Advanced Approaches to Assure Pharmaceutical Product Quality- Lifecycle Management in Taiwan

Mei Fang Chen, Ph.D.
mfchen@fda.gov.tw
Senior Reviewer, Division of Medicinal Products, Taiwan
Food and Drug Administration (TFDA)

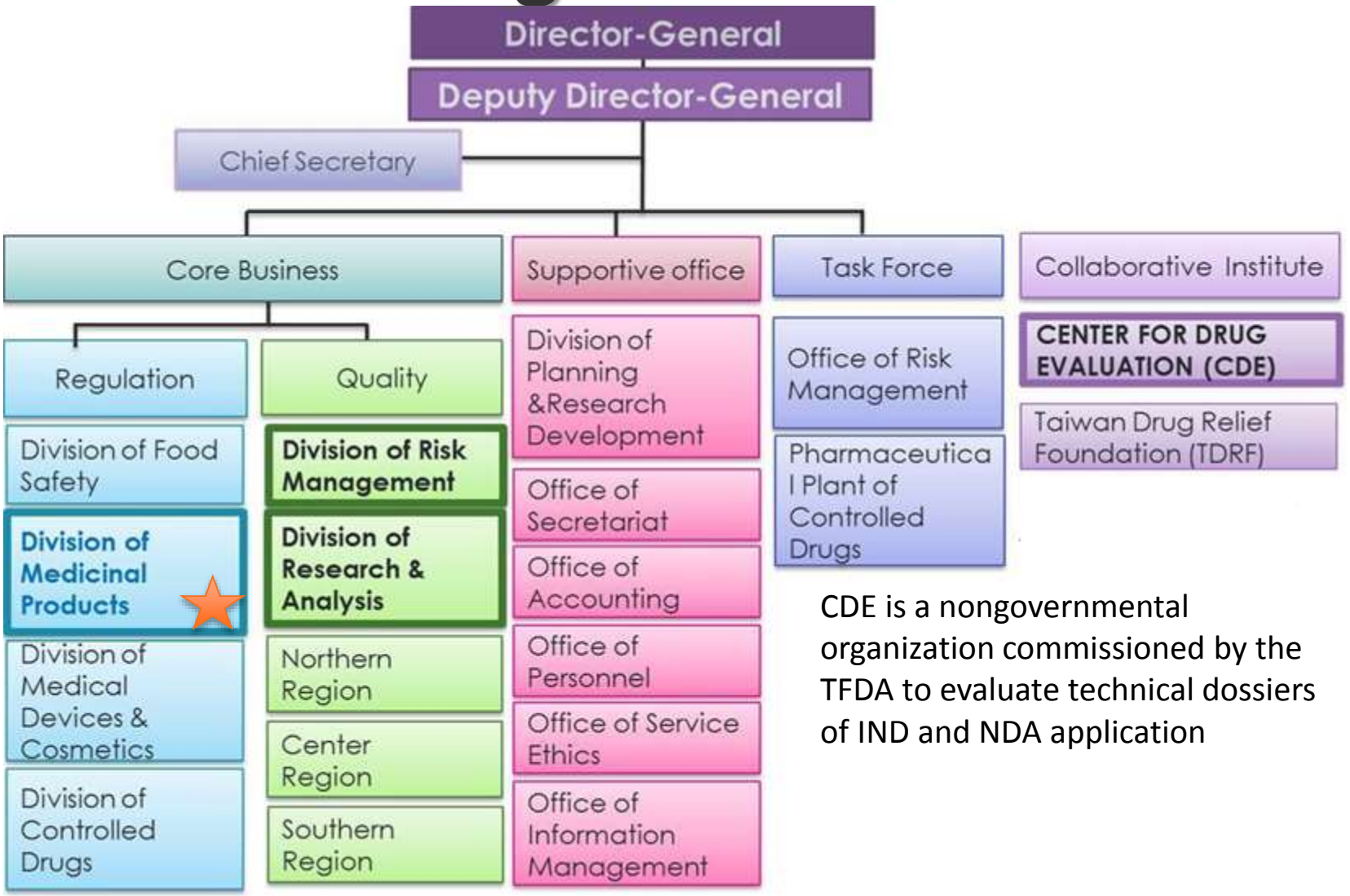
衛生福利部
食品藥物管理署
Food and Drug Administration

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

Outline

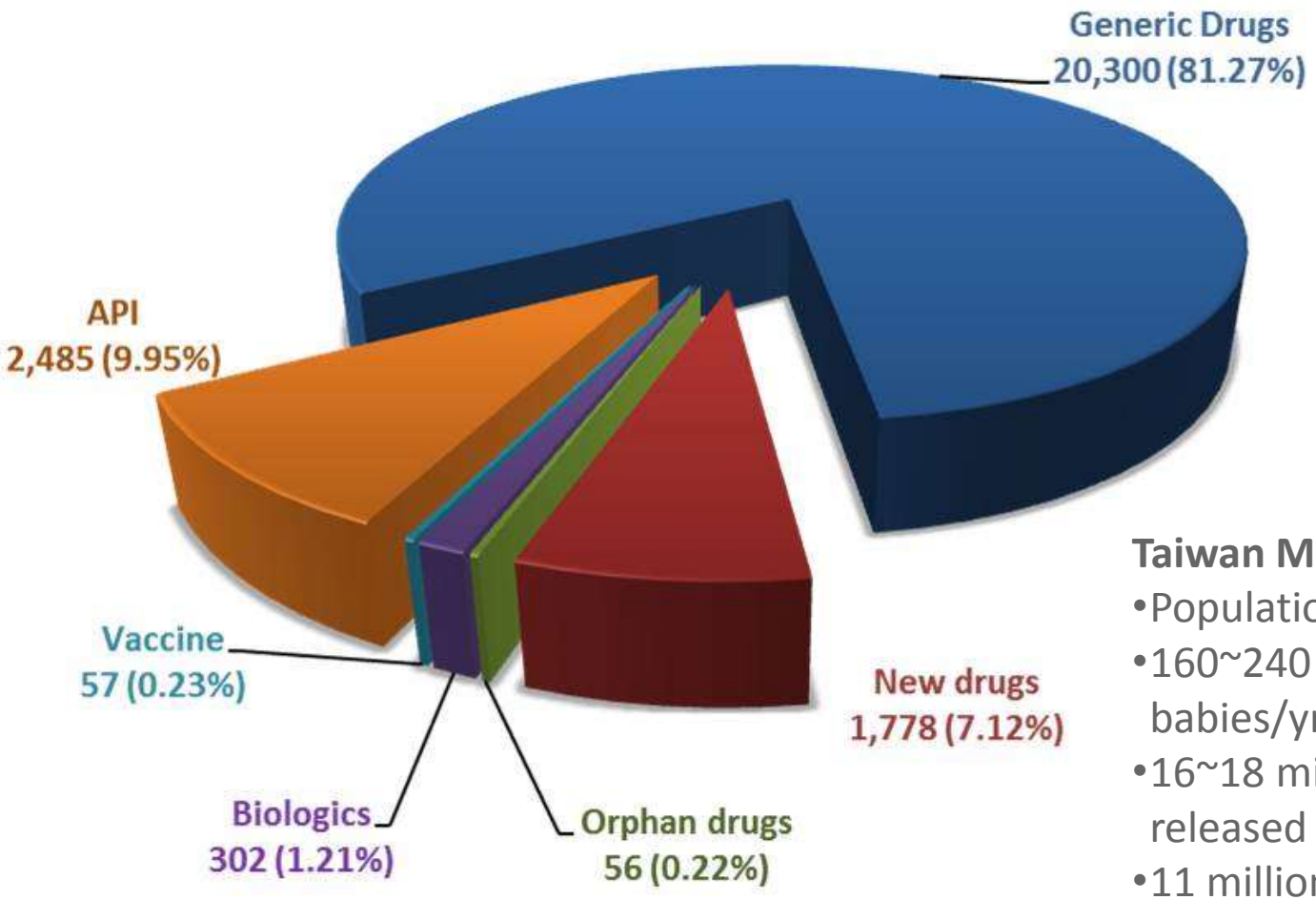
- Introduction of TFDA
- Lifecycle Management of Drug in TFDA
- Pre-market Evaluation Process
- Post-market Control
- Conclusion

TFDA Organization Chart



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

License Numbers of Drugs in 2016



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: 24,978

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Life Cycle Management of New Drug

Pre-Market Approval

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

Post-Market Control

- Lot release
- Post-approval changes (i.e., new indication or facility…)
- GDP
- GPvP
- GPP
- ADR & Product Defect Reporting
- Drug Injury Relief
- RMP

PICS/GMP

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: Vaccine, blood derived product and Toxin

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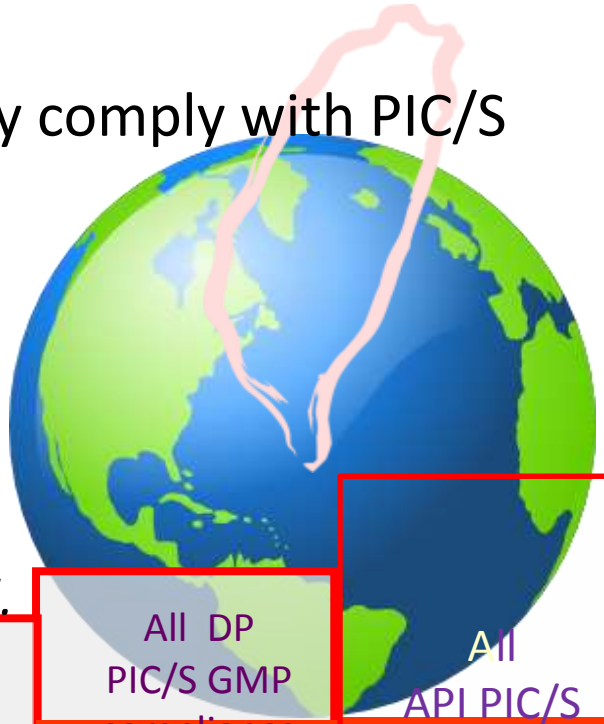
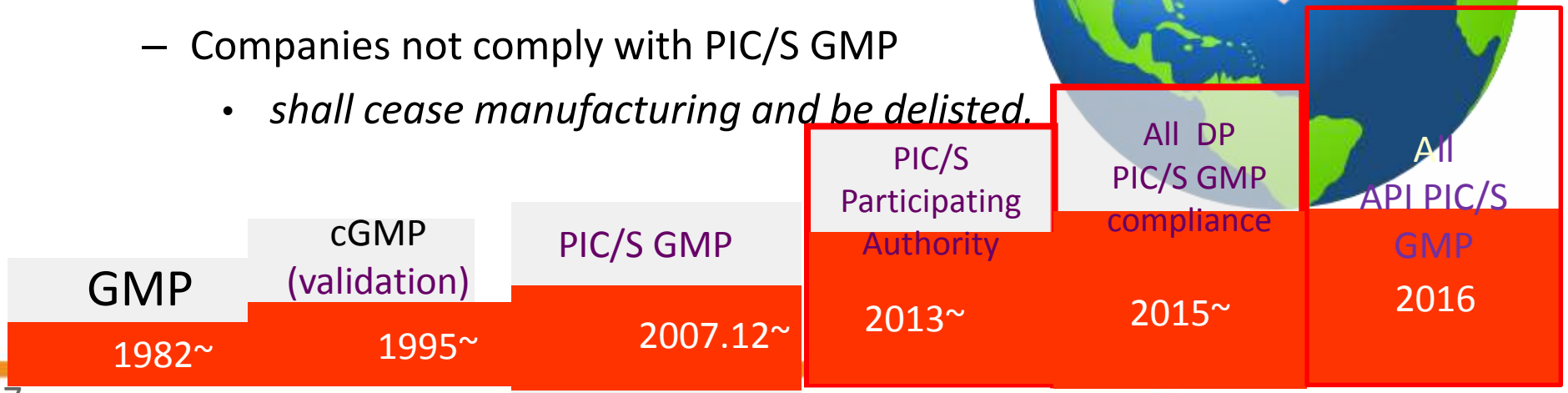
Manufacture

- PIC/S Participating Authority since 2013
- All drug product manufacturers shall fully comply with PIC/S GMP Guide since 2015
- All drug substance manufacturer shall fully comply with PIC/S GMP Guide since 2016
- Current status: (up to 2th October 2017)
  - Domestic pharmaceutical drug product manufacturers: **137**
  - Companies not comply with PIC/S GMP
    - *shall cease manufacturing and be delisted.*





API GMP

API quality control system

Products

API source

In-house API

API license

Quality certificate for specific areas e.g.

China (July 2013) or India (2014)

Domestic: Similar CTD (1995)

Stage I

API CTD system (2009)

API CTD format(2013)

2016-1-1

Stage II

API license and Product license(API) has fully compliance with GMP

API source registration

2017-7-1

Variation API

API CTD format

Transport

Manufacture

- **GMP**

Good Manufacturing Practices

Storage, Transportation

- **GDP**

Good Distribution Practices

Hospital, Pharmacy, Patients

- **GDP**

Good Dispensing Practices

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

Quality Assurance

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

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

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Evaluation Process

Application submitted to TFDA

Documentation Evaluation

Integrated Medicinal Products Review Office (iMPRO)

Administrative	**Technical part**				
	CMC	**Pharm/Tox**	**PK/PD**	**Clinical**	**Statistics**
Administrative	**CMC**	**Bio-equivalence(BE) or dissolution test**			

Assessment Report

Advisory Committee

Asking for suggestion

if necessary

Providing opinion

Final Decision made by TFDA

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Post –Marketing Management System

Post –Approval Change (1/2)

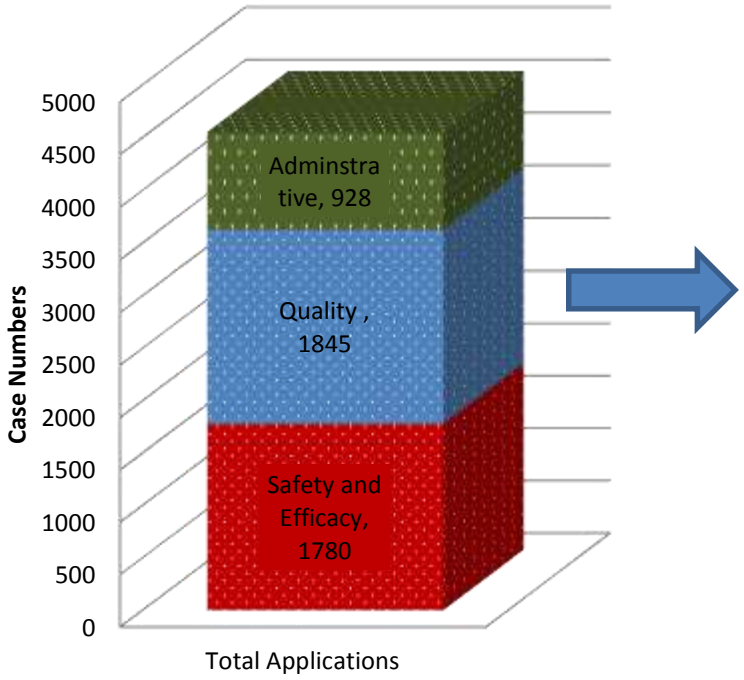
Variation	Type	Regulations for Registration of Medicinal Products	Response Time
Quality(CMC) variation	Changes in active ingredient	48, 53	120 days
	Changes in excipients	56	
	Changes of drug testing specifications, methods and product appearance Manufacture process, in process controls, batch size	57	
	Changes of immediate packaging materials	58	
	Changes in drug storage conditions	68,45	
	Others	…	

Post -Approval Change(2/2)

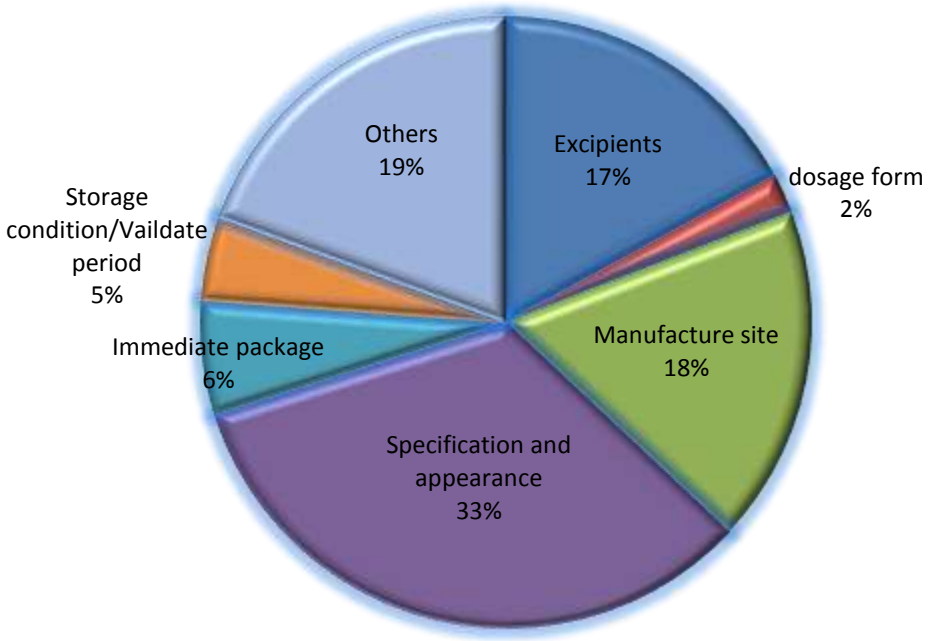
Variation	Type	Regulations for Registration of Medicinal Products	Response Time
Safety variation	Changes in indications	54	180 days
	Changes in drug administration and dosage	55	
	Changes in package inserts, labels	63	
Administrative variation	Changes in the Chinese or English product name	50	60 days
	Changes in drug categorization	51	
	Changes in the pharmaceutical company's name, drug company name, drug manufacturer's address	60, 61, 62	
	Others	…	

Statistic Analysis on Variation

Post Market Variation



Quality Variation



The statistic analysis is from 2017.1.1 to 2017.10.31

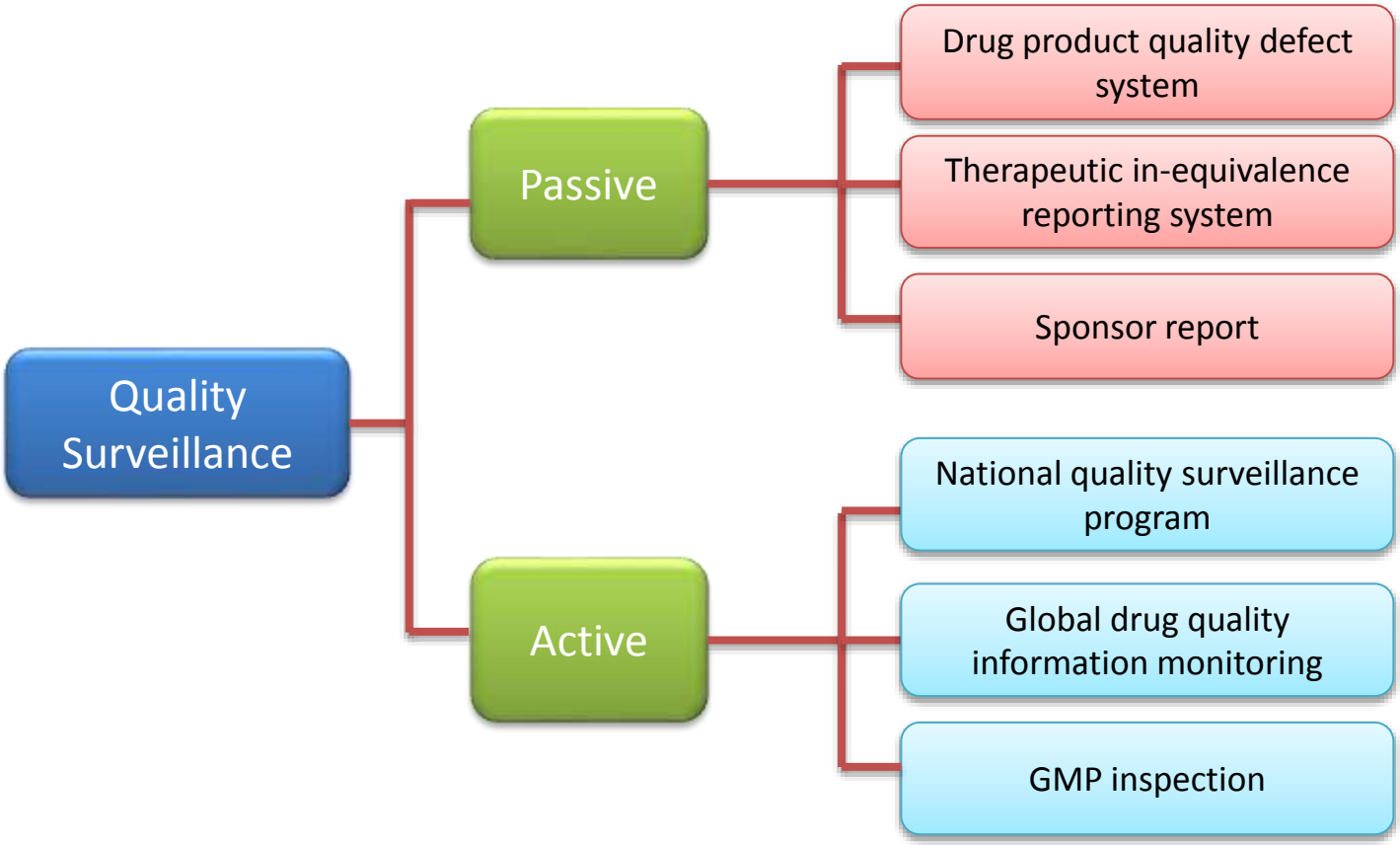
Categorisation of Post Approval CMC Changes

- **Prior-approval:** The changes are considered to have sufficient risk to require regulatory authority review and approval prior to implementation
- **Notification:** The changes are moderate- to low-risk and judged to not require prior approval and generally require less information to support the change.

Post-Approval Change Reporting Categories

Risk	Taiwan (TFDA)	Japan (MHLW)	U.S.A (FDA)
High	Major Change (Prior Approval Change)	Partial Change Approval Application (Application for approval of variation)	Major Change (Prior Approval Supplement (PAS))
Moderate	Minor Change (Prior Approval Change)	Minor Change Notification (Notification within 30 days after implementation or shipping)	Moderate Change (Supplement-Changes Being Effected in 30 days (CBE30)) (Supplement-Changes Being Effected (CBE))
Low	Non-approved matters	Non-approved matters	Minor Change Annual Report (AR)

Post -Market Quality Surveillance

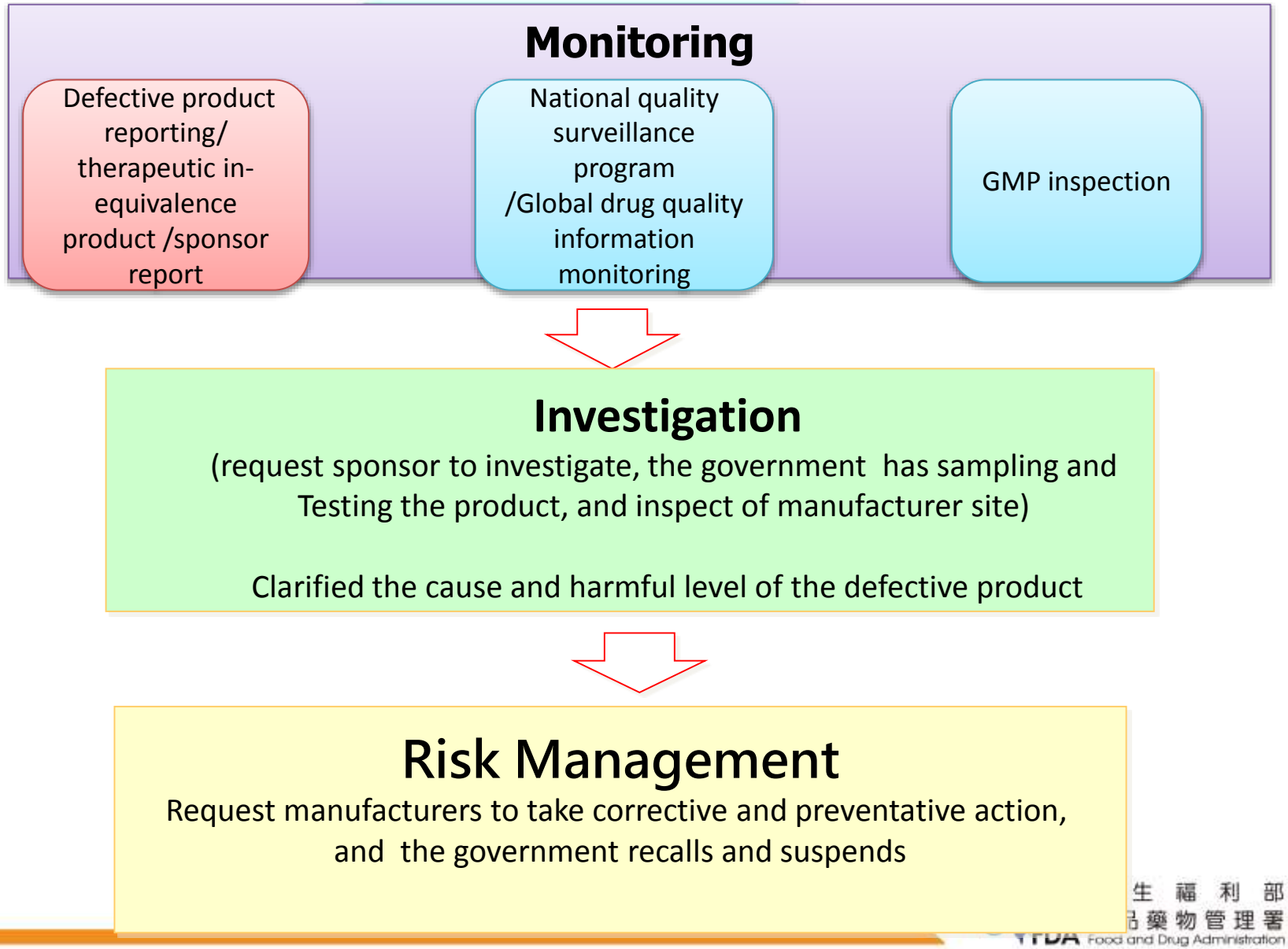


“Drug Product Quality Defect System” vs ” National Quality Surveillance Program”

Complementary

Item	Drug Product Quality Defect System	National Quality Surveillance Program
Monitoring category	Passive	Active
Reporting	Spontaneous report from healthcare providers	The government takes proactive action
The spread of Surveillance	All license drug product	Specific item of drug product
The detail of Surveillance	The abnormal appearance and abnormal package	The overall analysis e.g. Assay, impurity and dissolution test…

Flowchart for Risk Management



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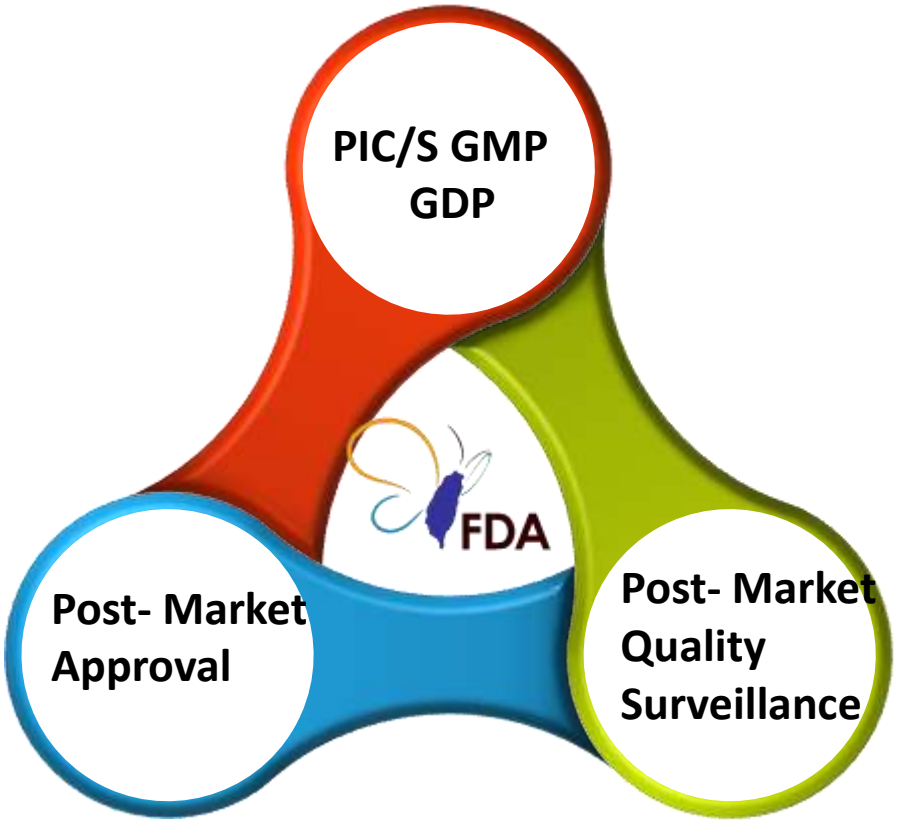
Conclusion


PIC/S GMP
GDP
FDA
Post- Market
Approval
Post- Market
Quality
Surveillance

Thank You for Your Attention

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