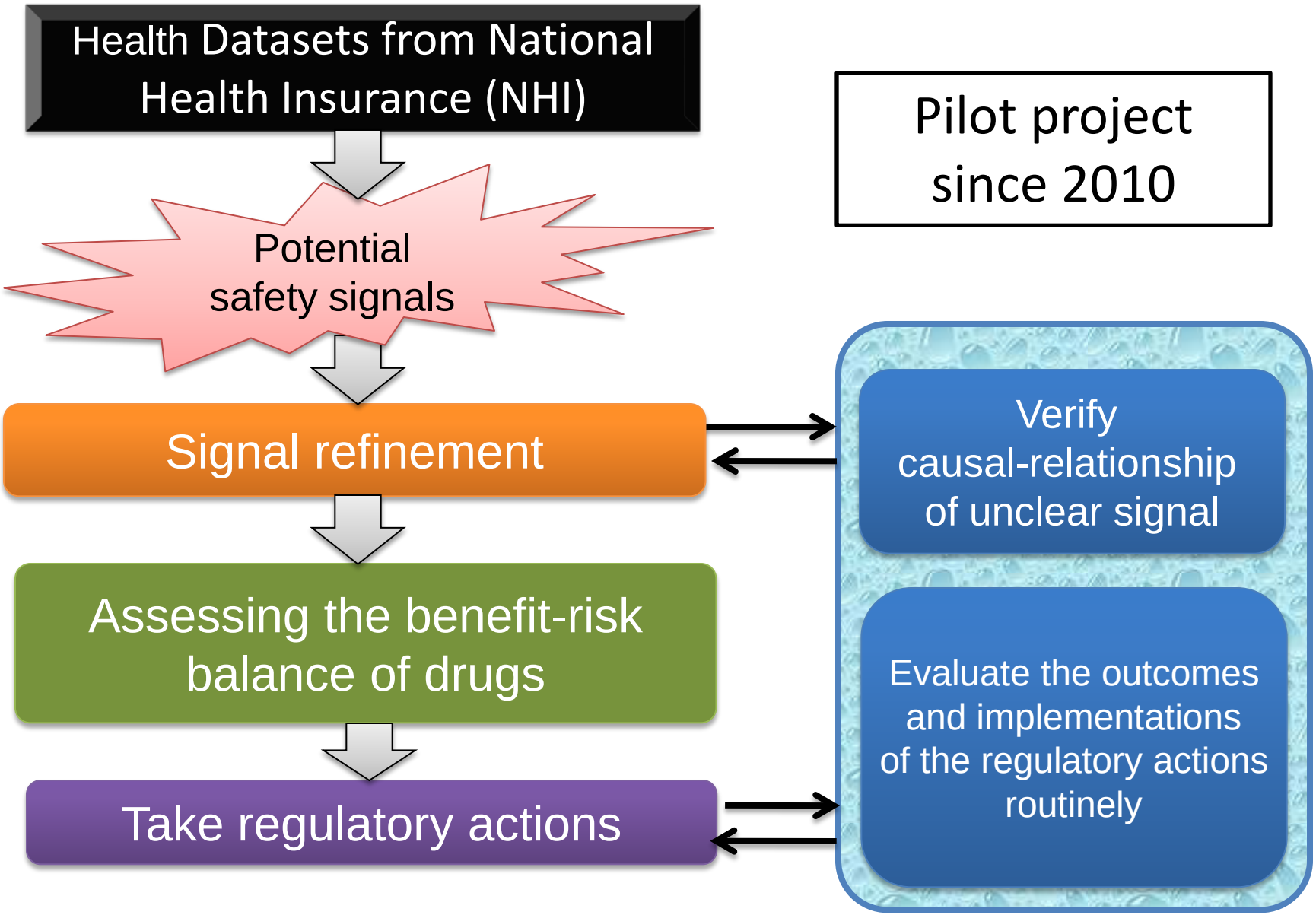
Total Cases (102.6.30)	NDA Approval	NDA Review	Phase III	Phase II	Phase I	Others
22	2	2	7	7	3	1

Recent Trend of Post-Marketing Management in Taiwan

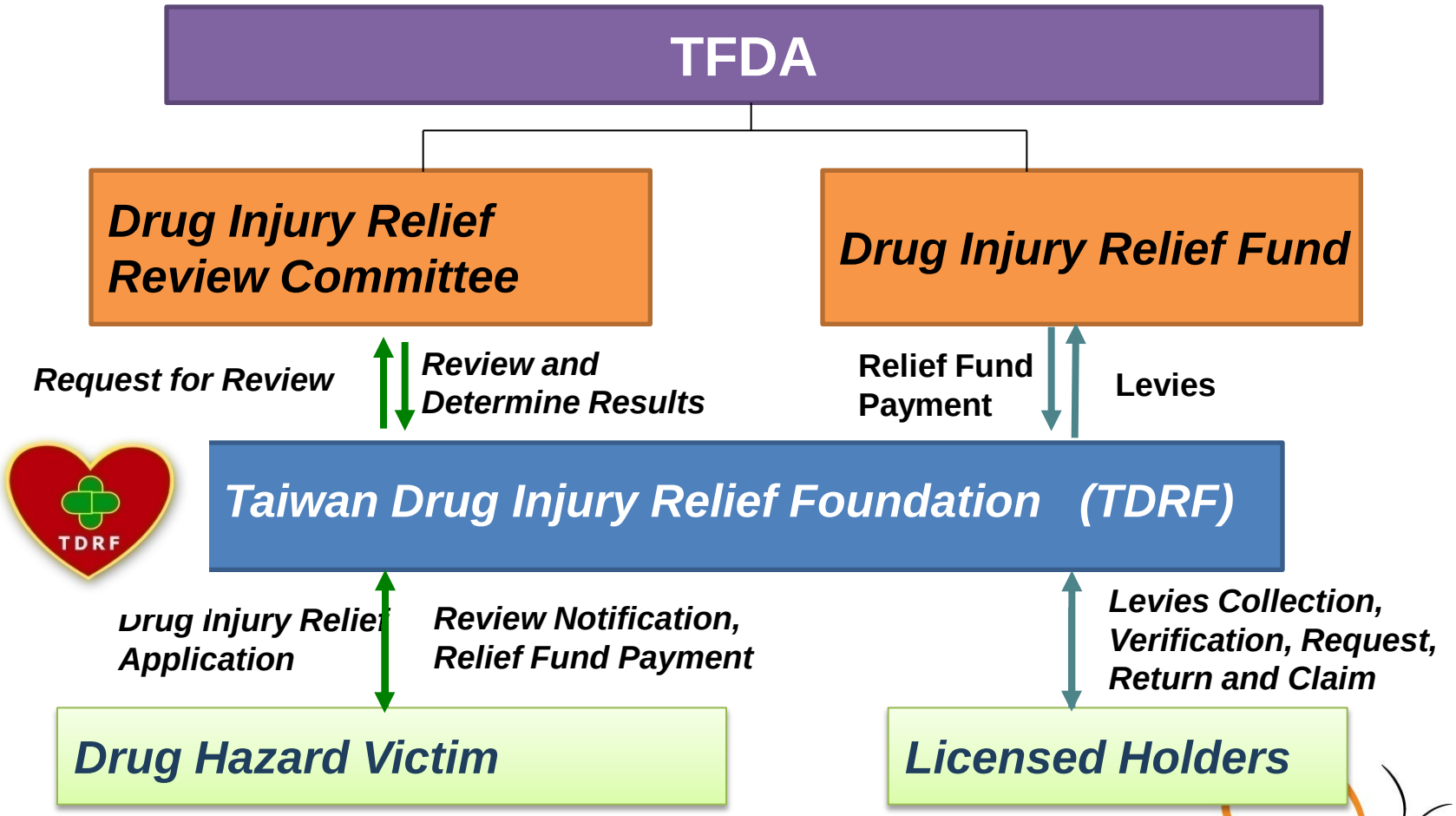
Post-Marketing
Safety and Quality Surveillance
—Risk Management



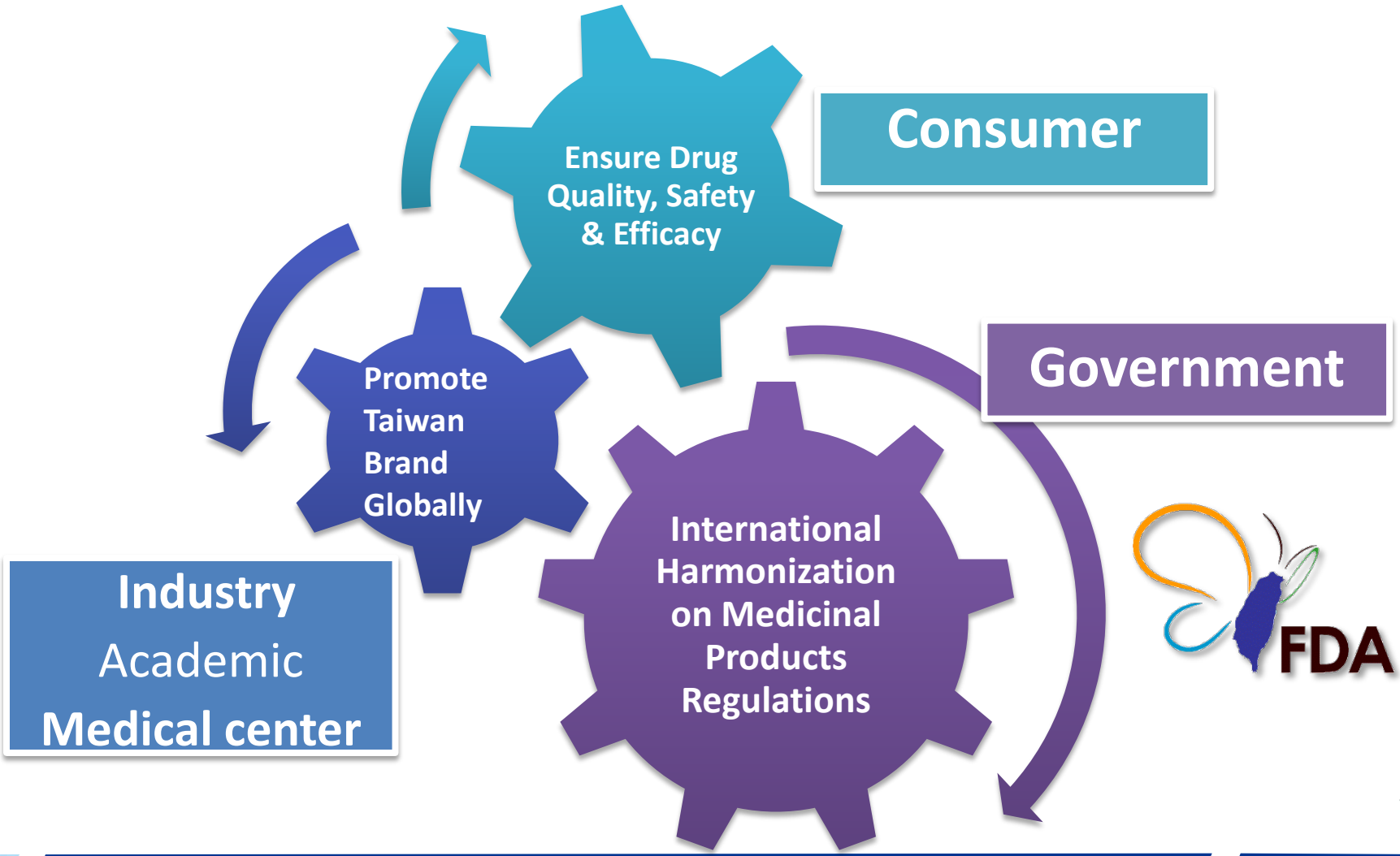
Active Assessment of Drug Safety



Taiwan Drug Injury Relief System



Future Prospects



Thank You For Your Attention!