Overview of Early Access Regulatory Pathways for Vaccine in Taiwan

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Outline

1. Organization and Responsibility of TFDA
2. Current Regulatory Framework of Vaccine
3. Application and Evaluation Process
4. Prospects of the future

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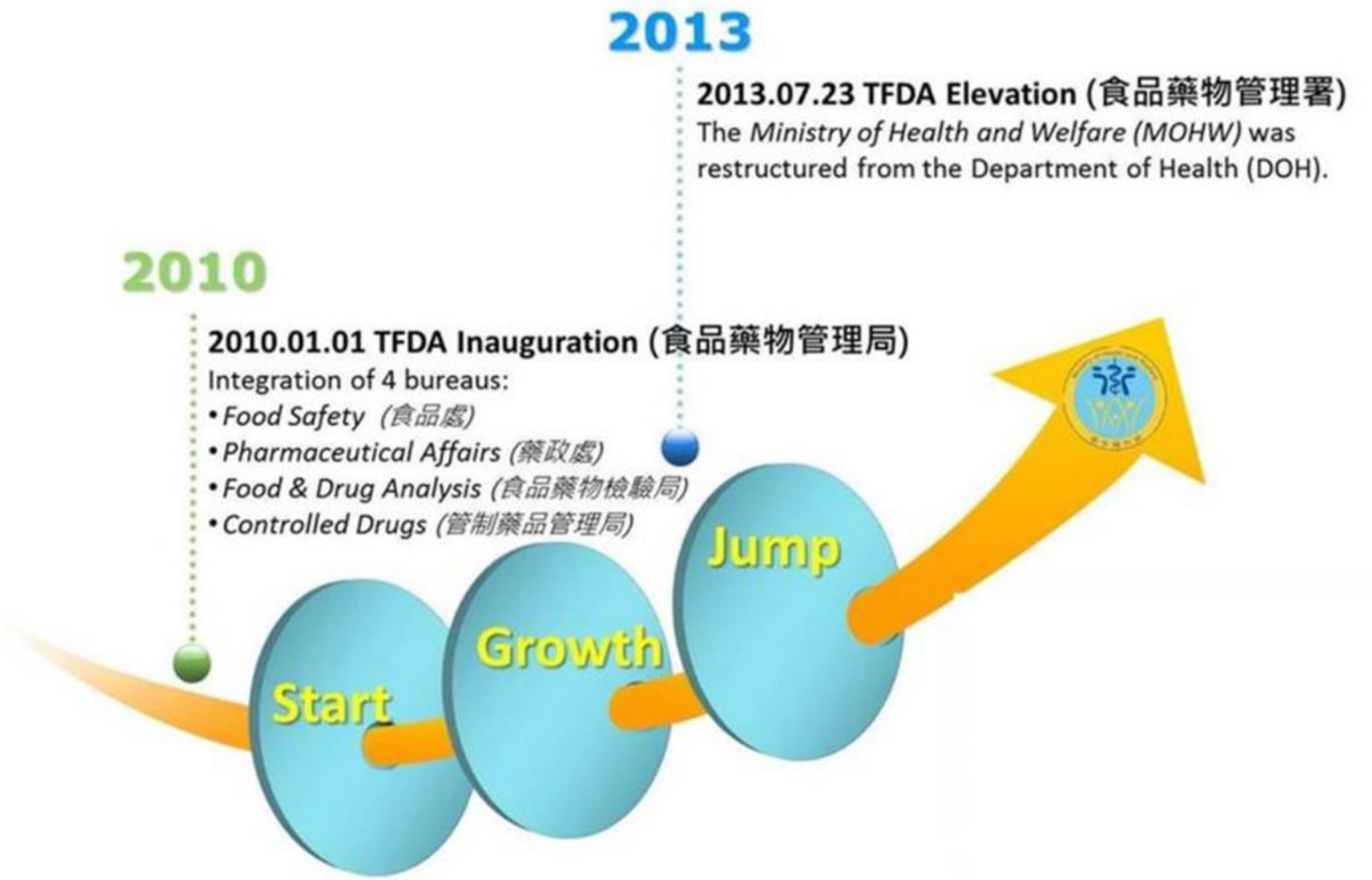
Establishment of TFDA



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The Role of TFDA in in Pharmaceutical product management

Protect

Assure **Quality, Safety, Efficacy** of Medicinal Products

Promote

Facilitate the **Development** of Innovative Medicine and Speed **Drug Accessibility**

Profession

Service

Quality

Innovation

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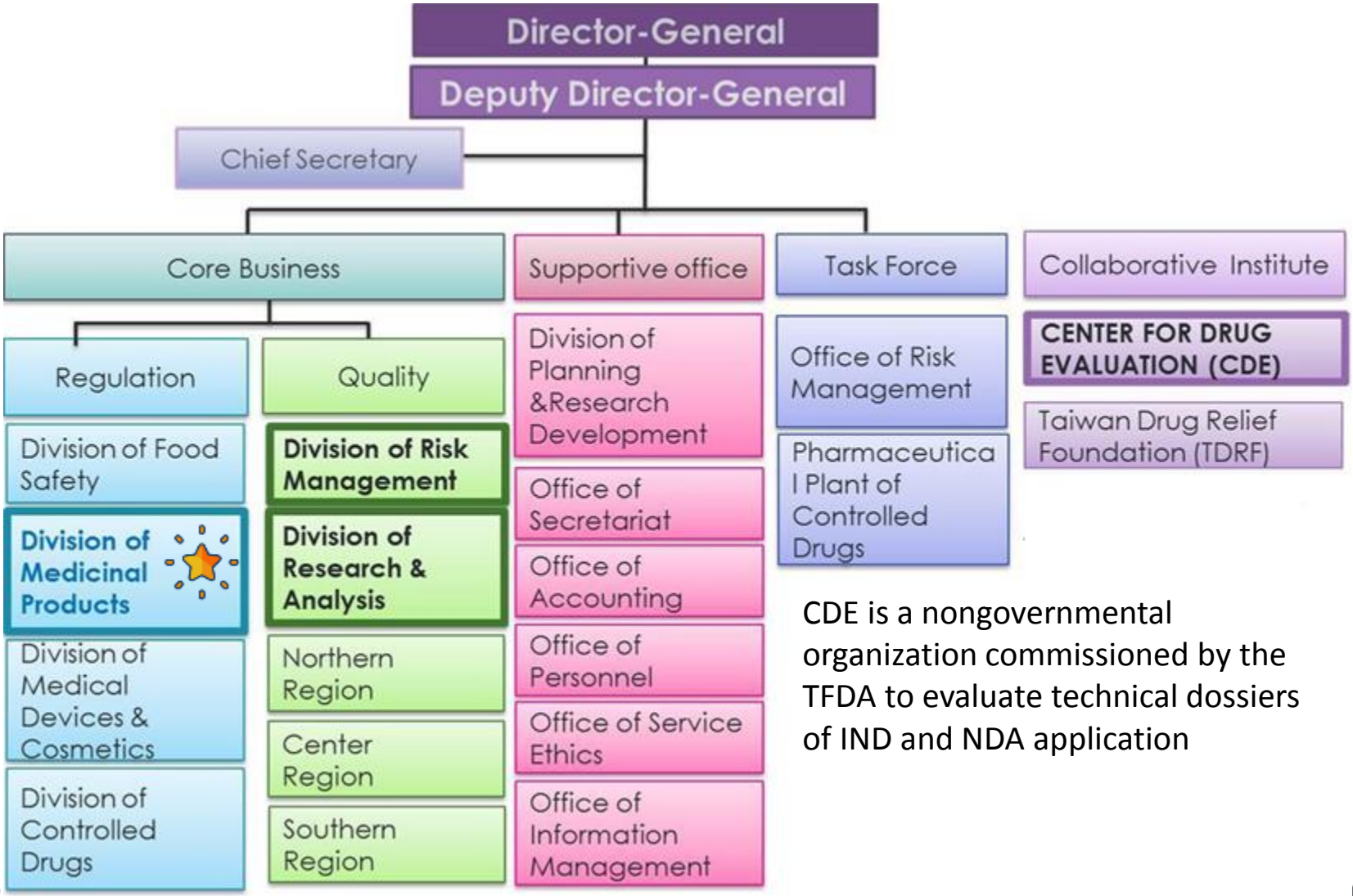
TFDA Organization Chart



CDE is a nongovernmental organization commissioned by the TFDA to evaluate technical dossiers of IND and NDA application

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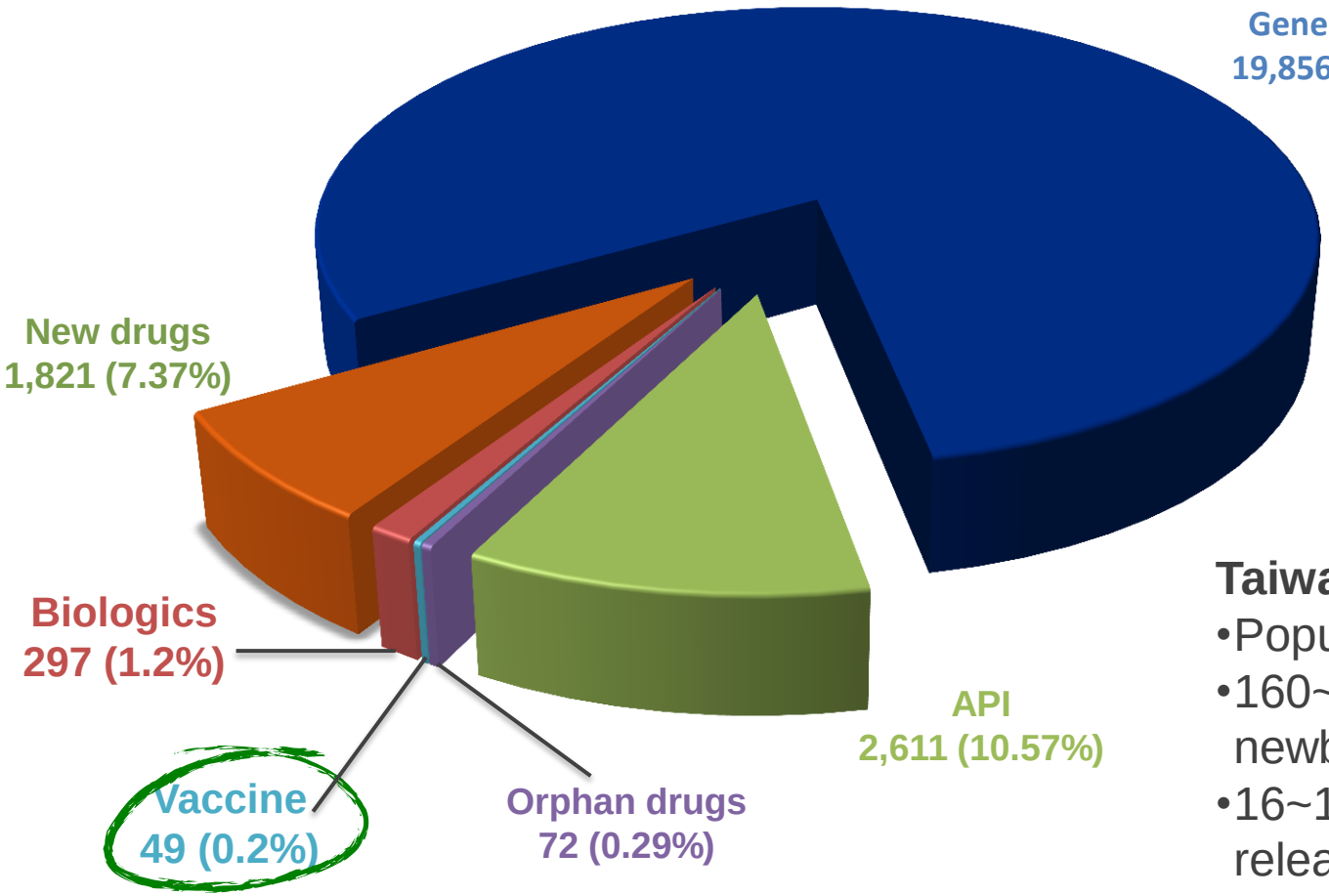
License Numbers of Drugs in 2017



Taiwan Market

- Population: 23 millions
- 160~240 thousand newborn babies/yr
- 16~18 million doses/yr released by TFDA
- 11 million doses/yr for EPI

Total license: 24,706

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Licensed Vaccines in Taiwan

Approved Vaccine

Domestic

- Bacille Calmette-Guerin vaccine (BCG)
- Mouse brain-derived JE vaccine
- Seasonal flu vaccine
- Tetanus toxoid

Import

Vaccinations for The Expanded Program on Immunization (EPI)

- Hepatitis B vaccine (HepB)
- DTaP-Hib-IPV 5 in 1
- DTaP
- Inactivated polio vaccine (IPV)
- Pneumococcal vaccine (PV)
- Varicella vaccine (Varicella)
- Measles, mumps and rubella vaccine(MMR)
- Cell –based JE vaccine
- Seasonal flu vaccine

Others

- Rotavirus vaccine (Rotavirus)
- Hepatitis A vaccine (HepA)
- DTaP-IPV-HepB-Hib 6 in 1
- DTap-IPV 4 in 1
- Rabies vaccine (Rabies)

HPV Vaccine

- Human Papillomavirus vaccine Type 16 and 18
- Quadrivalent Human Papillomavirus (Types 6,11,16,18)
- Human Papillomavirus 9-valent Vaccine, Recombinant

Specific Import by CDC

- Typhoid fever vaccine (Typhoid)
- Yellow fever vaccine (YF)
- Meningococcal C conjugate vaccine (Men C_conj)
- Others (Vaccines in Delay or Shortage)

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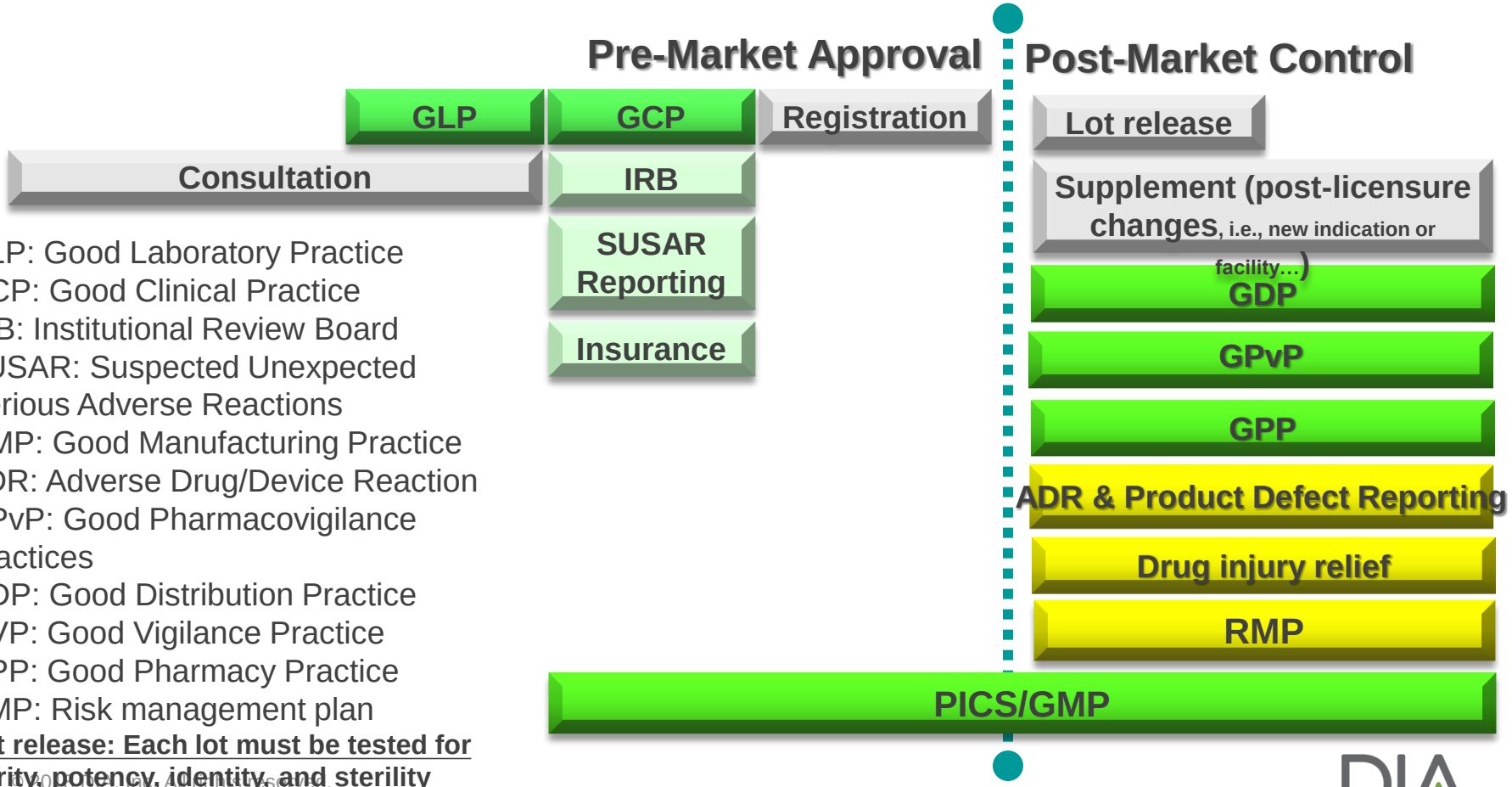
Life Cycle Management of Vaccine



GLP: Good Laboratory Practice
GCP: Good Clinical Practice
IRB: Institutional Review Board
SUSAR: Suspected Unexpected Serious Adverse Reactions
GMP: Good Manufacturing Practice
ADR: Adverse Drug/Device Reaction
GPvP: Good Pharmacovigilance Practices
GDP: Good Distribution Practice
GVP: Good Vigilance Practice
GPP: Good Pharmacy Practice
RMP: Risk management plan

Lot release: Each lot must be tested for purity, potency, identity, and sterility

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Legislation and Regulation

Legislation and Regulations on Vaccine	
Law	Pharmaceutical Affairs Act Medical Care Act
Regulation	Regulation for Registration of Medicinal Products Regulations on Human Trials Regulation on Good Clinical Practice (GCP) Regulation on Good Manufacture Practice (GMP) Regulation of the Lot Release Procedures for Biologics
Guidance	Guidance for Registration of Vaccines Guidance for Registration of Pandemic Influenza Vaccines Guidance for Strain Change Supplements of Seasonal Flu Vaccines
International Guidance	ICH/EMA/FDA/WHO guidance which are issued in an issue-specific manner are taken into reference E.g., viral safety, expression construct, specification, cell substrate, individual vaccine

Emergency Use Authorization (EUA)

§ PAA 48-2

When a special case happened in the following circumstances…

01

- For the **life-threatening, severely disability diseases**
- **No** appropriate drugs or alternative treatment

02

In responding to the necessity of emergency public health circumstances

TFDA can approve to manufacture and import the specific drugs that are not licensed in Taiwan, ex. Yellow Fever Vaccine (YF).

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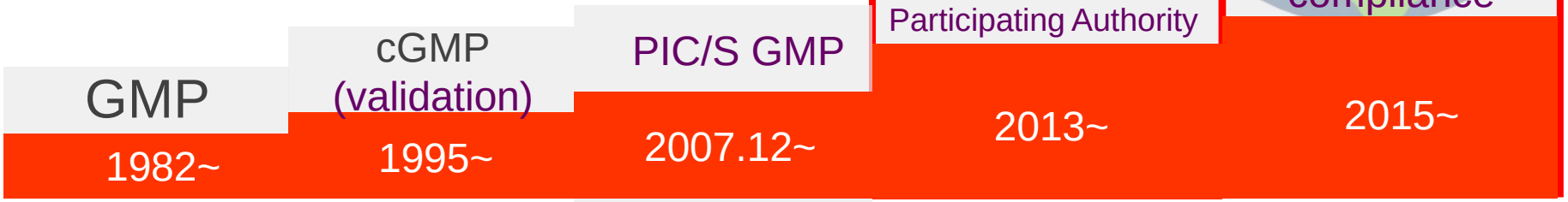
Enhance Drugs Supply Chain Integrity

§ PAA 6-1

- **Government:**
  - ✓Announcing drug items to be **tracked and traced**
  - ✓**Establishing e-reporting system**
- **Stakeholders:**
  - ✓Uses unique identification number to uniformly used by manufacturers, wholesalers and pharmacies
  - ✓Documentation retention period: 5 years

Optimize regulations for quality-1

- PIC/S Participating Authority since 2013
- All manufacturers shall fully comply with the current version of PIC/S GMP Guide since 2015
- Current status: (up to 31th Dec 2017)
  - Domestic pharmaceutical drug product manufacturers: **137**
  - Companies not comply with PIC/S GMP
    - *shall cease manufacturing and be delisted.*



Optimize regulations for quality-2

Manufacture

- **GMP**

Good Manufacturing Practices

Storage, Transportation

- **GDP**

Good Distribution Practices

Hospital, Clinics to Patients

- **GDP**

Good Dispensing Practices

Ensuring the quality and package integrity during the manufacturing, storage and transportation.

Quality Assurance

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Implementation Schedule of GDP

Announcement of " Guide to Good Distribution Practice for Medicinal Products" 【2015-7-16】

NEW

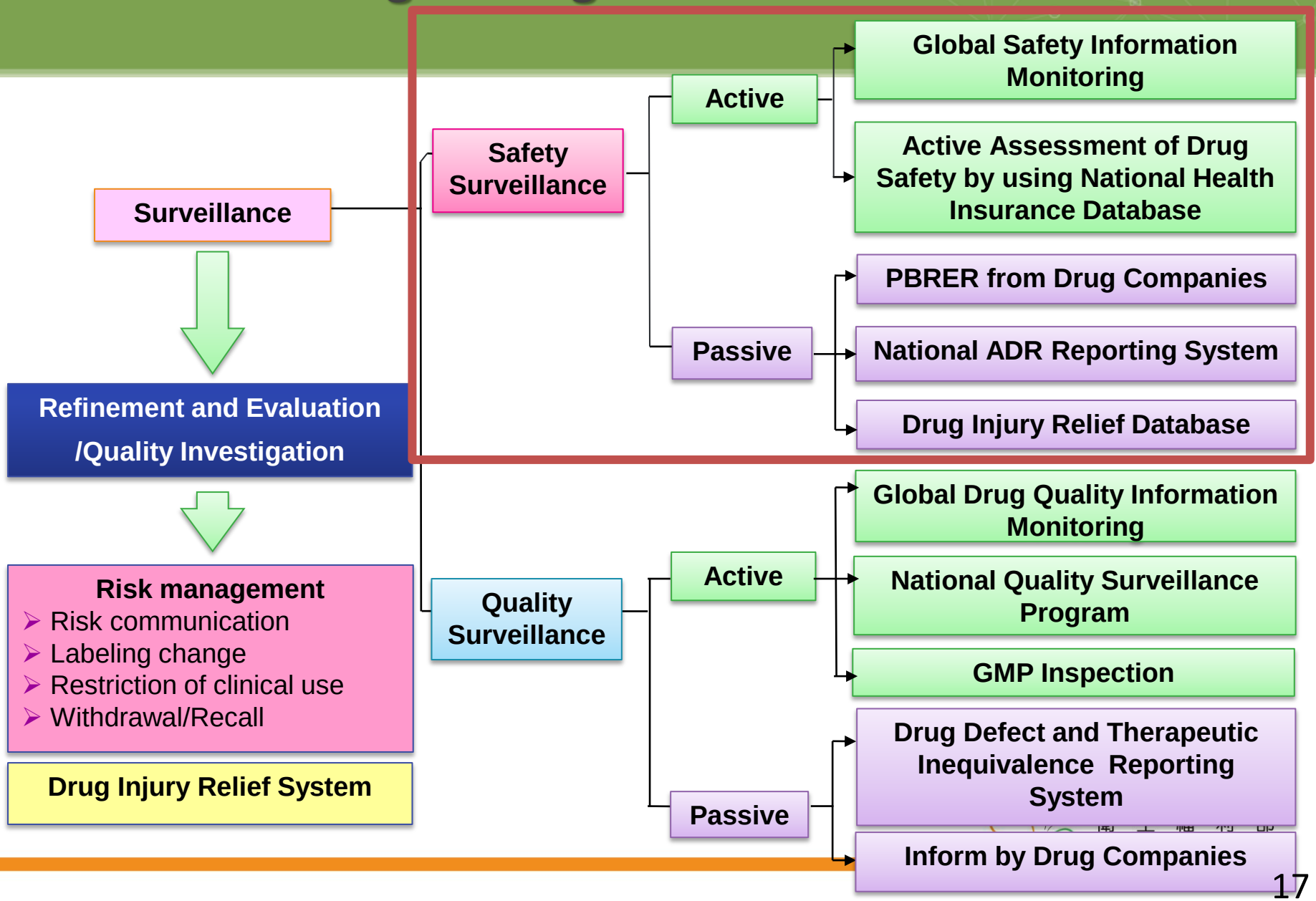
From July 1, 2016, all **new** manufacturer, logistics company and **license applicator** shall comply

ALL

By January 1, 2019, the **existed** manufacturers, logistics companies and **license holder** shall comply

Inspection: with GMP, or application before 2017-12-31, whichever comes first

Post-marketing Management



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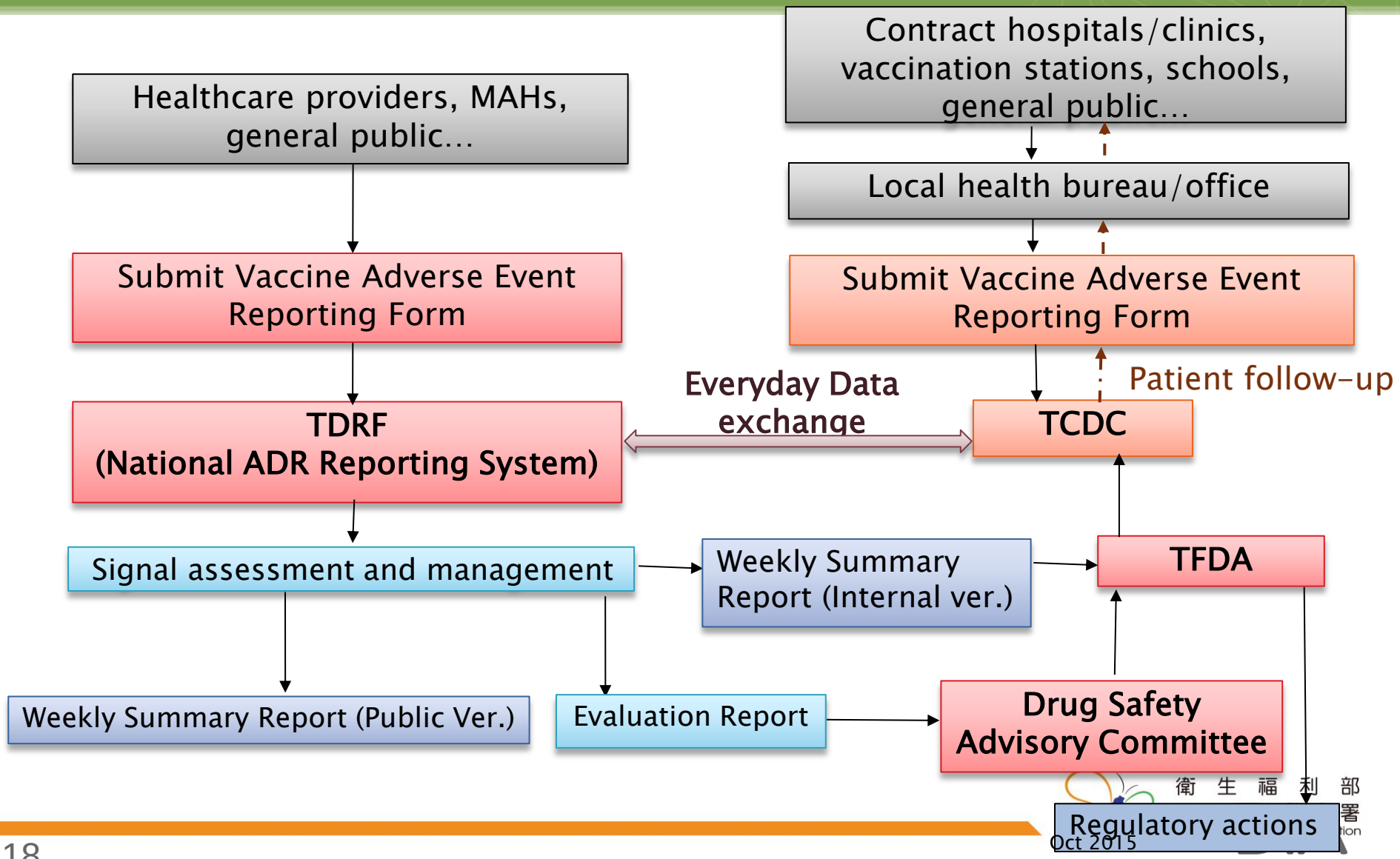
Schematic Flow of Information within the Passive Surveillance Program



AEFI Reports Monitoring for Annual Seasonal Influenza Vaccination

- During 2009 pandemic influenza A (H1N1) season, the ADR reporting system was integrated into the mass influenza vaccination campaign program operated by Taiwan Centers for Disease Control (TCDC) to serve as a tool for Adverse Event Following Immunization (AEFI) collection and vaccine safety signal detection
- This collaborative surveillance mechanism has then been routinely conducted during the following influenza seasons.

DIA DEVELOP INNOVATE ADVANCE

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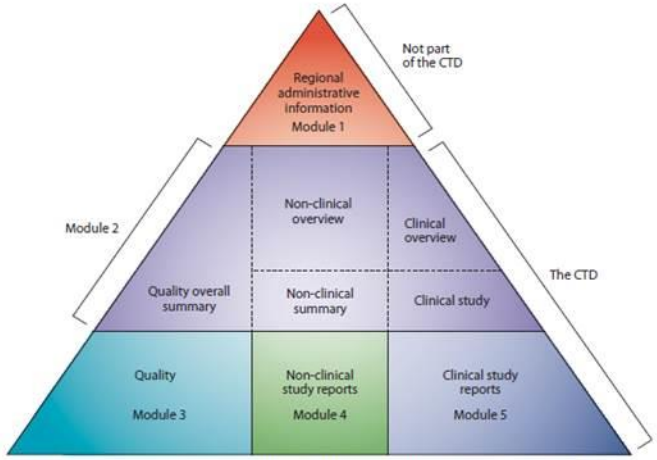
Common Technical Document Format

2012 November 01

When submitting NDA, ICH Common Technical Document (CTD) Format should be used.

1. **Regulatory administrative information**
2. **Overall summary (Quality, Non-clinical, Clinical)**
3. **Quality**
4. **Non-clinical study reports**
5. **Clinical study reports**



The CTD triangle, the Common Technical Document is organized into five modules. Module 1 is region specific and modules 2, 3, 4 and 5 are intended to be common for all regions.

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Technical Document

Quality

- Source Controls (Reagents, Excipients)
- Virus or Cell Banks (Size, Passage number)
- Characterization
- Manufacturing
- Process Control
  - **Safety issues**
    - Sterility
    - Purity/Impurities
    - Identity
  - **Efficacy issues**
    - Potency
    - Stability
- Batch analysis
- **Stability**

Non-Clinical

- Pharmacology (relevant animal models of disease; injury if possible)
- Toxicology (relevant healthy a nimal species)

Clinical

- Current clinical experience
- Study design (administration procedure, proposed dose levels, regimen, escalating)
- Selection of patients (inclusion/exclusion criteria)
- Safety evaluations
- Efficacy evaluations
- Statistical considerations

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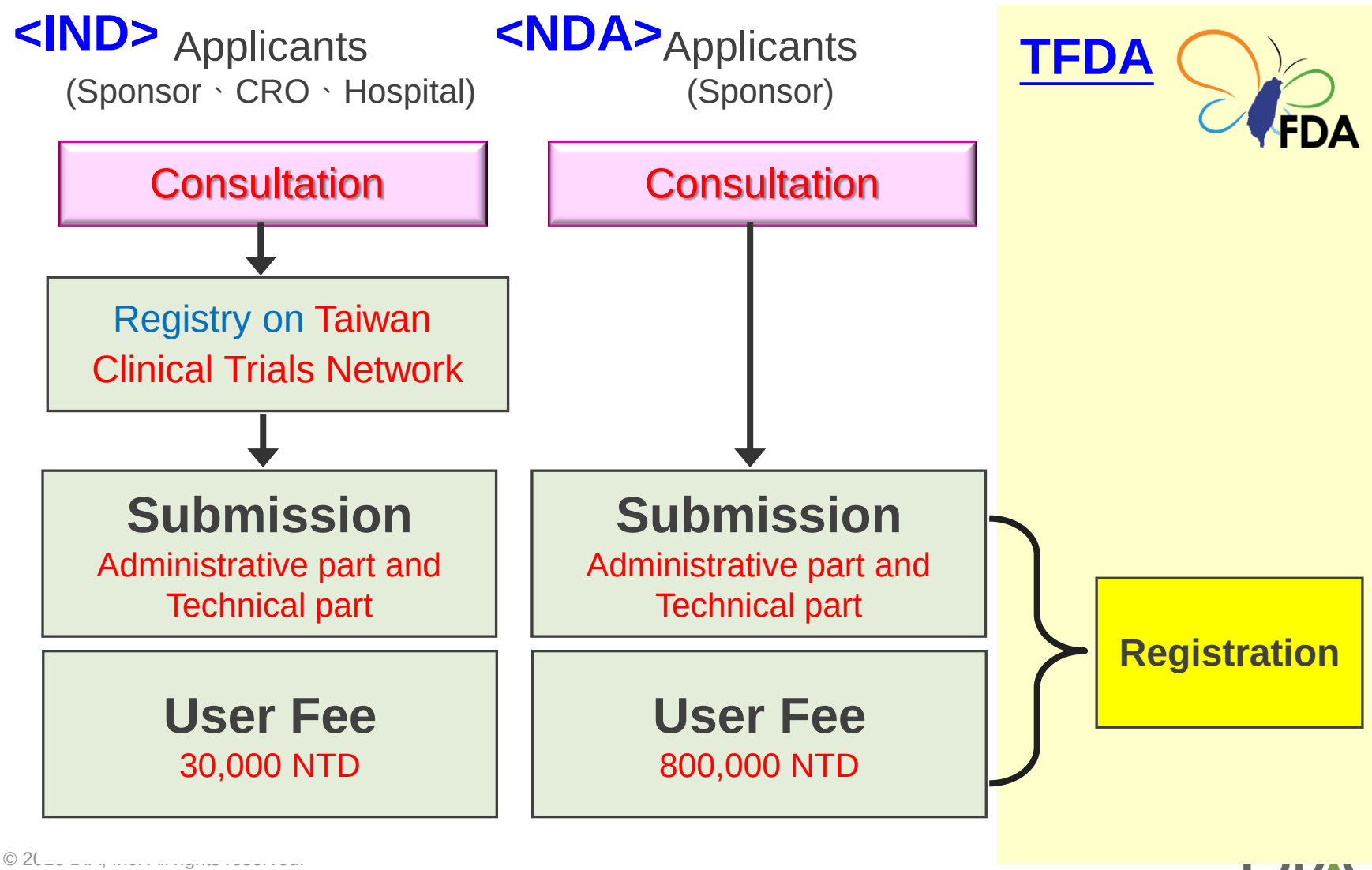
Application Process



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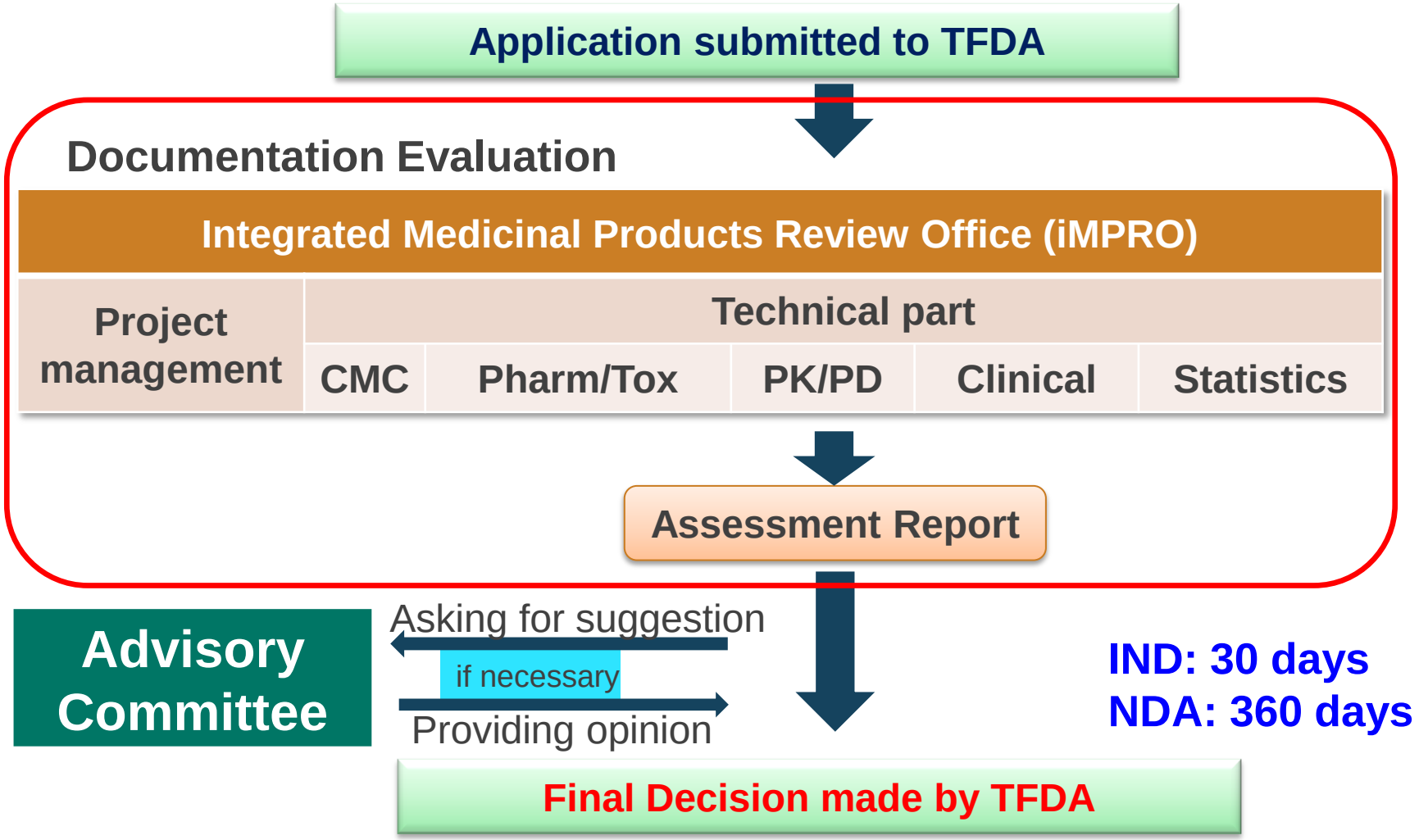
Evaluation Process



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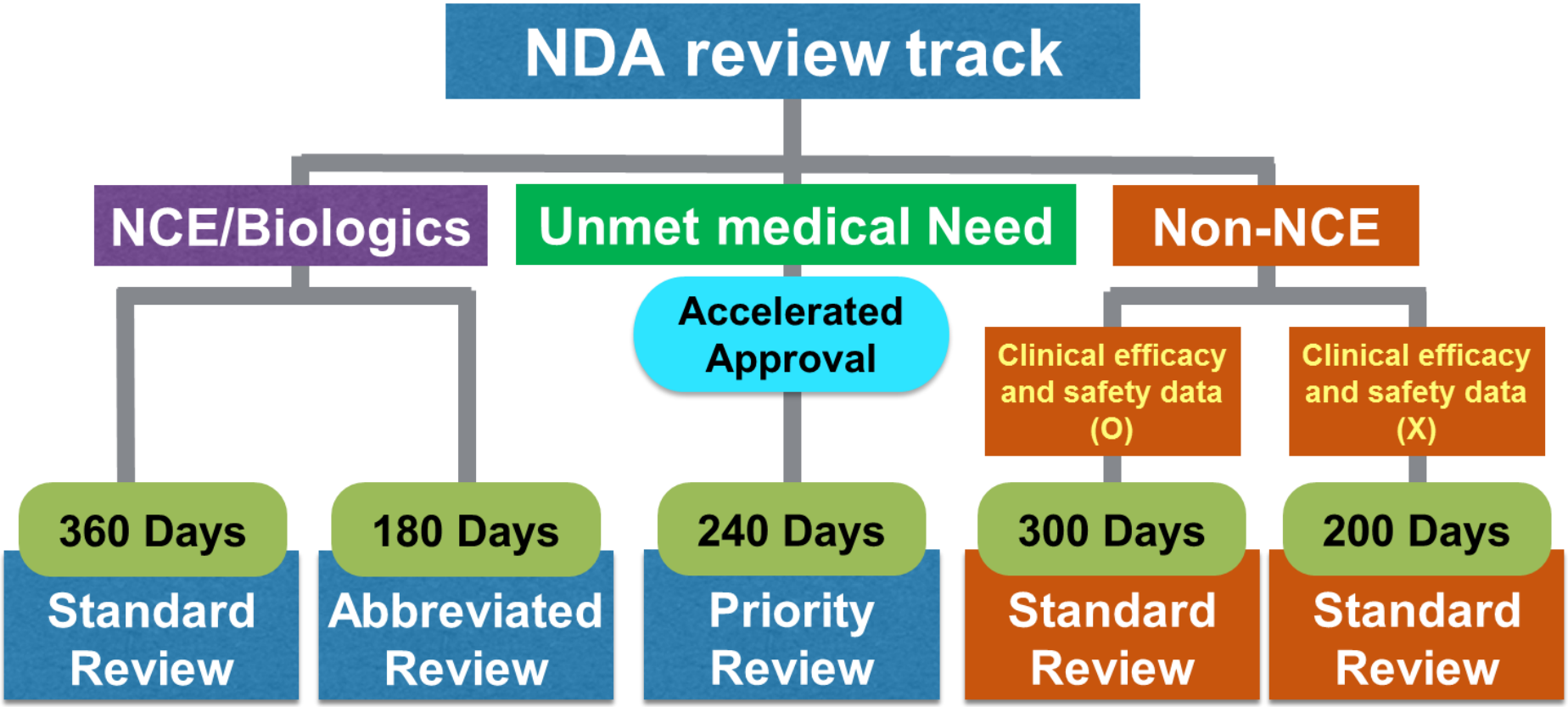
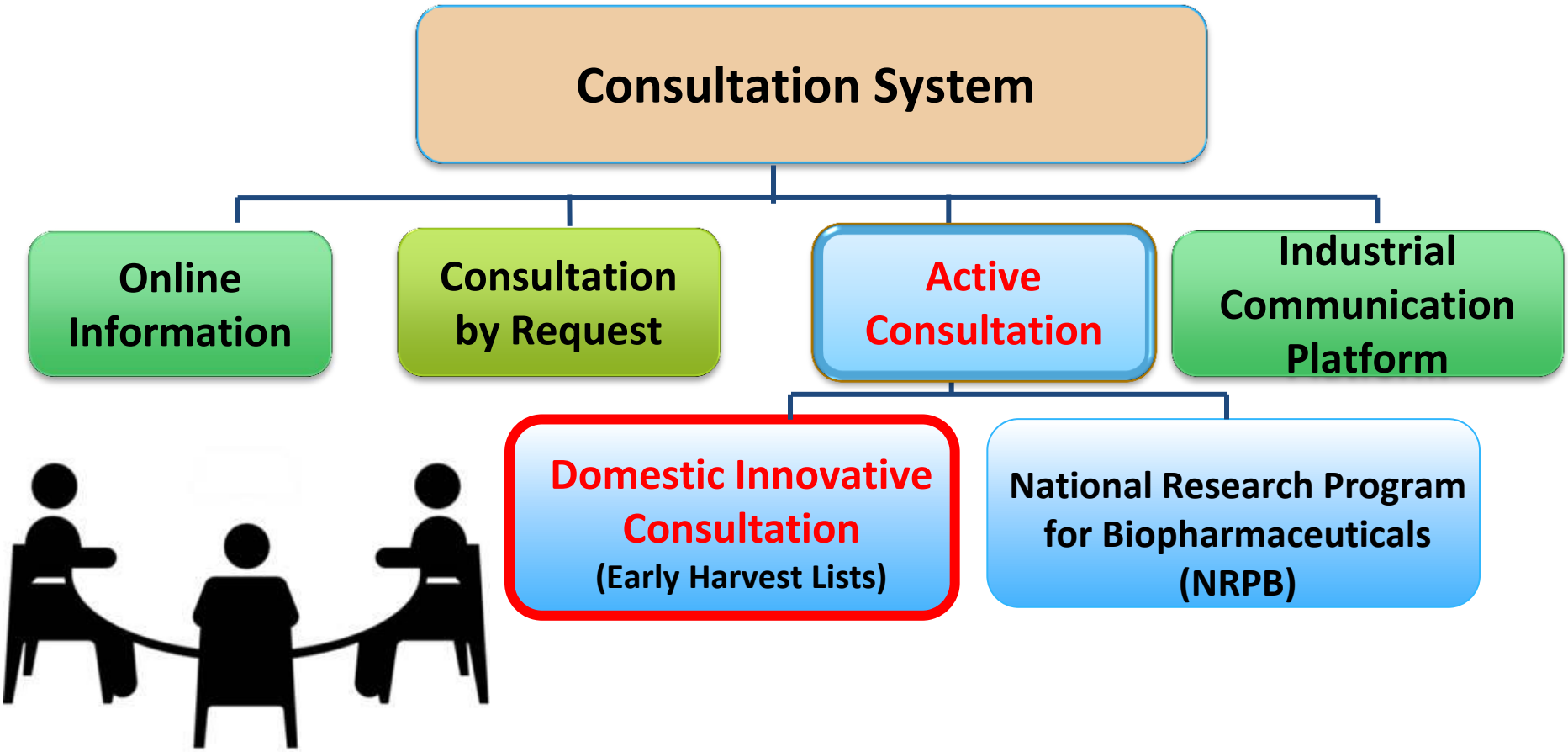
Expedited Programs for NDA



*Priority Review (meet 2 of the following criteria):
- new drug
- serious disease + unmet medical needs
- priority counseling + R&D grants + unmet medical need

*Abbreviated Review: NCE + US FDA, EMA, MHLW approved (2 out of 3)

Consultation System



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Domestic Innovative Consultation

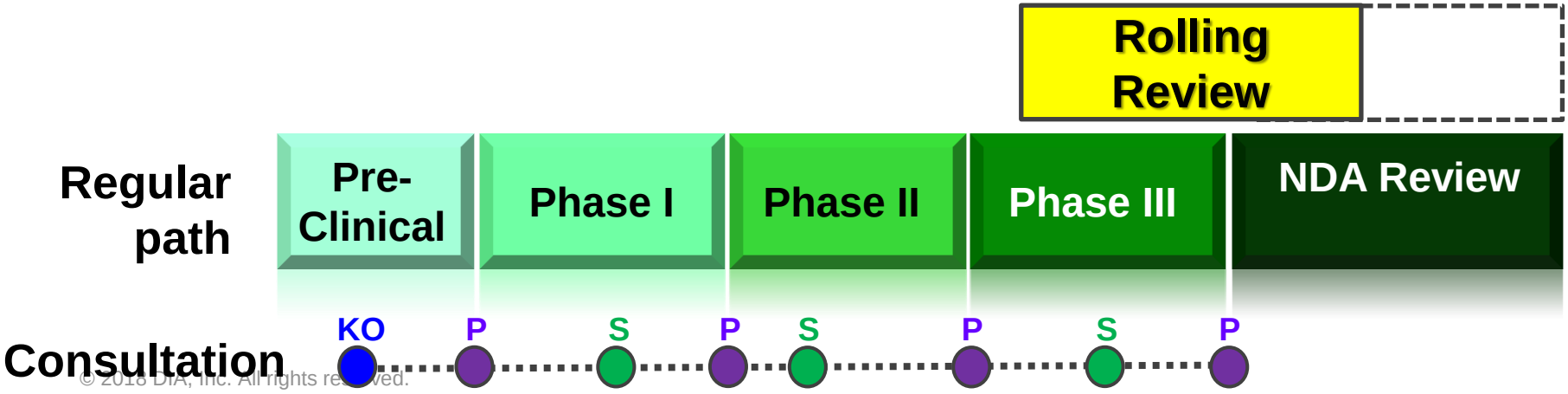
To facilitate medicinal products development and marketing approval

Meeting types:

- Kick-off meeting
- Sponsor meeting
- Pre-filing meeting

What is needed at consultation?

- Well-developed & -controlled manufacturing information
- Preclinical studies to show safety and effect of products
- Provide evidence to support human dosing and scientific rationale



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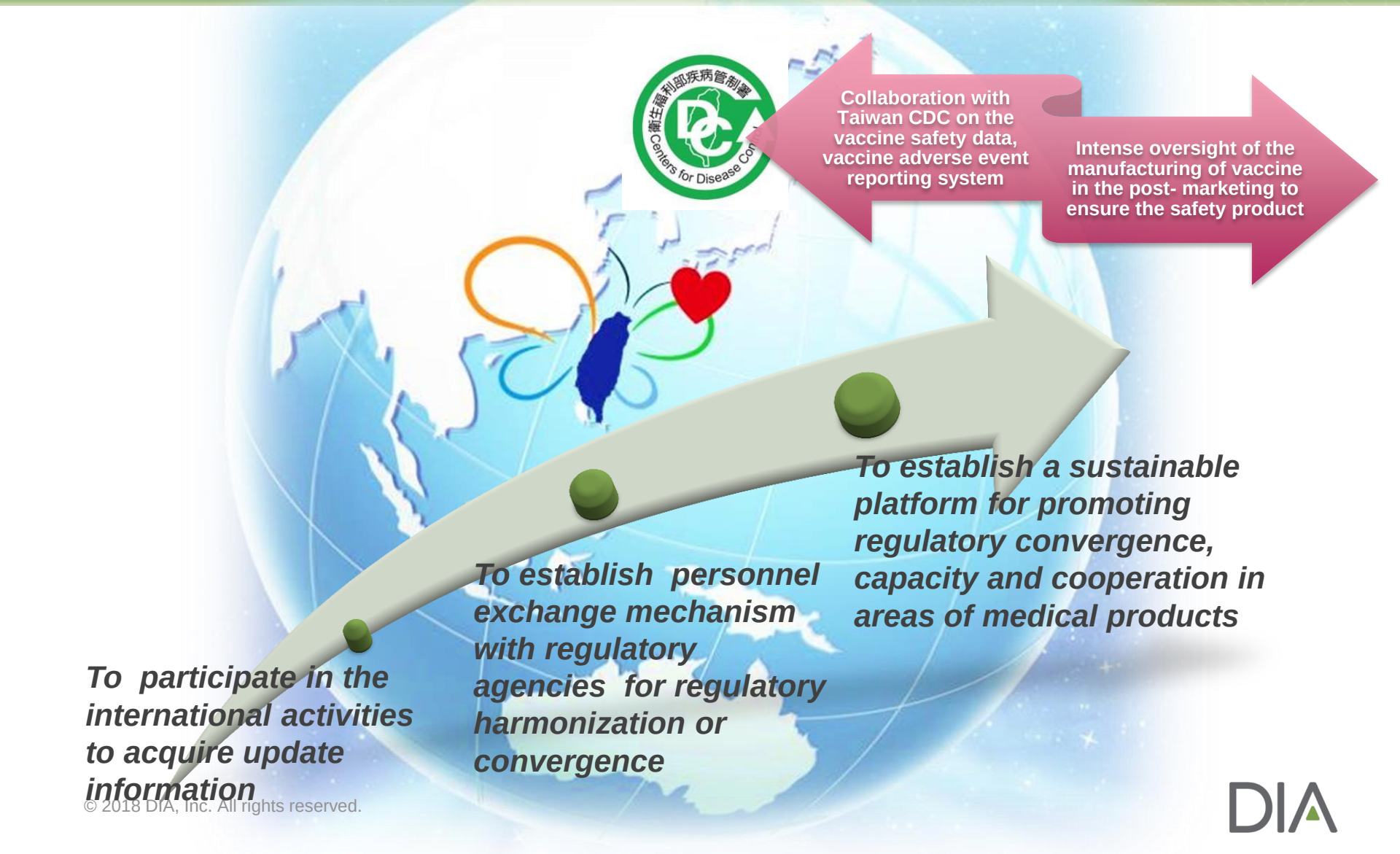
Regulatory Cooperation



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Triple-Win Situation

Ensure drug safety, efficacy, quality and accessibility

Harmonization with international regulations

Product promotion

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Thank You for Your Attention!






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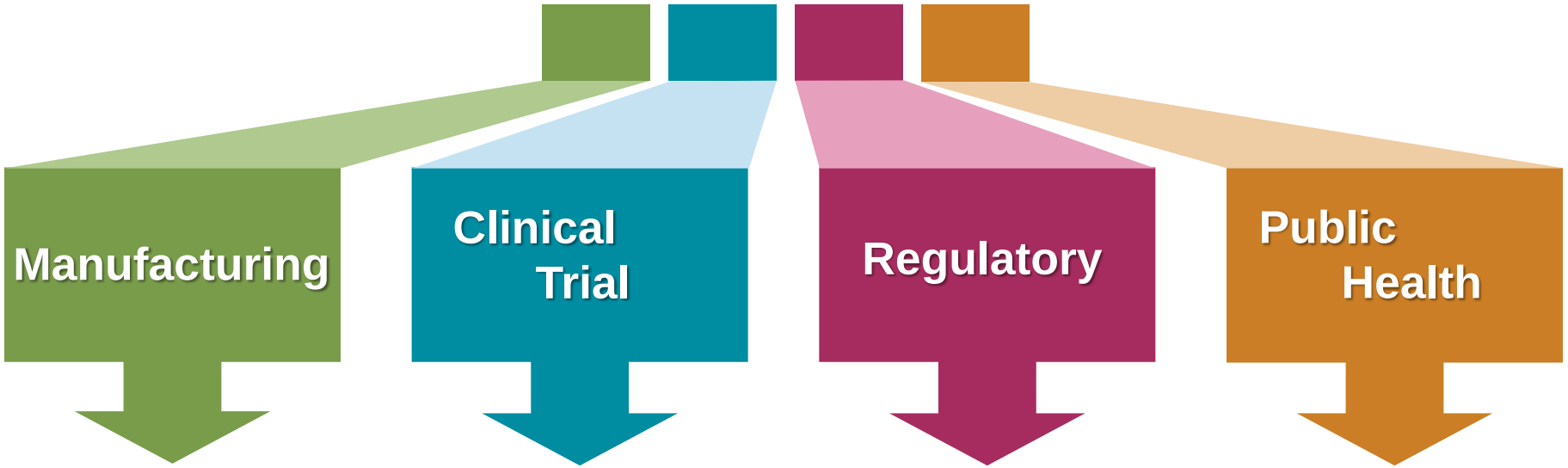
Challenges for pandemic vaccine development

Considerations



Seed virus development
Potency testing method and reagents

Antigen dose, number of doses
Timing of availability of clinical data

Pathways and regulatory process to speed vaccine approval
Facilitating vaccine manufacturing and availability

Vaccination program
Assuring safety and public confidence

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