The 9th Asia Regulatory Conference

Good Registration Management (GRM) to Strengthen the Product Registration System in Asia

-Regulator and Industry Views from APEC CoE Pilot Training-

Product Registration System in Taiwan and the Training

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Tokyo, Japan

April 6, 2017

衛生福利部
食品藥物管理署
FDA Food and Drug Administration

http://www.fda.gov.tw/

Outline

01 Introduction of TFDA

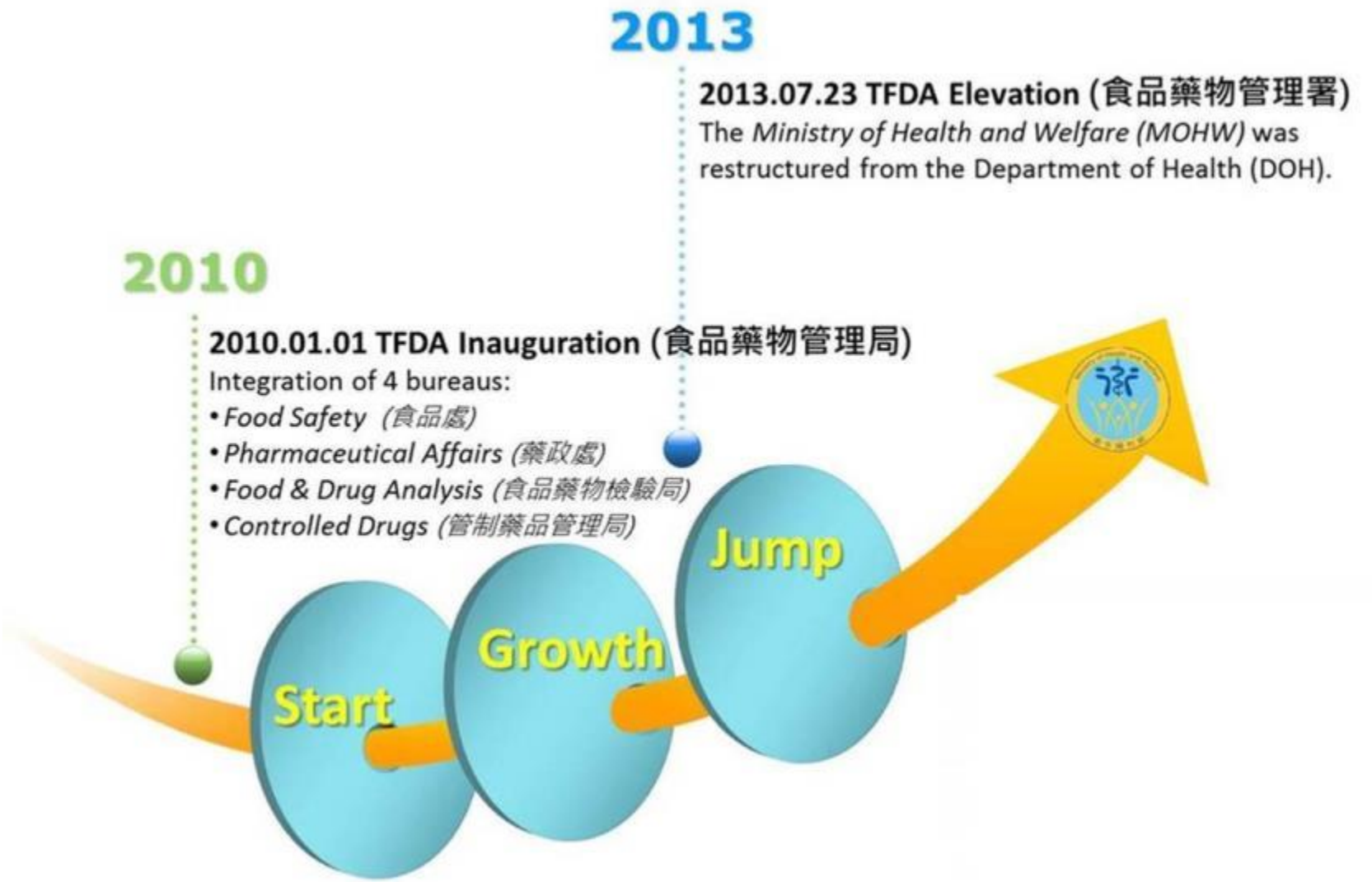
02 Life Cycle Management of Medicinal Porducts

03 Current Registration System

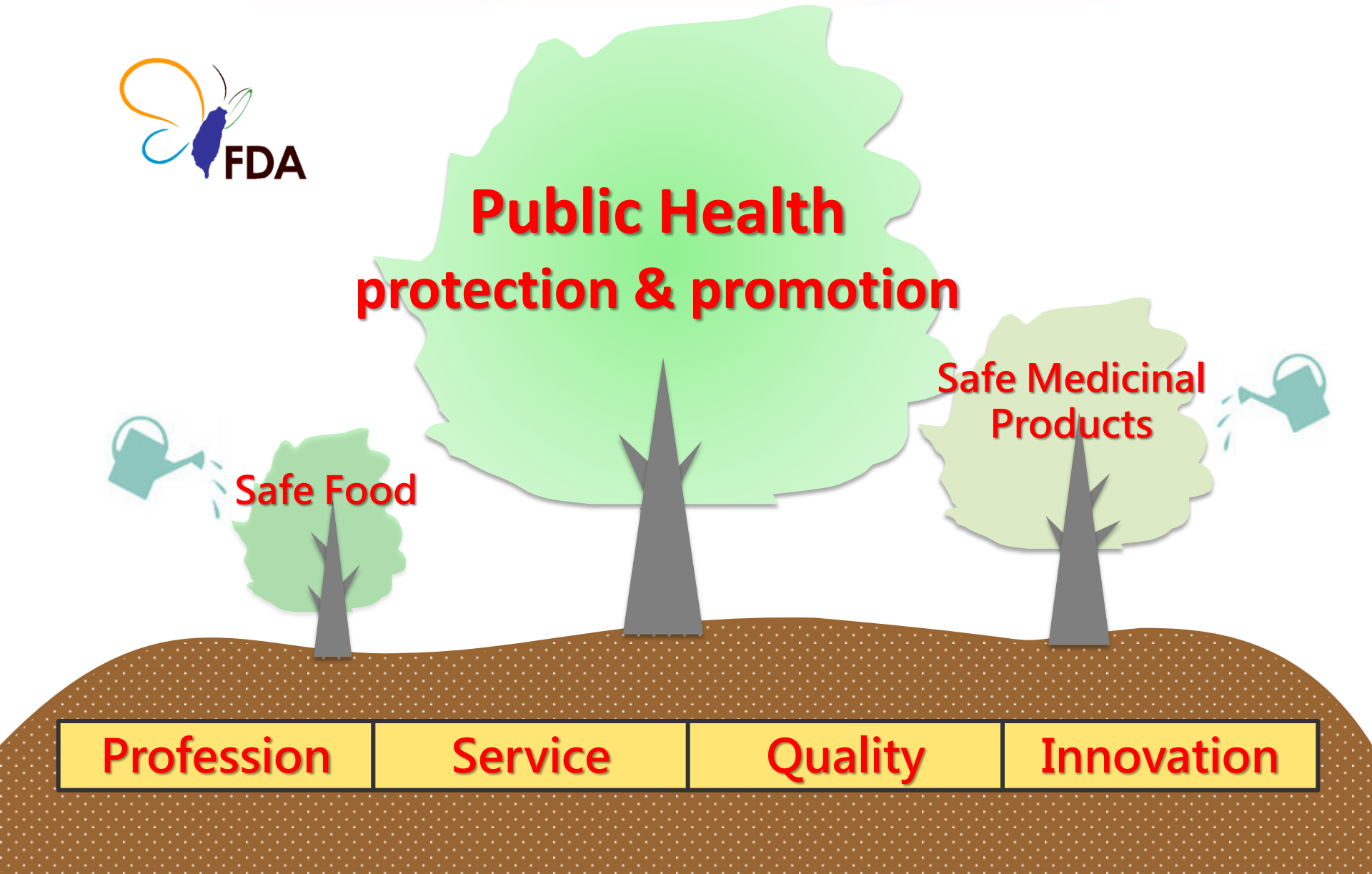
04 Training and Continuing Education

05 Future Prospects

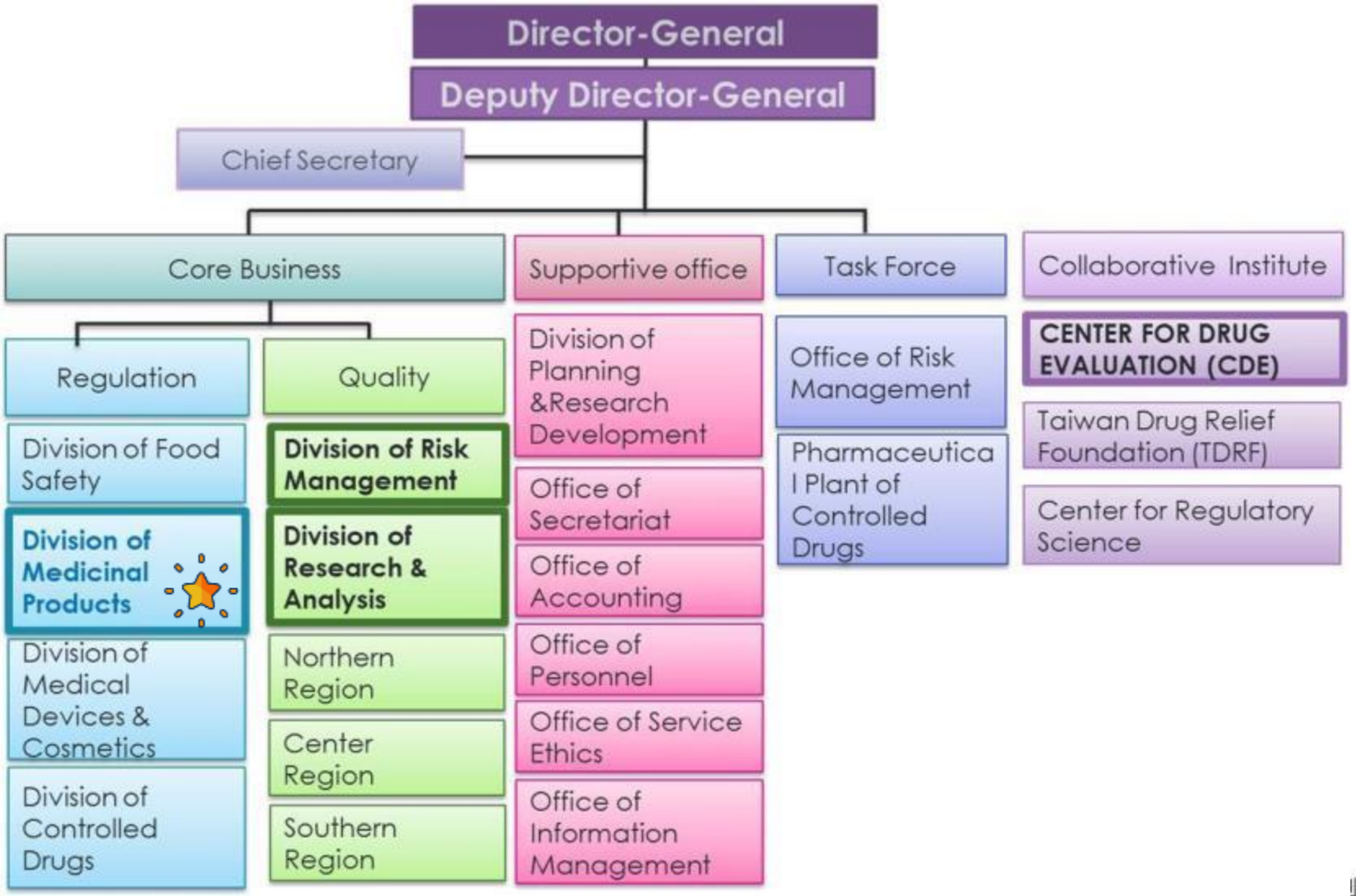
Establishment of TFDA



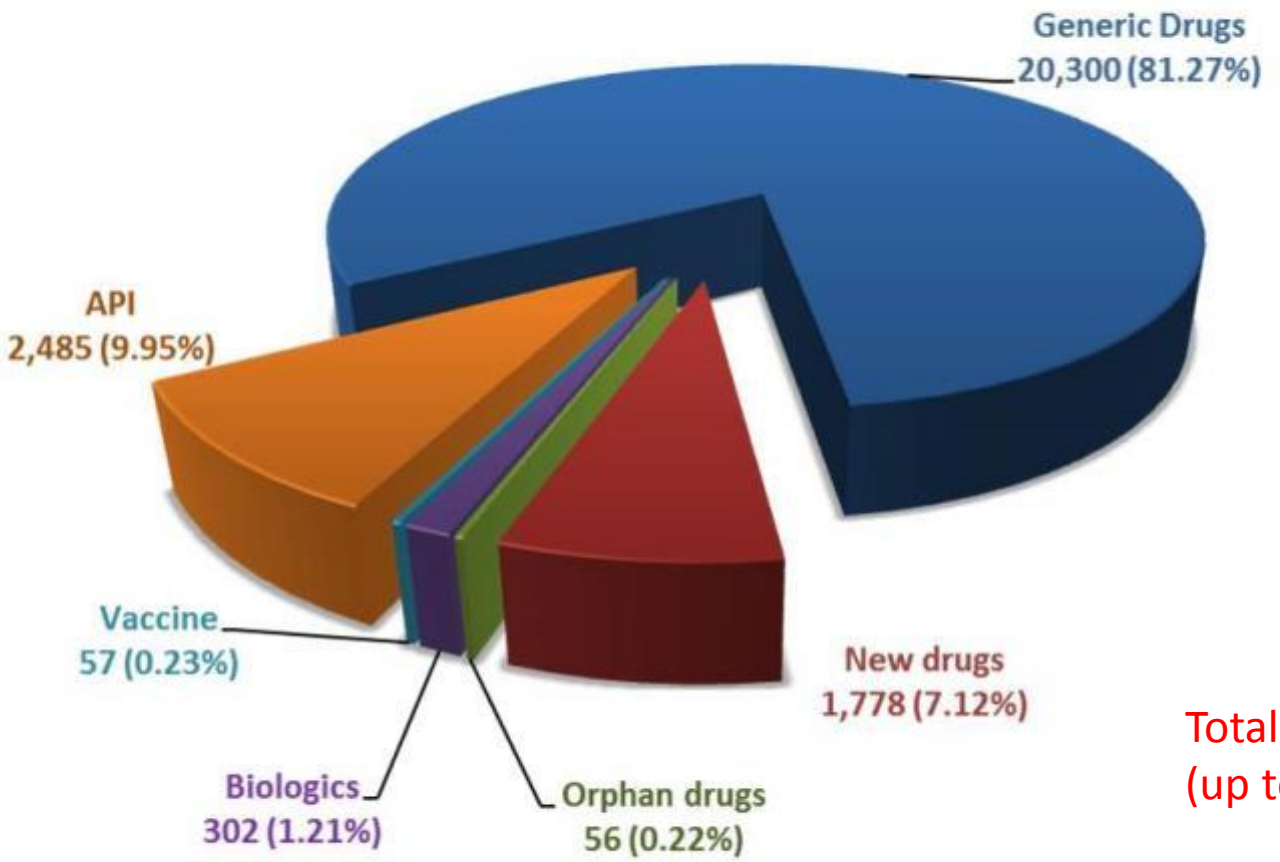
Mission, Vision, and Core Value



TFDA Organization Chart



Statistics on Pharmaceutical Licenses



Total: 24,978
(up to Dec 31, 2016)

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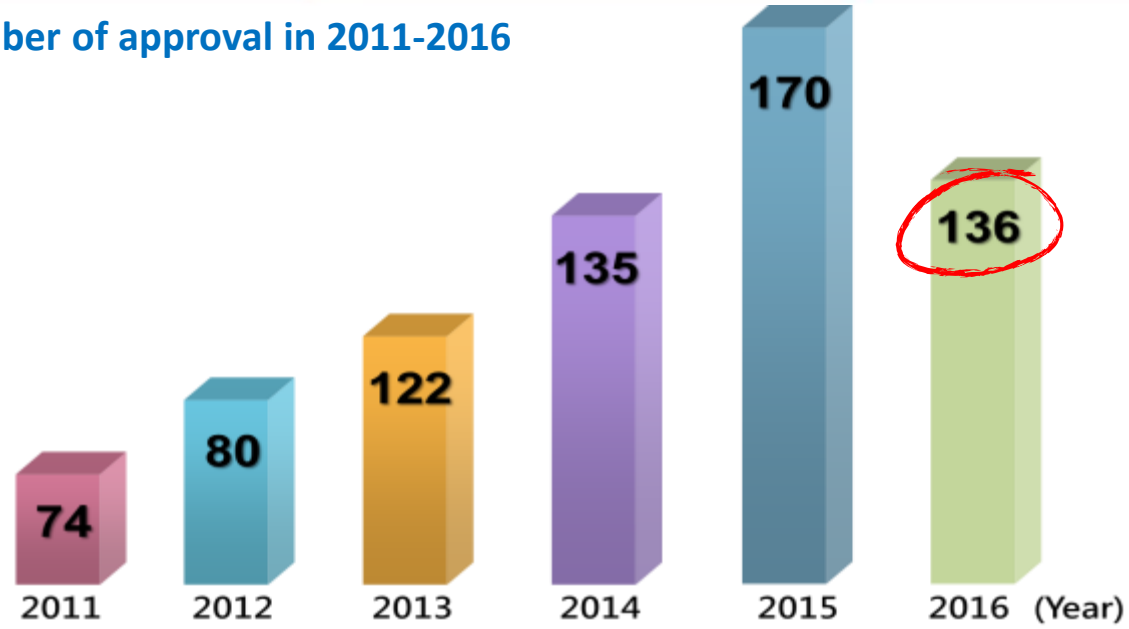
The Statistics of New Drug Approval in Taiwan

The number of approval in 2011-2016



Number of approvals	136											
Types	Domestic						Import					
Numbers (%)	8 (6%)						128 (94%)					
Types	Chemical			Biologics			Chemical			Biologicals		
Numbers	8			0			99			29		
Numbers	New chemical entity	2	4	Vaccine	0		New chemical entity	42	67	Vaccine	3	
	New combination	2		Plasma derivative	0		New combination	15		Plasma derivative	0	
	New indication	0		Toxoid	0		New indication	4		Toxoid	0	
	New route of administration	0		Genetically engineered drugs	0		New route of administration	6		Genetically engineered drugs	26	
	New dosage forms	3	4				New dosage forms	14	32			
	New administration doses	0					New administration doses	2				
	New unit strengths	1					New unit strengths	16				

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Life Cycle Management of Medicinal Products

Medical Care Needs/Basic Research → Product Development → Pre-clinical Studies → **IND** Clinical Trial → **NDA** Market licensing → Production → Postmarket Surveillance

Pre-Market Approval

- GLP
- GCP
- Registration
- Consultation
- IRB
- SUSAR Reporting
- Insurance

Post-Market Control

- Lot release
- Supplement (post-licensure changes, i.e., new indication or facility…)
- GDP
- GPvP
- GPP
- ADR & Product Defect Reporting
- Drug injury relief
- RMP

PICS/GMP

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Legislation and Regulations

Legislation and Regulations on Medicinal Drugs	
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 Biotechnological Products Guidance for Registration of Biosimilar Products Guidance for Registration of Biosimilar monoclonal antibodies Guidance of Stability Testing of Biological Products Guidance of Comparability of Biological Products Guidance for Registration of Vaccines Guidance for Registration of Pandemic Influenza Vaccines Guidance for Registration of Blood Products Guidance for Registration of Allergenic products
International Guidance	ICH/EMA/FDA/WHO guidance which are issued in an issue-specific manner are taken into reference

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Regulations for Quality

- 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 23 February 2017)
  - Domestic pharmaceutical manufacturers: **130**
  - Companies not comply with PIC/S GMP
    - *shall cease manufacturing and be delisted.*

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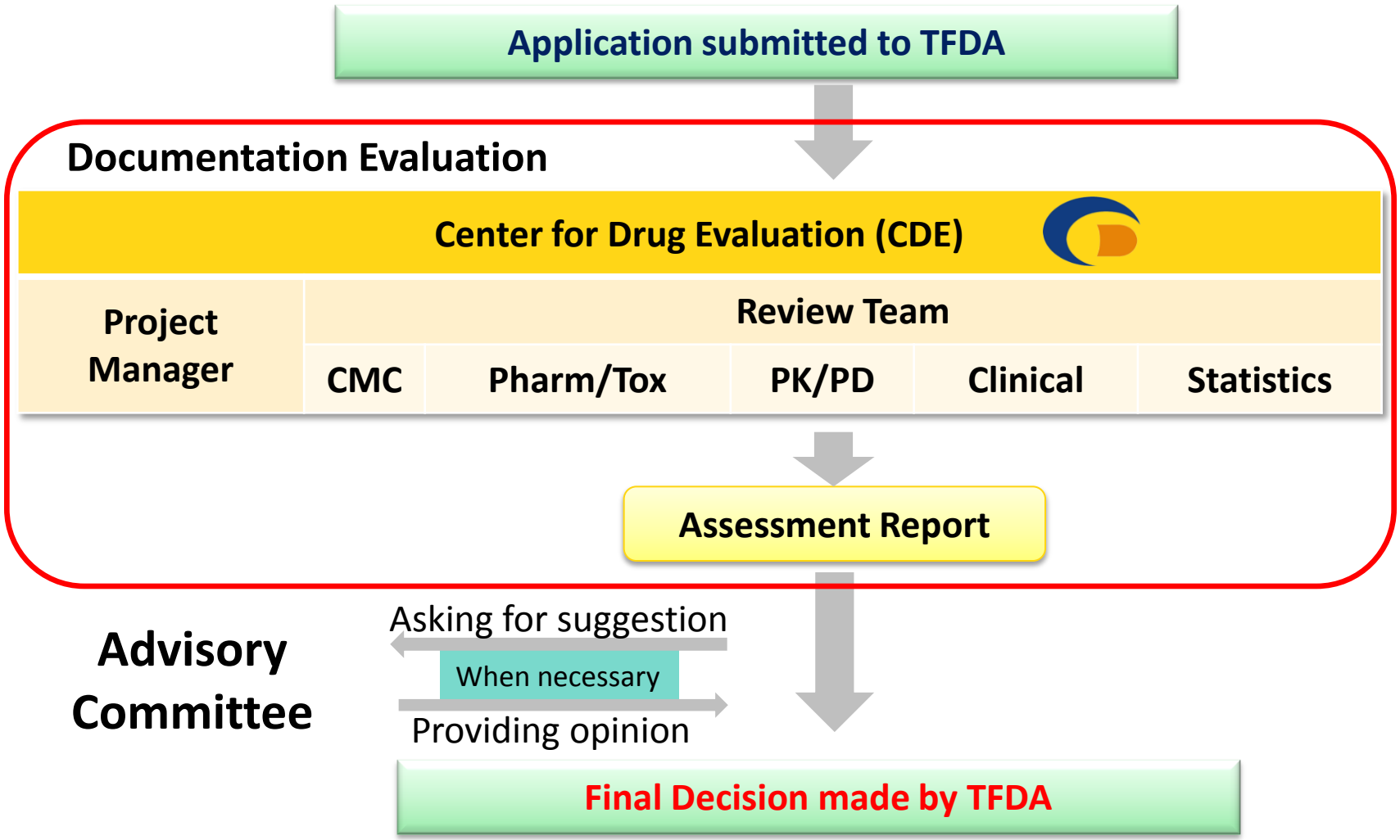
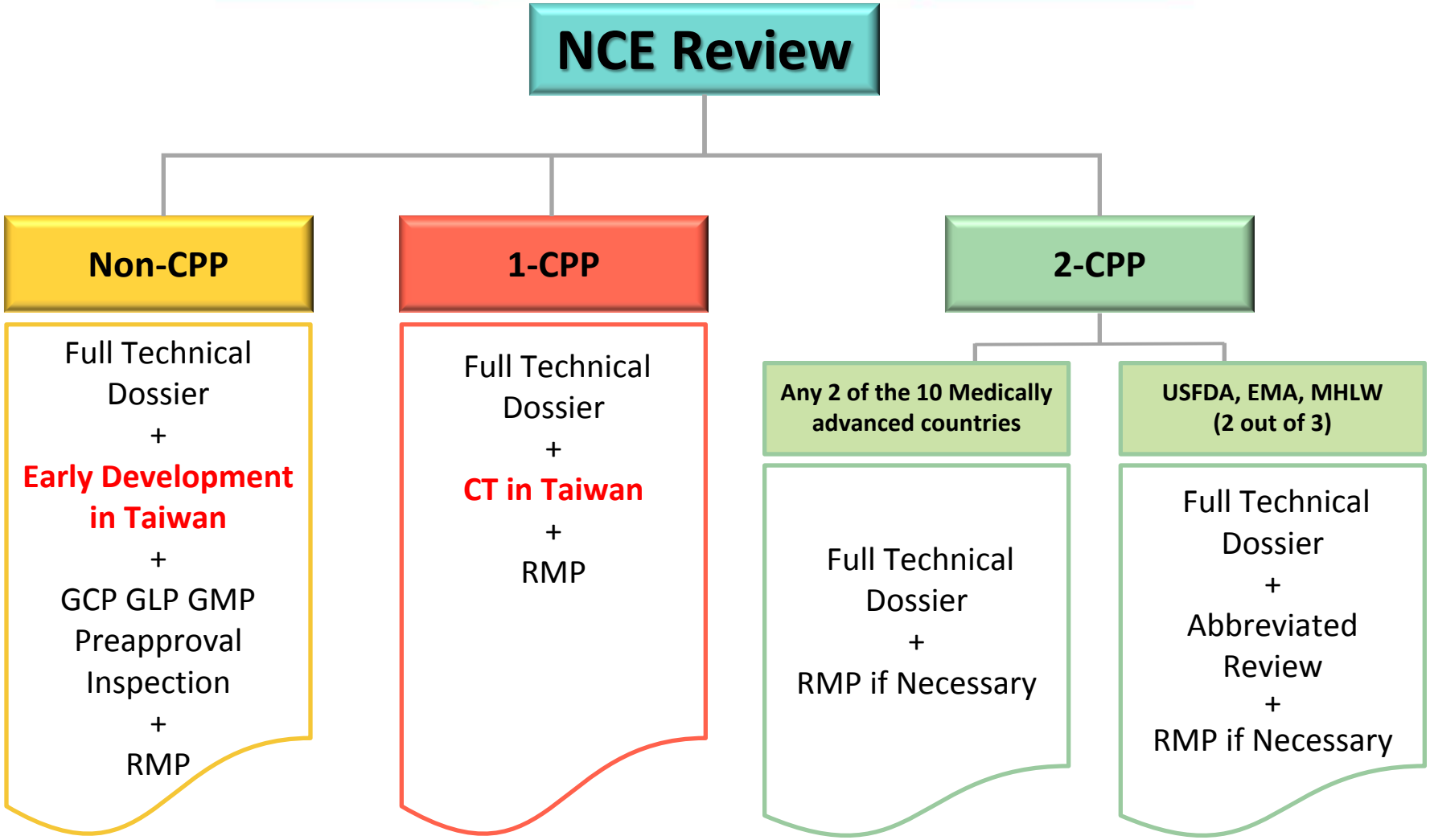
Review Process



Rationalization of CPP Requirements



CPP: Certification of Pharmaceutical Products
RMP: Risk Management Plan

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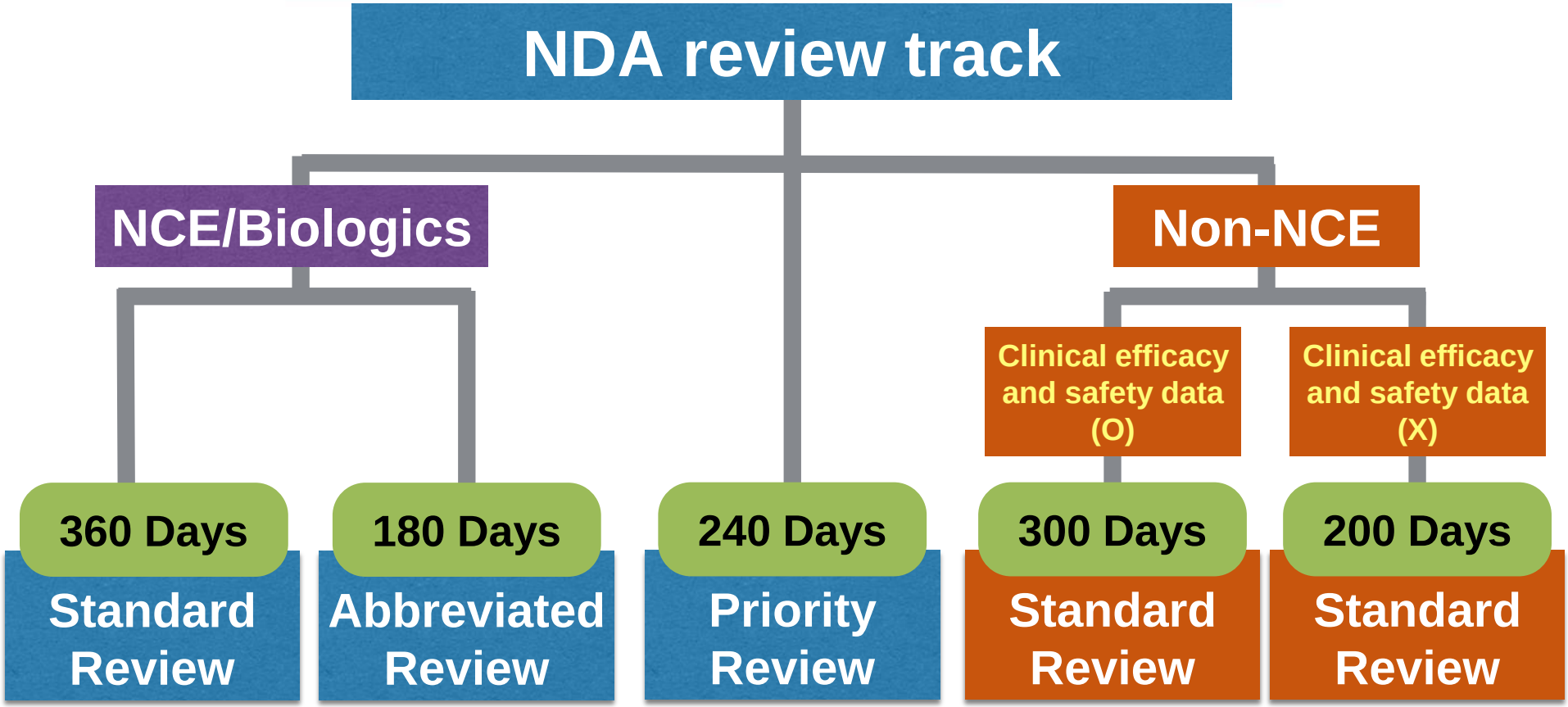
Expedited Review Process

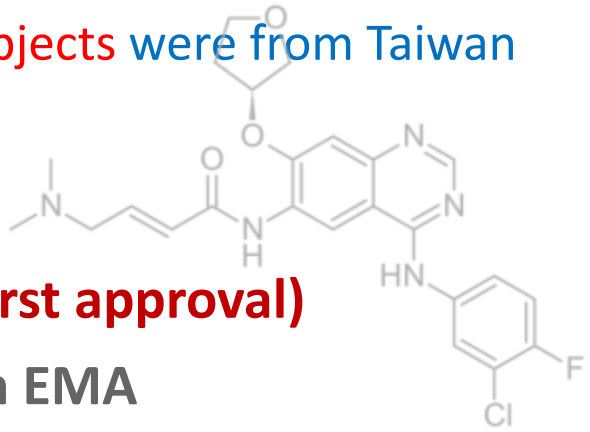


*Priority Review (meet 2 of the following criteria):
- new drug
- serious disease + unmet medical needs
- priority counseling + R&D grants + unmet medical need

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

Case Sharing

- **Afatinib dimaleate**
  - Target therapy drug for advanced non-small cell lung cancer
    - New Chemical Entity
    - Multinational Trials were led by Investigator in Taiwan
      - Phase II : 80% of subjects were from Taiwan
      - Phase IIb/III and Phase III : 20% of subjects were from Taiwan
    - Non-CPP
- **Review Time: 89 days**
- **Approval: May 17, 2013 in Taiwan (globally first approval)**
- **Approval: July 12, 2013 in US, July 25, 2013 in EMA**



MRCT + ***Fast Track*** = ***First approval in the world***

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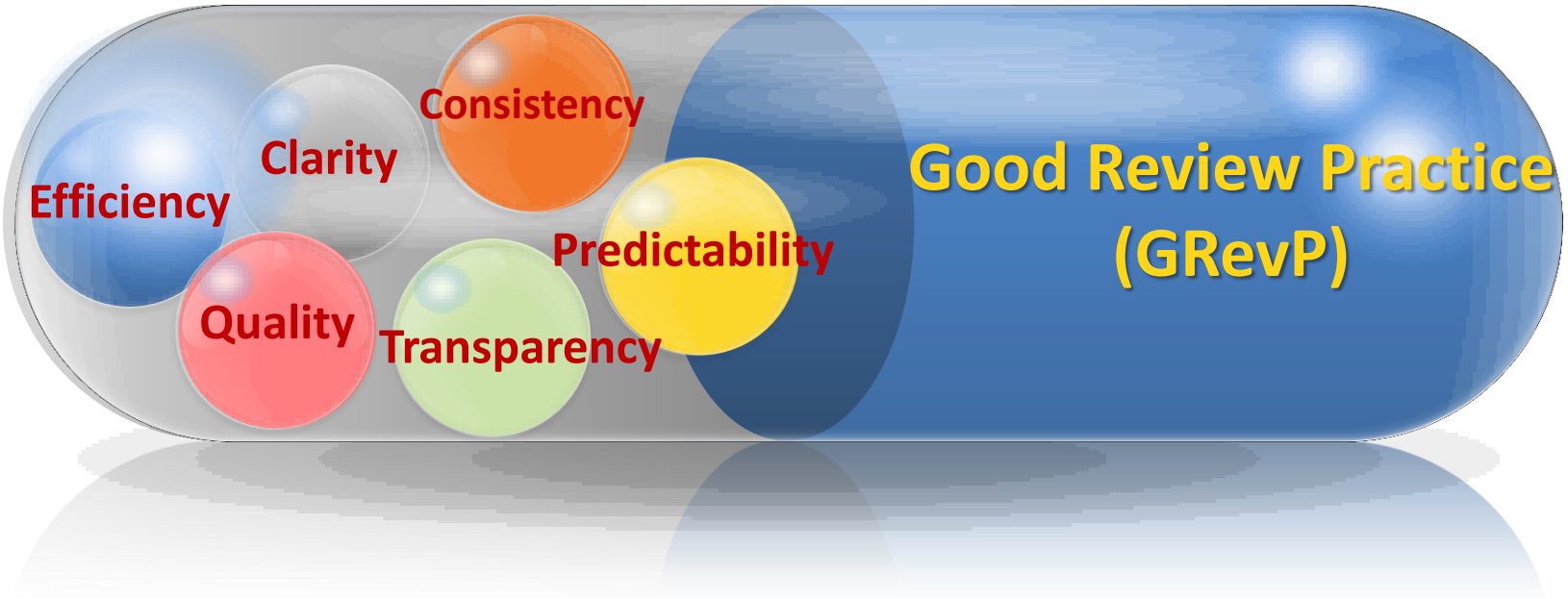
Implementation of Good Review Practice (GRevP)



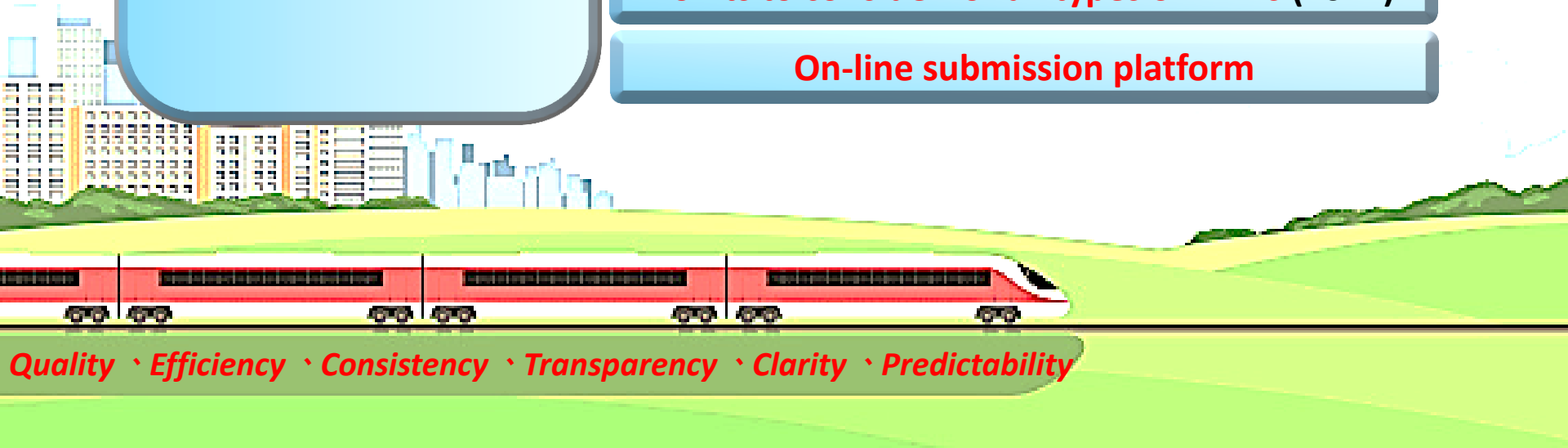
Enhancing Review Efficiency

Efficiency

Pre-clinical | **Clinical** | **Marketing Approval**

Consultation and **Rolling Review** (2016)

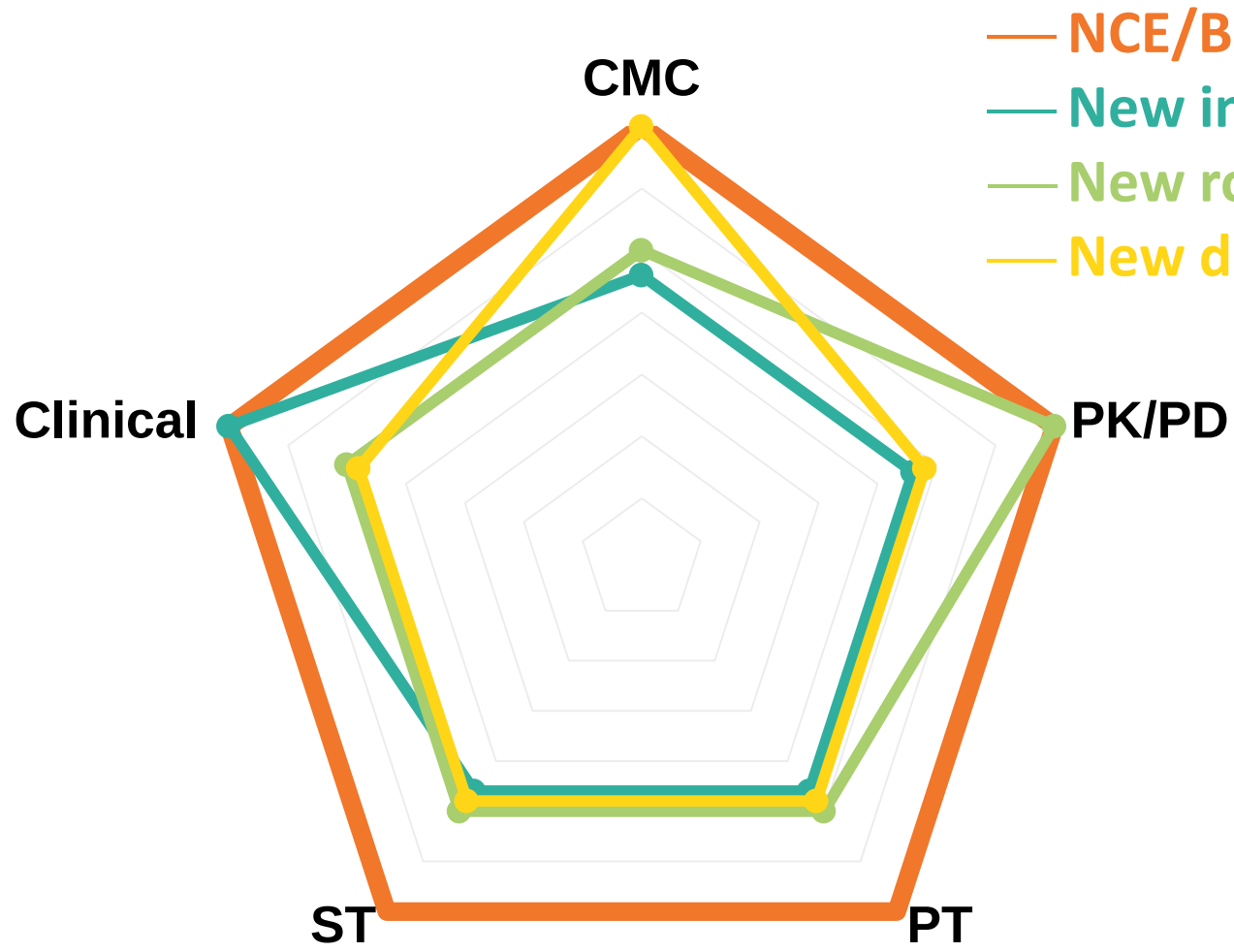
- **Review process and Timeline** (2016)
- **Review time for non-NCE NDA** (2016)
- **Refuse-to–File** (2016)
- **Pre-NDA meeting** (2016)
- **Points to consider for all types of NDAs** (2017)
- **On-line submission platform**



Quality、Efficiency、Consistency、Transparency、Clarity、Predictability

Points to Consider for All Types of NDAs

Clarity



- NCE/Biologics
- New indication
- New route of administration
- New dosage forms

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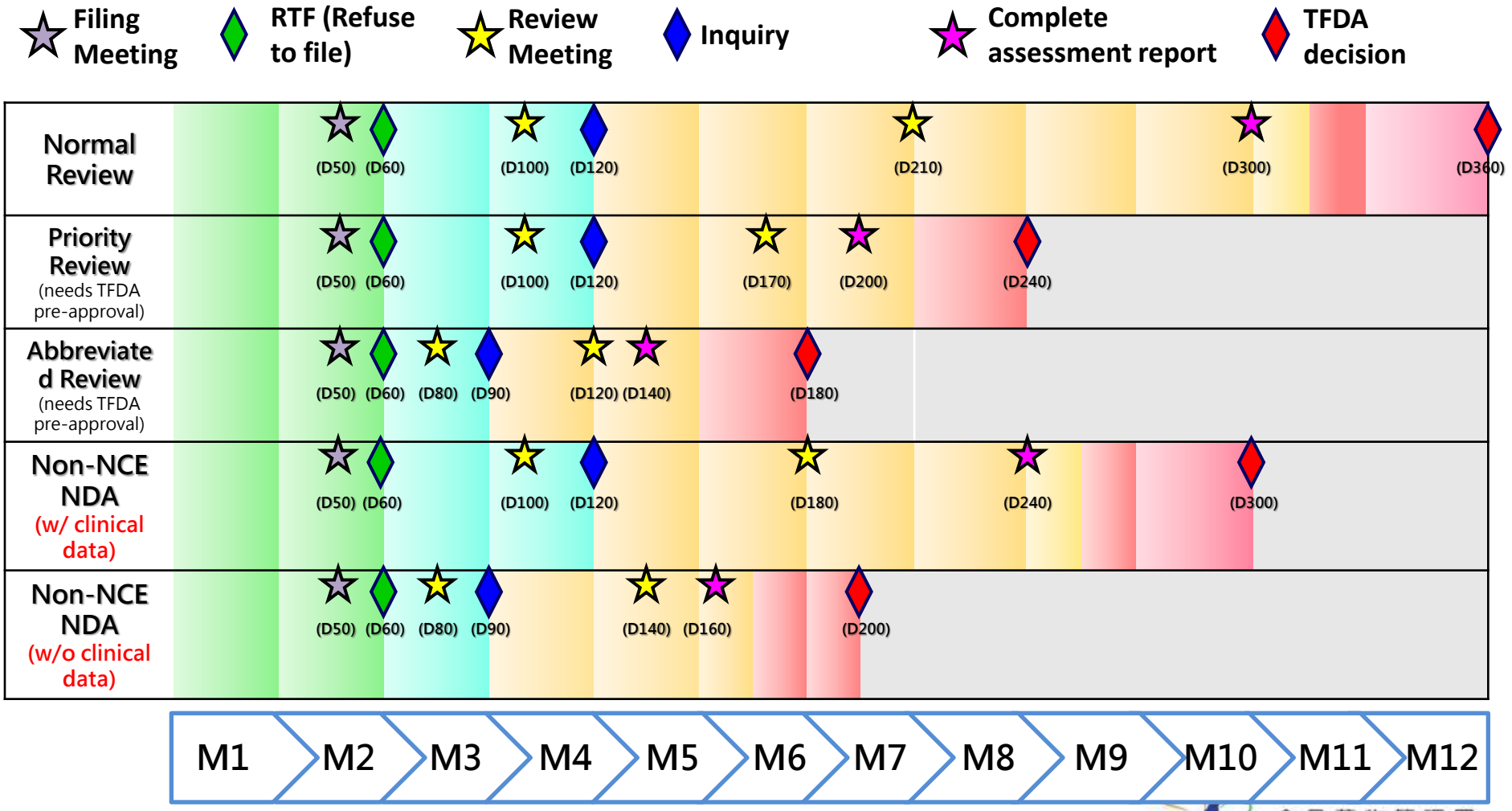
Review Timeline Management

Predictability



QA/QC Meeting

Quality

Integrated **M**edicinal **P**roduct **R**eview **O**ffice

↑ Internal Control Monitoring & Auditing

↑ Resource Integration

↑ Job Integration

↑ Process Integration

Consultation System

Transparency

- Consultation System
  - Online Information
  - Consultation by Request
  - Active Consultation
    - Domestic Innovative Consultation (Early Harvest Lists)
    - National Research Program for Biopharmaceuticals (NRPB)
  - Industrial Communication Platform

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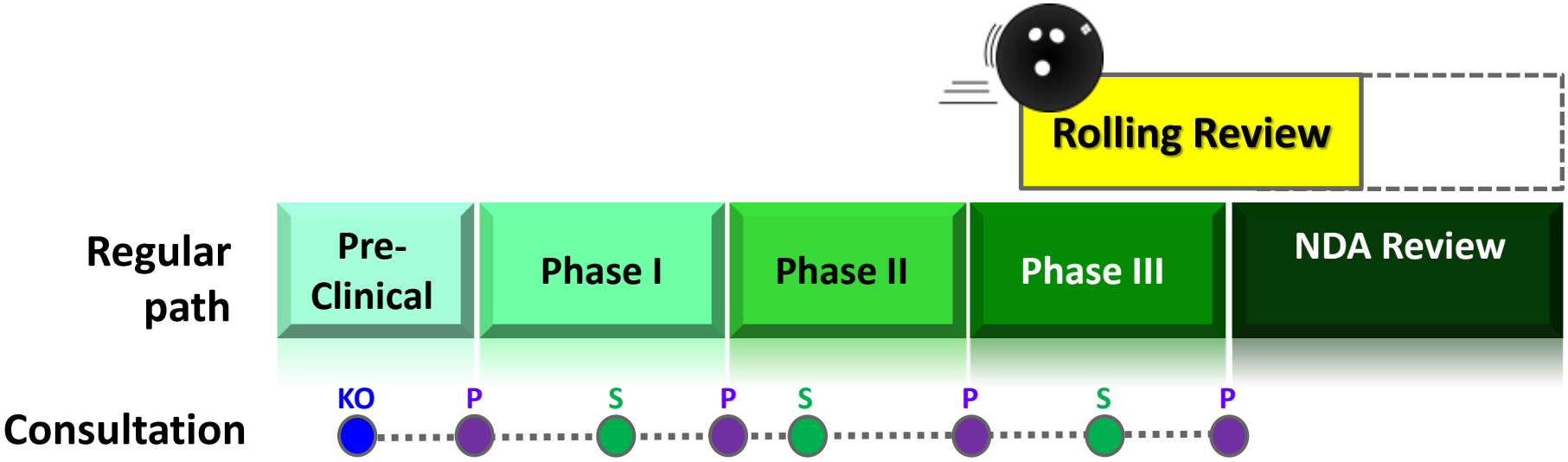
Domestic Innovative Consultation

Transparency

To facilitate medicinal products development and marketing approval

Meeting types:

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



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Domestic Innovative New Drugs Approved in 2014-2016

Nemonoxacin

- NCE
- Treatment of community-acquired pneumonia

Flu Vaccine

- Flu vaccine with adjuvant (Virosome)
- Flu prevention

Ferric citrate

- NCE
- Control of hyperphosphatemia in adult patients with chronic kidney disease

Irinotecan liposome

- New indication & new formulation
- Treatment of pancreatic cancer

Methtlene blue

- Orphan drug
- Treatment of methemoglobinemia

Phenylbutyrate

- Orphan drug
- Treatment of urea cycle disorders

Fomepizole

- Orphan Drug
- Antidote for ethylene glycol or methanol poisoning

Omega-3-acid Ethyl Esters 90

- NCE
- Treatment of hypertriglyceridemia

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The Median Approval Time of NDAs in 2014-2016

	2014	2015	2016
NCE/Biologics	359	346	361
Priority Review	304	171	273
New Indication	181	161	149

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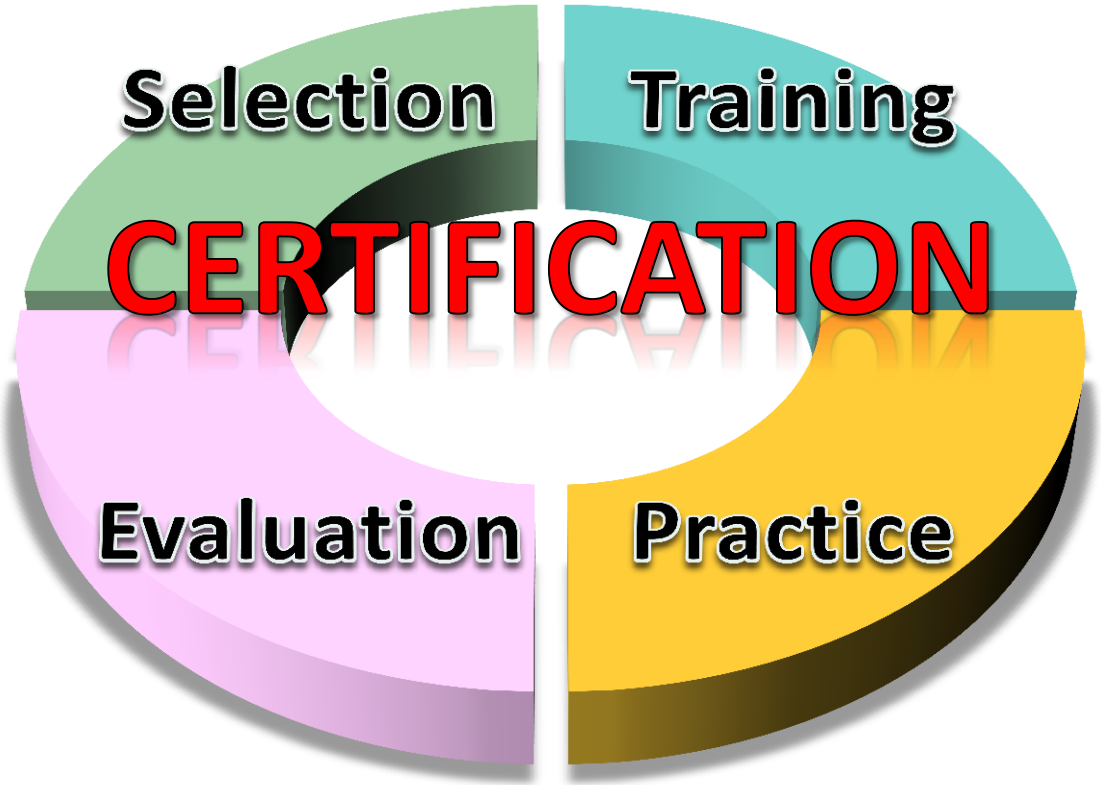
Selection, Training, Evaluation & Practice



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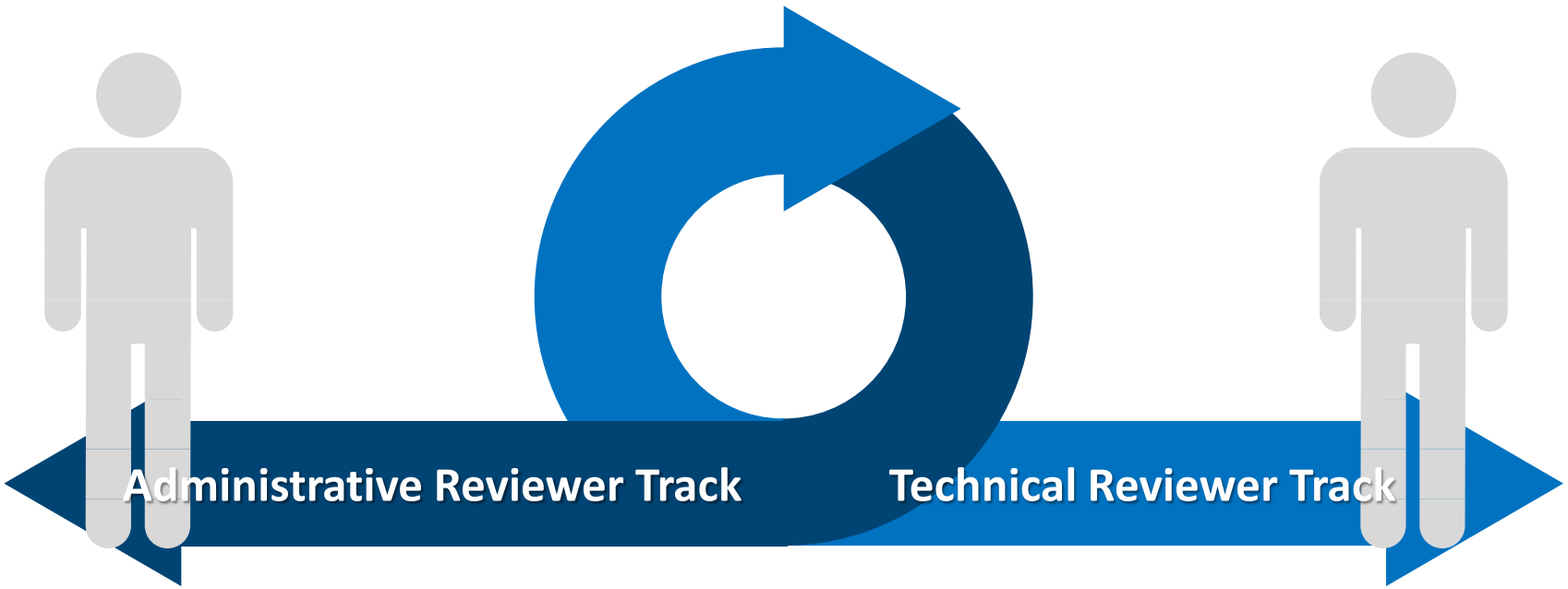
Selection

- Medical related Background
- Master Degree and Above
- Start as a Primary Reviewer

- CMC, Pharm/Tox, PK, MD, Stat.
- MD, Master and/or Ph.D Degree
- Start as a Primary Reviewer



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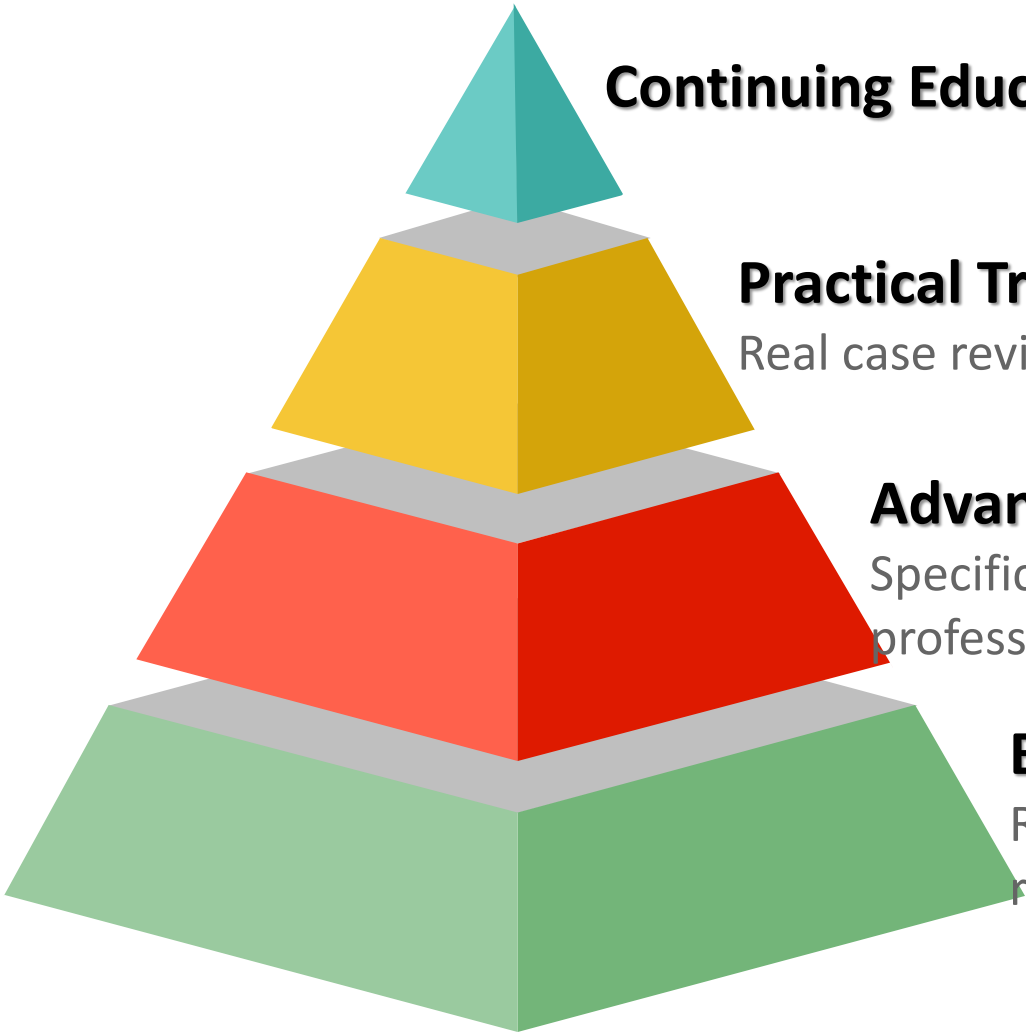
Training

30 hours every year

Continuing Education



Practical Training

Real case review under mentor supervision

Advanced Training

Specific guideline, case study and professional lectures

Basic Training

Regulation, review process and review principle

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Evaluation

■ **Qualified for average seniority of the employees and recommended by supervisors.**

■ **Assessment and approval by the Board of Certification Evaluation Committee.**

- Board Chairperson is designated by TFDA Commissioner
- Meeting will be held at least every 6 months, or more if necessary
- If nominee gets rejection, re-nominee will be made 1 year later

Practice

Administrative Reviewer Track		Technical Reviewer Track
• General Affairs • As Preceptors to Guide New Staff • Guideline drafting • Specialized Projects	**Senior Reviewer**	• General Affairs • As Preceptors to Guide New Staff • Secondary Case Review • Guideline drafting • Specialized Projects
• General Affairs • As Preceptors to Guide New Staff • Assist Guideline drafting	**Secondary Reviewer**	• Review Technical Dossier • As Preceptors to Guide New Staff • Secondary Case Review • Assist Guideline drafting
General Affairs	**Primary Reviewer**	Review Technical Dossier

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ExPREES (E Platform for Review & Submission)

The E Platform for Review & Submission (ExPRESS) is for accepting electronic regulatory submissions. The ExPRESS enables the secure submission of premarket and postmarket regulatory information for review.

Information Database

Easy to Retrieve

Paperless

Enhancing Review Efficiency

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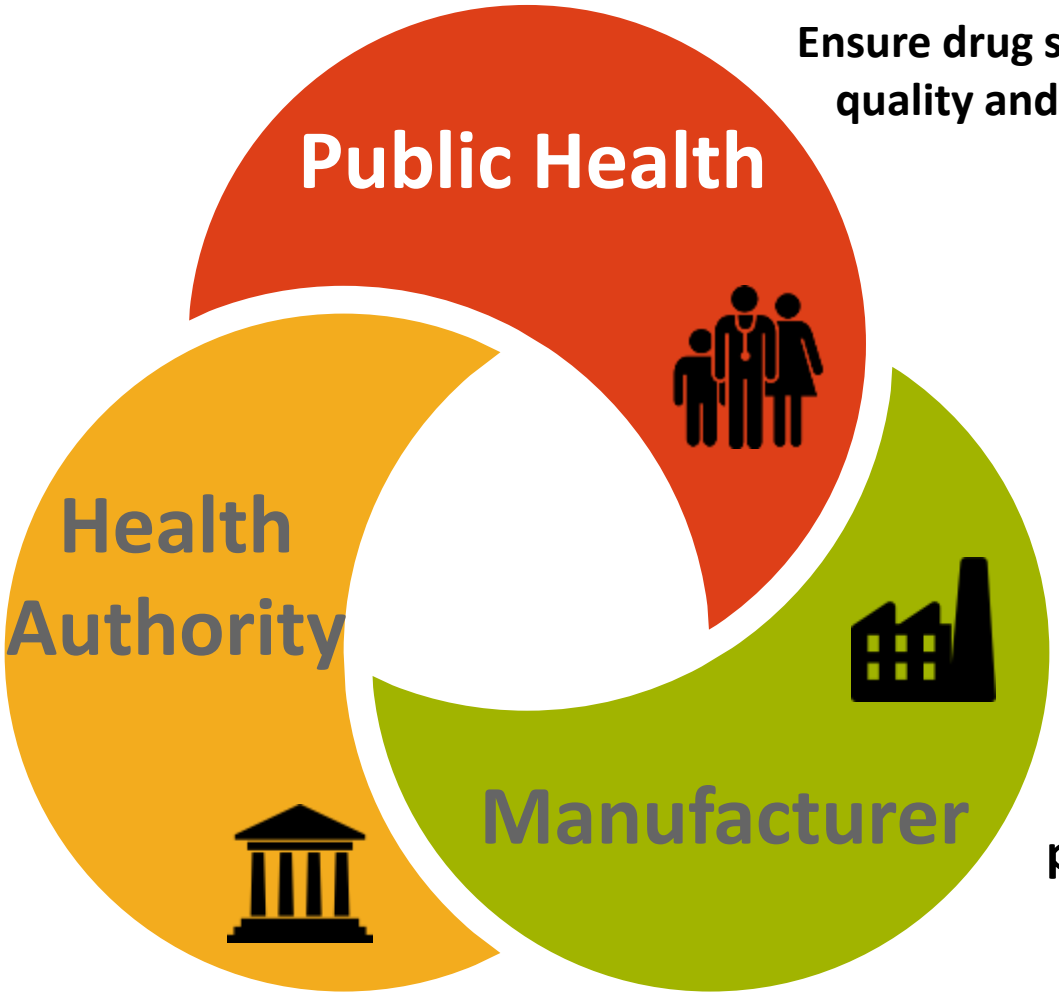
Win-Win-Win Situation



Ensure drug safety, efficacy, quality and accessibility

Harmonization with international regulations

Product promotion

Thank You for Your Attention

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