5th Joint Conference of Taiwan and Japan on Medical Products Regulation

Regulatory Updates in Taiwan

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Dec. 1, 2017

Outline

- Mission, Vision, and Core value
- Life Cycle Management of Medical Products
- Innovation-Modernization of Regulatory System for Medical Needs
  - Advancing regulations for innovation
  - Enhancing accessibility of medical products
  - Ongoing new strategies
- Progress of Working Group in 2017

Mission, Vision, and Core Value

Quality and Safety of Food and Medical products
(藥求安全 食在安心)

Safe Food

Safe medical products

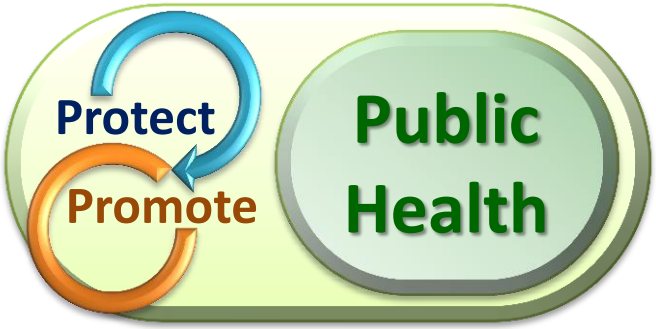
To safeguard national health
To lead the nation to a new era
of food and drug management

- **Profession (專業)**
- **Service (服務)**
- **Quality (品質)**
- **Innovation (創新)**

Mission of Taiwan FDA

Protect

Assure Quality, Safety, Efficacy of Medicinal Products



Promote

Facilitate the Development of Innovative Medicine and Speed Drug Accessibility

Life Cycle Management of Medical Products

Pre-Market Approval/ Control

- Product Designation
- GLP/GTP
- GCP
- Registration (Approval/ Listing)
- General/Case Consultation
- IRB
- SUSAR Reporting
- Insurance
- ICH –Based Regulations
- MD Advisory Committee

Post-Market Management / Control

- ADR & Product Defect Reporting
- GPvP/ GVP
- GDP
- GPP
- Drug injury relief

- Manufacturer's Quality System Audit (GMP)-MD
- PICS/GMP-Drugs
- RMP

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

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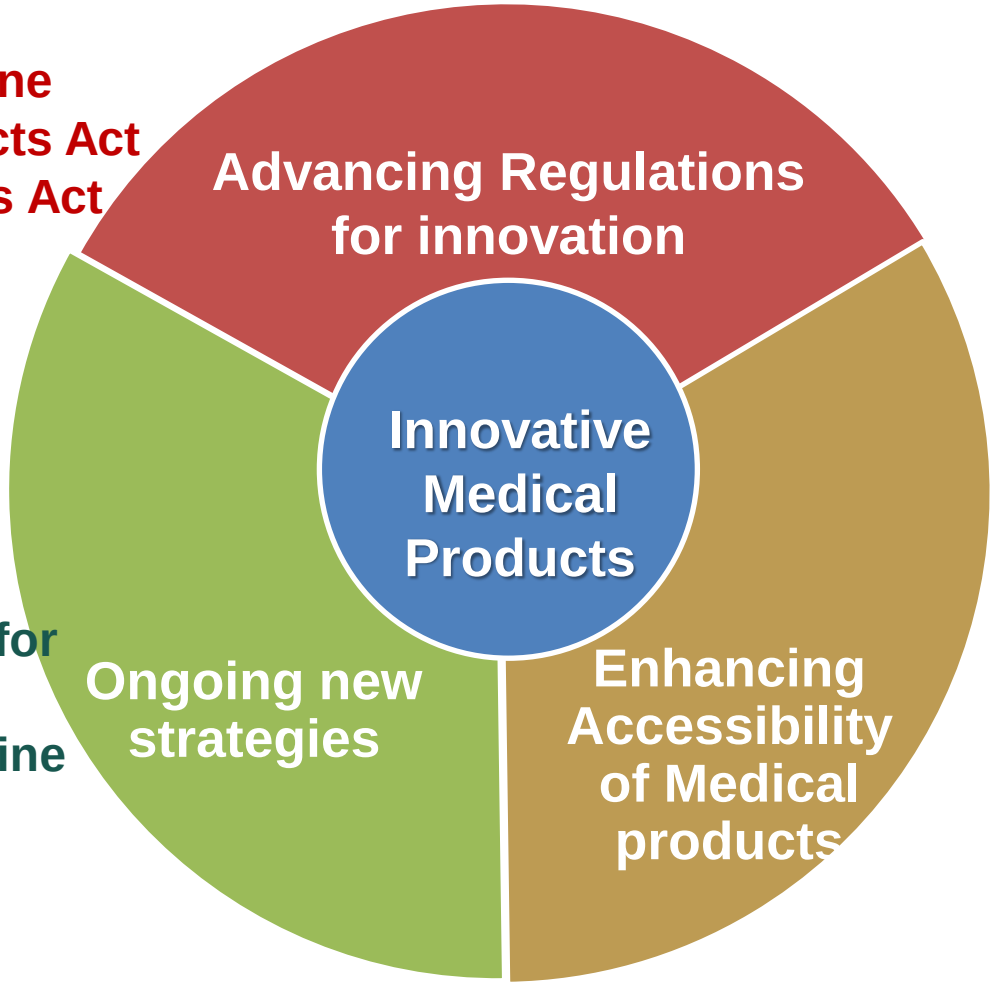
Innovation-Modernization of Regulatory System for Medical Needs

(Drafting)

- **Cellular and Gene Therapy Products Act**
- **Medical Devices Act**



- **Trace and Track system; GDP**
- **Simplify review for ICF approval**
- **Precision Medicine and LDT**

- **Enhancing Review Efficiency**
  - **Promote Good Registration Management in APEC**
  - **Implement New Measures:**
    i.e. Refuse to File, Rolling Review, etc.

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Regulation of Cell Therapy Products in Taiwan

Pre-marketing | Post-marketing

Product Development → **IND Clinical trials** → **NDA Market licensing** → **Production** → **Marketing**

Product Development	IND Clinical trials	NDA Market licensing
Consultation 2011.08.02	Guidance on **Donor Eligibility** Determination 2015.10.02	Guidance on Cell Therapy Products Application 2015.07.13
	Guidance on Investigational Cell Therapy Products 2014.09.17	
	Guidance on Good Tissue Practice (GTP) 2002.12.13	

Cellular and Gene Therapy Products Act (draft) 2017.7.26

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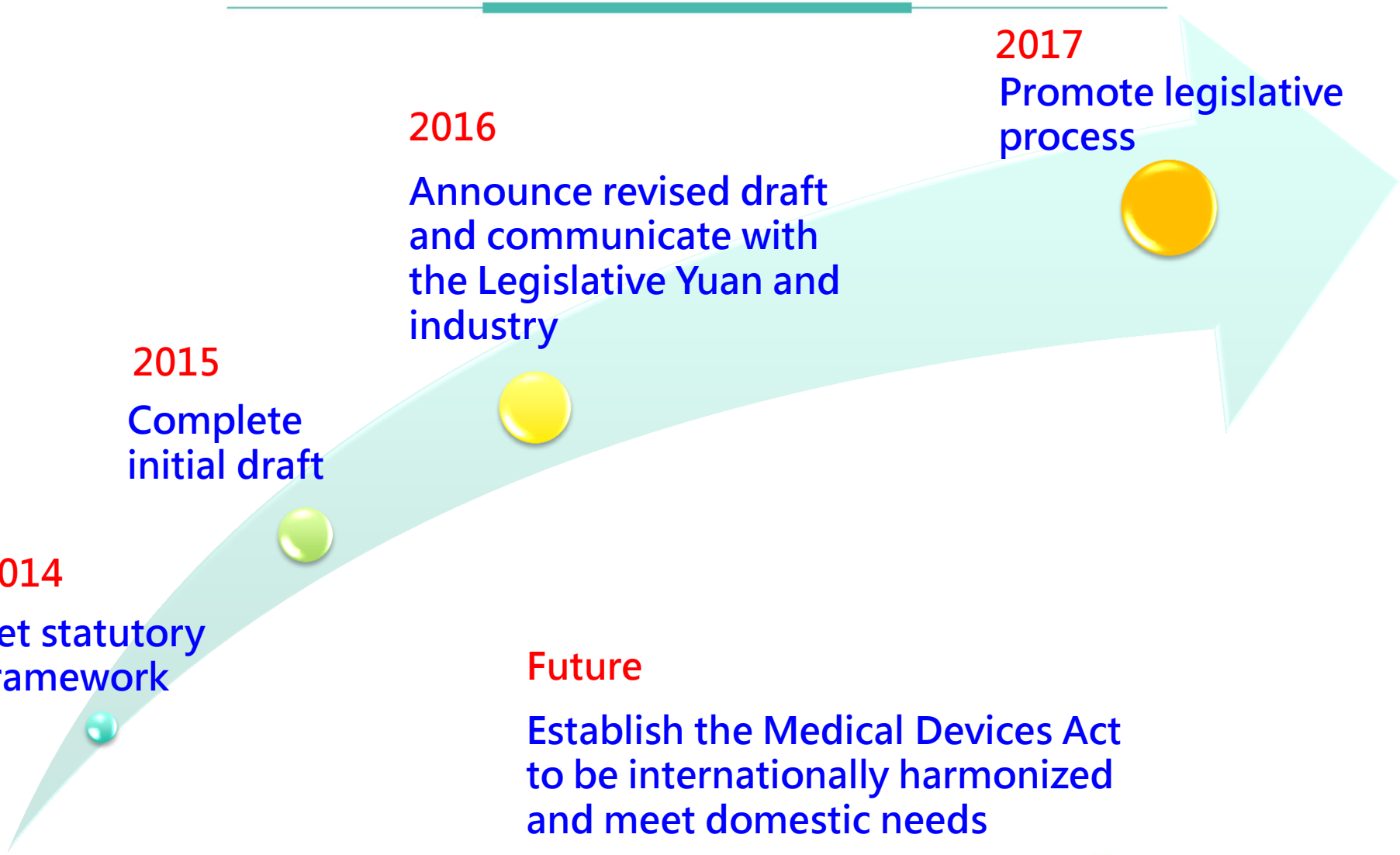
Establishing Medical Devices Act



Announcing guideline/guidance/ standards

Drugs

- **Guidance【2017】**
  - Summary for BA/BE guidance (revision) 【2/15】
  - Regulatory consultation guidance (revision) 【3/3】
- **Rules 【Dec 2016 - 2017】**
  - Announce the list of essential drugs 【Dec. 2016】
  - Refuse-to-File mechanism 【01/01】
  - Clinical trial application for cell therapy products (revision) 【01/17】
  - Announce drug items to be traced and reported 【4/20】 【10/31, up to 20 items 】
  - Advanced process of review for clinical trial application 【8/10】
  - The list of orphan drug items (revision) 【9/27】
- **Law 【2017】**
  - Data exclusivity and patent linkage in PAA (draft Aug. 2016)

Medical Devices

- **Guidance【2017】**
  - Guidelines for Registration of In Vitro Diagnostic Medical Device (revision) 【3/15】
- **Rules 【2017】**
  - Priority Review Mechanism for Medical Device Registration“ 【1/9】
  - Medical Devices Sellable on the Internet via Distance Sales and Items Required to Be Registered by Pharmaceutical Firms and Pharmacies (revision - for the inclusion of menstrual cup, blood pressure cuff, etc.) 【3/16】
  - Amendment to Partial Articles of the Regulation for Registration of Medical Devices " to explicitly indicate the regulatory scope for skin stimulators with energy (e.g., electric current, light energy, ultrasound, etc.) 【3/30】
  - Amendment to Annex I of Article 3 and Annex II of Article 4 of the "Regulations for Governing the Management of Medical Device“ 【7/25】
- **Law 【2017】**
  - Medical Devices Act to the Executive Yuan (draft) 【8/30】

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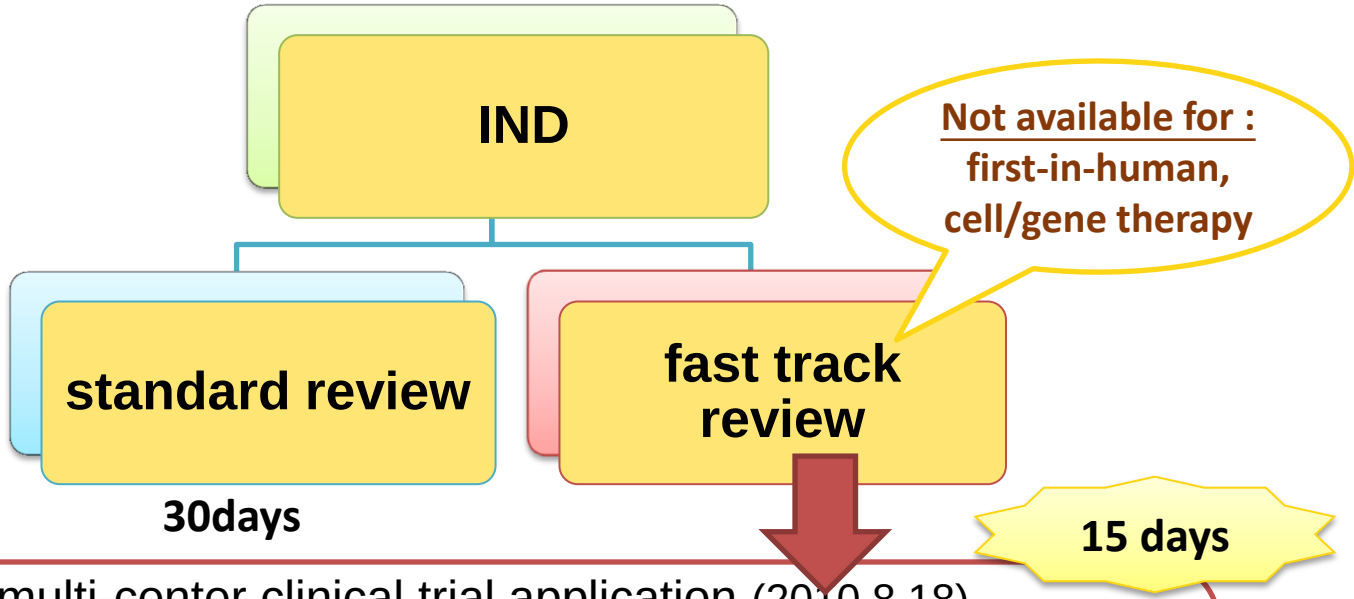
Enhancing Accessibility of Medical Products

Enhancing review efficiency

Enhancing review efficiency

IND Review



Multi-national multi-center clinical trial application (2010.8.18)

- If with both of the following items:
  - With the protocol number same as that conducted in one of advanced countries
  - The clinical trial is planned to be conducted in any medical center in TW

Announcement for the Improvement of IND Review

2017.08.10

To simplify the process for first in human clinical trial

Fast track review for cell/gene therapy clinical trial

30 days

If (1)multi-national multi-centers CT, not first in human, or (2) the product manufactured from the Lab with the other products previously approved for CT.

Establish the priority of review for clinical trial protocol change

- ✓ **Enhancing review efficiency**
- ✓ **Improving accessibility of innovative medical products**

To accelerate the development of biotech medicine, the non-infection clinical samples **used for research, teaching, and/or for examination** will not need to make an application for **import/export** to TFDA. (from 2017/12/01)

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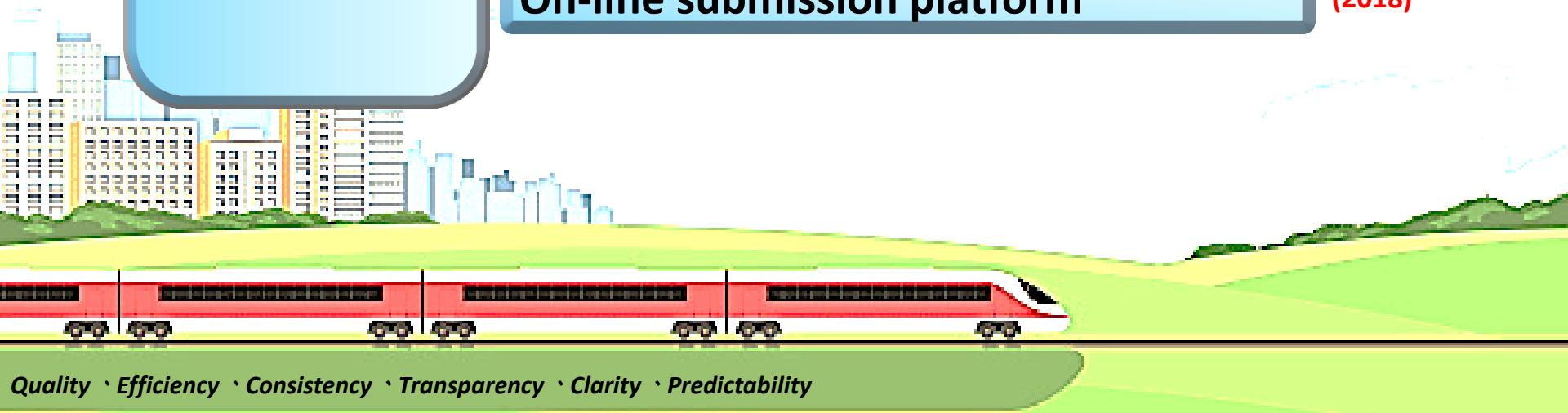
Enhancement of Review Efficiency

Pre-clinical → Clinical → Marketing Approval

Consultation and Rolling Review
(2016.12.12 announcement rev)

- Review process and timeline (2016.10.27 announcement rev)
- Refuse-to–File (2017.01.01 Implementation)
- Pre-NDA meeting (2017.01.01 Implementation)
- Points to consider for NDAs (2017.03.03 announcement)
- On-line submission platform (2018)



Quality、Efficiency、Consistency、Transparency、Clarity、Predictability

Domestic Innovative Consultation

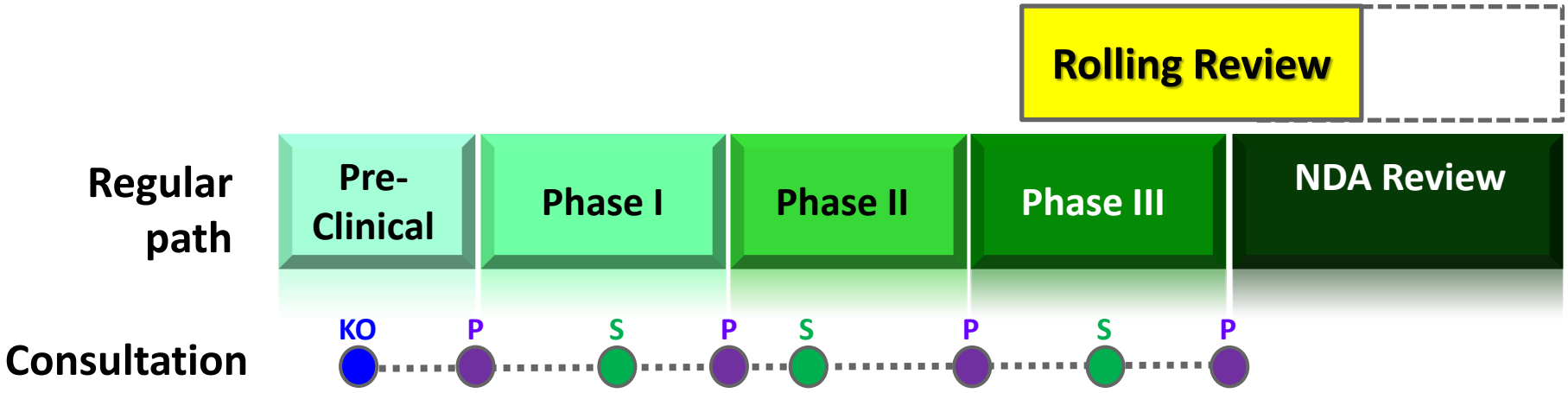
To facilitate medicinal products development and marketing approval

Meeting types:

- Kick-off meeting
- Sponsor meeting
- Pre-filing meeting (pre-IND or pre-NDA)

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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Refuse to File (RTF) - New Drugs

Rule

- Without completed administrative documents
- Without completed technological information
- Not pay the submission fee

Refuse if with anyone of these deficiencies

Timing

- Refuse within 60 days after receiving the submitted documents, but not returning the submission fee.
- Allow to submit again within 4 months after RTF.

Performance

- Up to June, 2017, among 63 applications for NDA, there are 8 RTF events due to the technological documents not completed,
  - RTF (domestic): 30%
  - RTF (import): 9%

Refuse to File (RTF) – Generic Drugs

Rule

- Without completed administrative documents
- Without completed technological information
- Not pay the submission fee

Refuse if with anyone of these deficiencies

Timing

- Refuse within 14 days after receiving the submitted documents; but returning ¾ of submission fee for drugs, 3/5 of submission fee for drugs.
- Resubmission with the total of submission fee after RTF.

Performance

- Up to June, 2017, among 94 applications for ANDA, there are 44 RTF events due to the technological documents not completed,
  - administrative: 6 events
  - CMC: 35 events
  - PK: 11 events

- RTF (domestic): **28.3**%
- RTF (import): **48.1** %

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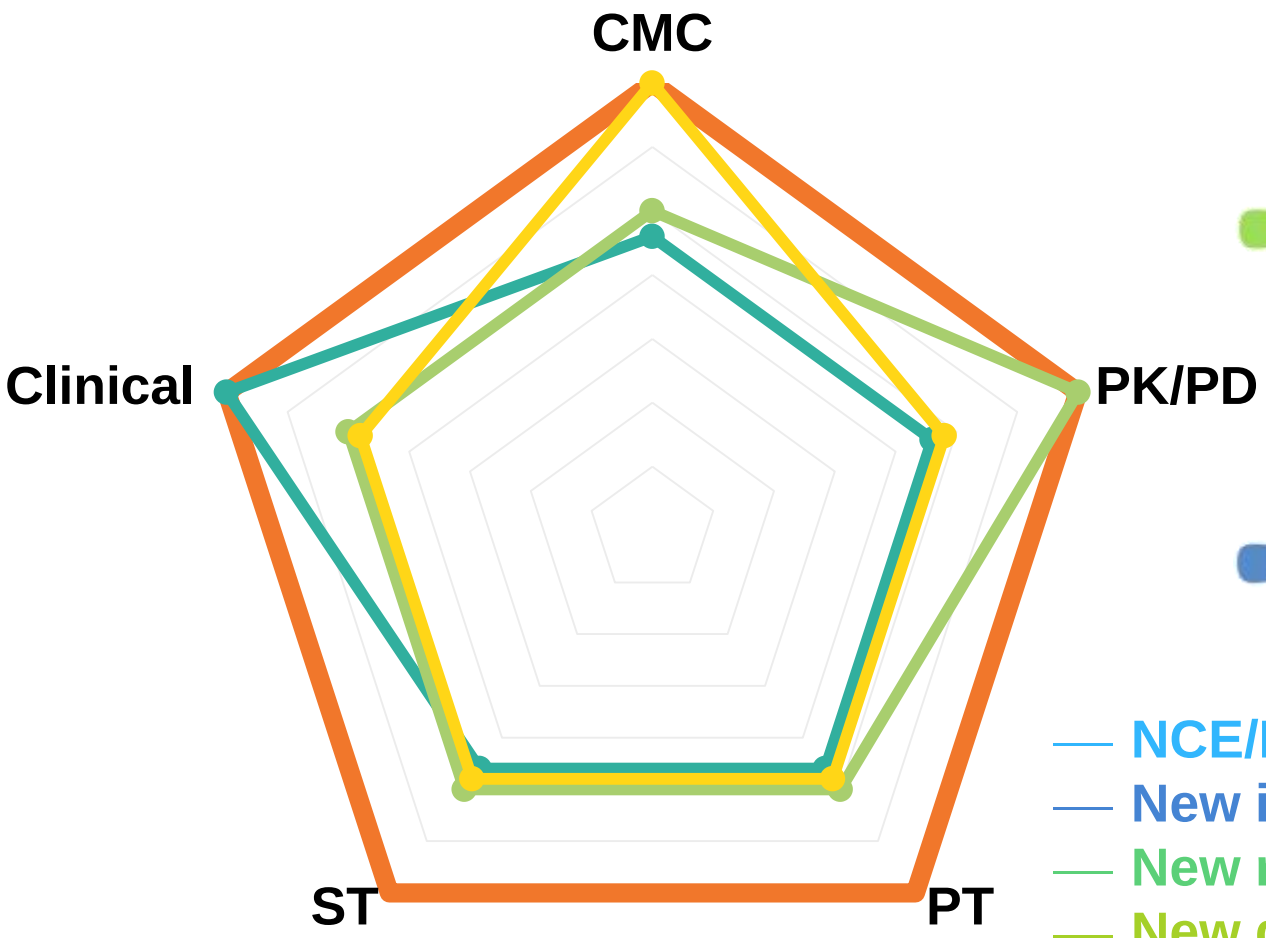
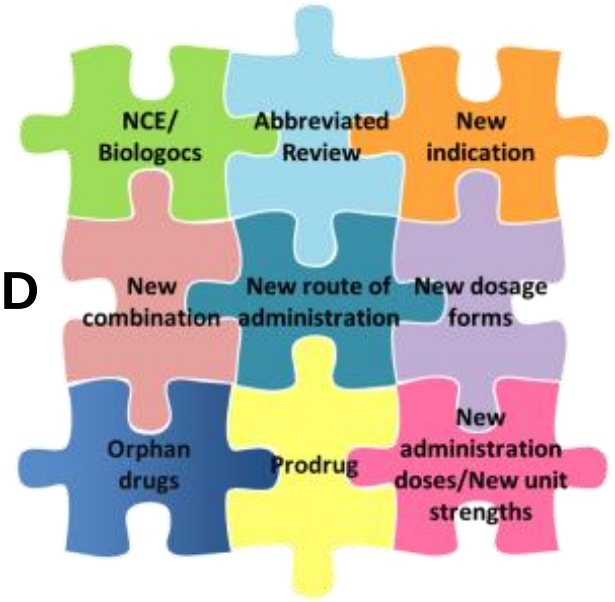
Points to Consider for NDAs





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

E platform for Review & Submission

- Systemic Database
- Paperless
- Quick Searching
- Review Efficiency

License Extension (pilot) → Post-marketing change；Registration for NDA, API (pilot) → Implementation

2017 APEC GRM CoE Workshop

The 2017 workshop gathered representatives from the government, academy, and industry of 13 different countries. The total number of participants was more than 120.

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Enhancing Supply Chain Integrity of Medical Products

Implementation Schedule of GDP in TW

Wholesale Distribution

Drug Manufacturer

From July 1, 2016, all **new** manufacturers, logistics companies and product **license applicators** shall comply

Drug Dealers

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

Announcement of "Guide to GDP for Medicinal Products" 【2015-7-16】

Trace and Track system

Items to be traced and reported in accordance with PAA §6-1

【2017/4/20】 【2017/10/31】

20 items, such as:

- Plasma derivatives
- Vaccines
- Botox
- Crestor 10mg Film-Coated Tab
- Exforge Film -Coated Tab
- .....etc

Pharmaceutical Affairs Act (PAA) §6-1 (new)

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

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Amendment of Medical Law- 55th enforcement rule

Clinical Trial ICF

Draft

Review for ICF approval

If the clinical trial: (1)only used clinical research, but not for registration; or (2) ICF change, the ICF can be reviewed/ approved by study site IRB committee. (2017/4/5 pre-announcement)

ICF template

To revise the ICF template adding with the information regarding the clinical samples, personal information protection, etc. (2017/8/22 announced)

Regulatory System for Precision Medicine

Value Chain for Precision Medicine (PM)

Testing Service → **Diagnostic Services** → **Treatment Services** → **Monitoring Services**

Testing Service

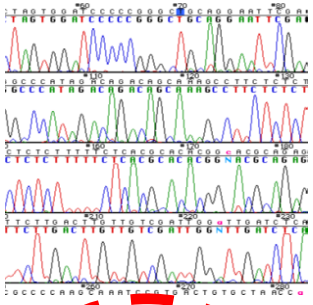
Database

- disease target
- resource

1. Collaboration grant for Precision Medicine
2. Cancer Moonshot

Diagnostic Services

Regulations



LDT (Laboratory Developed Tests) Guidance

Treatment Services

- Drug Discovery
- Medical Device – (IVD-CDx)

The products used for identifying the treatment targets especially on oncology

Monitoring Services

- Liquid biopsy
- Mobile & Wearable

Technology and products development

Personalize / Predictive / Prevention / Participatory

Precision Medicine

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International cooperation

Bilateral Cooperation:

- Japan: Arrangement
- China: Agreement
- Philippines: MOU
- Australia: MOU
- Austria: MOU
- Poland: MOU
- UK: Confidentiality MOU
- EDQM: Confidentiality Agreement
- Germany: Joint Declaration

Multilateral Cooperation:

- ICH: 15 Working Groups
- IGDRP: Quality and Bioequivalence
- APEC: LSIF-RHSC
- IPRF: Gene Therapy Products, Cell Therapy Products, Nanomedicine, and Biosimilar
- WTO

Collaboration with Japan

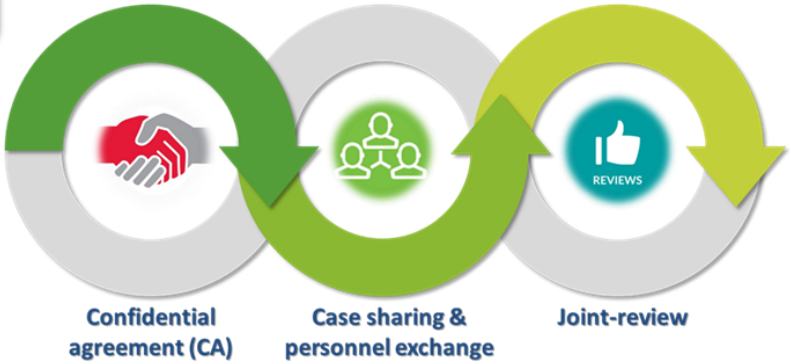
New drug

- Review points sharing/comparison
- Short-term personnel training
- *Future: review cooperation*

GBO (Generic /BE/OTC)

- Revision of BE regulation
- *Future: recognition of BE reports*

- Comparisons of regulations
- *Future: market expansion*



Information Sharing model established
Direct contact of post-marketing surveillance information

Avoiding duplicated review / inspection

Progress for the QMS Working Group of Medical Devices

2017

- EoL was modified to MoC format
- MoC was confirmed by relevant authorities
- Start of Phase III after signing of MoC

2016

- Start of Phase II for QMS Working Plan (Road Map), and monitored audit for SGS Japan, PMDA, TUV Rheinland and BSI Japan
- Meeting of QMS WG in Japan for revising of QMS Working Plan (Road Map)
- 4th Joint Conference of Japan and Taiwan on medical product regulation and confirmation of EoL

2015

- 3rd Joint Conference of Japan and Taiwan on medical product regulation and QMS Working Plan was proposed
- Start of Phase I for QMS Working Plan (Road Map)

2014

- Establishment of QMS WG
- 2nd Joint Conference of Japan and Taiwan on medical product regulation

Progress for the QMS Working Group of Medical Devices (2)

Outcome & Next Steps

- Both sides will endeavor to complete administrative procedures for MoC before the end of 2017 and sign the document by sending it to their respective signatories: Japan-Taiwan Exchange Association & Taiwan-Japan Relations Association.
- Both sides have agreed to conduct future exchange in practice according to the work items of Phase III. This will include: holding regulatory workshops, having exchange of audit reports and certifications, notifying each other of their inspection schedules, etc. Japan has informed Taiwan about its inspection schedule for Jan. 2018.
- Japan intends to charge relevant fees to RCBs for Taiwan's observation of their inspections. Further discussion with RCBs would be needed before a response is available for Taiwan.

Progress for Product Registration Working Group of Medical Devices

Work Items & Outcome in 2017

- Results of case study conducted regarding **dental implants** are summarized and presented in this conference.
- Case study of dental implant will be continued and focused on the review of mechanical properties. It is being considered to have discussion by teams of reviewers during the review task in order to enhance and accumulate comprehensive experience, as well as to help reach consensus on the differences.
- Taiwan and Japan have collaborated in preparing two separate Q&As for each other as proposed by the industries. They will be published for the benefit of stakeholders.

Thank You

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