Regulatory Updates in Taiwan

Shou-Mei Wu, Ph.D.
Director-General, Taiwan FDA
Chairperson, Taiwan CDE

Oct. 1, 2019
Outline

01. Mission, Vision, and Core value

02. Medical Products Management

03. Innovation - Modernization of Regulatory System for Medical Needs

04. International Collaboration

05. Progress of Working Group in 2019

06. Future Prospects
Mission, Vision and Core Value

Protect
Assure Quality, Safety, Efficacy of Medicinal Products

Promote
Facilitate the Development of Innovative Medicine and Speed Drug Accessibility

Profession
Service
Quality
Innovation
Pharmaceutical Management

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

ICH - Based Regulations

Supplement (post-licensure changes, i.e., new indication or facility...)
Lot release
Drug injury relief
ADR & Product Defect Reporting
RMP
PICS/GMP

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

Pre-Market Approval
Post-Market Control
Medical Device Management

- Medical Device Management
  - Preclinical Validation
  - Clinical Study
  - Premarket Application
  - Production
  - Postmarket Surveillance

- General/Advanced Consultation
- Laboratory Practices (GLP/GTP)
- Clinical Trial Inspection (GCP)
- Clinical Study Protocol Review (TFDA/IRB)
- Registration (Approval/Listing)
- MD Advisory Committee
- Manufacturer’s Quality System (GMP)

- 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

ADR & Product Defect Reporting
Safety Surveillance & Alert Collection (GVP)
Consumer Health Education Promotion
Good Distribution Practice (GDP)
Comprehensive Regulatory System

Introduce Medical Devices Act establishment and New Regulatory Framework for Regenerative Medicine

Accelerate Review Efficiency

Renew Pharmaceutical Regulations
  • Patent Linkage System of Drugs

Enhance medication information access for Patients
  • E-labeling

Establish Electronic-Platform
  • E-submission System
  • Track and Trace system

Assure Products Safety and Quality
### Announcing Guideline/Guidance/ Standards

#### Rules 【2017-2018】
- Guidelines on the Review of Instruction Drugs (revision) 【2018/10/5】
- Regulations for Registration of Medicinal Products (revision) 【2019/2/14】
- Regulations on Management of Medicament Samples and Gifts (revision) 【2019/4/11】
- Refuse-to-File RTF (Registration of generic drugs) 【2019/7/19】
- Guidelines on the Review of Instruction Drugs (revision) 【2019/8/5】
- Refuse-to-File check list 【2019/8/20】

#### Medical Devices
- Announced the guidance on **Laboratory Developed Test and Service (LDTS)** for Precision Medicine Molecular Testing 【2018.12.17】
- Initiated the draft of medical device cybersecurity guidance 【under development】
- Initiated the draft of In Vitro **Companion Diagnostics (IVD-CDx)** guidance 【under development】
- Announced the list of recognized standards for 2019 【2019.8.14】
- Announced and revised 10 technical and pre-clinical testing guidances between 2018 Q4 and 2019 Q2

#### Law
- Submitted the draft of **Medical Devices Act** to Legislative Yuan 【2017.12.15】
- Developed and formulated 15 regulations and 19 announcements that are relevant and complementary to the Medical Devices Act
Establishing Medical Devices Act

2014
Set statutory framework

2015
Complete initial draft

2016
Announce revised draft and communicate with the Legislative Yuan and industry

2017
Promote legislative process

2018-2019
Conducted article-by-article deliberation and inter-party negotiation

Future
Establish the Medical Devices Act to be internationally harmonized and meet domestic needs
Before the implementation of RMP Act, the application of clinical trial and product registration should follow the PHARMACEUTICAL AFFAIRS ACT and related regulations.
Implication of the Refused-to-File Procedure

Validation of applications before scientific review

- The Refused-to-file (RTF) procedure was announced in 2016
  - Originally implemented for New drug and Generic drug applications
  - A checklist for NDA required documents was announced in 2018
- The RTF procedure successfully improved the efficiency of NDA review by enhance the integrity of application dossiers
  - Now implemented for various applications.

<table>
<thead>
<tr>
<th>Year</th>
<th>Announcement</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>Announcement of RTF procedure for NDA applications</td>
</tr>
<tr>
<td>2018</td>
<td>Announcement of RTF checklist for NDA applications</td>
</tr>
<tr>
<td>2019</td>
<td>Announcement of RTF checklist for New drug and Biosimilar drug applications</td>
</tr>
<tr>
<td>2019</td>
<td>Announcement of RTF checklist for post-approval changes (changes of indications or dosage use)</td>
</tr>
</tbody>
</table>
Patent Linkage System of Drugs

Announced Aug. 20, 2019

Chapter 4-1”Patent Linkage of Drugs” in the Pharmaceutical Affair Act (2018.01.31)

Regulation for Patent Linkage of Drugs (2019.07.01)
Regulation for the notification of drug patent linkage agreements (2019.03.06)

Registration System for Patent Linkage of Drugs
Implementing the E-Submission System

TFDA ExPRESS
(E platform for Review & Submission)

- Implemented for the application of validity extension of drug license in 2017
- Gradually implemented to various applications including IND, NDA and ANDA, etc.
- Expect to be fully implemented on 2020

System Integration

Function Expansion

Promotion & Training

E-submission cases increased every year!

Enhance review efficiency
Information database
Easy to retrieve
Paperless

136 ‘16
158 ‘17
587 ‘18
717 ‘19
Promoting the E-labeling for Medicinal Products

Benefits
1. Healthcare professionals can obtain the most up-to-date information with a minimum of search time.
2. Advance the searching system of package insert in response to user needs.

- Convert them into Structured Data
- Opendata for Public to access
- Design a User-friendly search page
- Integrate with other database

2019-2020
Transition period
- Build up platform for pharmaceutical manufacturers to upload the package insert.
- Improve and Expand the system functions.

2021-2022
Phased implementation
- Gradually ask the pharmaceutical manufacturers to upload the package insert.

Screened PDF files/Printed Package insert

Benefits
1. Healthcare professionals can obtain the most up-to-date information with a minimum of search time.
2. Advance the searching system of package insert in response to user needs.

- Convert them into Structured Data
- Opendata for Public to access
- Design a User-friendly search page
- Integrate with other database

2019-2020
Transition period
- Build up platform for pharmaceutical manufacturers to upload the package insert.
- Improve and Expand the system functions.

2021-2022
Phased implementation
- Gradually ask the pharmaceutical manufacturers to upload the package insert.
Track-and-Trace System

**Expected Benefits**

1. To avoid counterfeit medicine entering supply chain under co-operation with GDP.
2. To commence drug recalls in a speedy manner when adverse drug events happen.

**LAW**

1. Pharmaceutical Affairs Act article 6-1
2. Regulations Governing the Trace and Track System for Medicinal Products

**Announce drug items to be tracked and traced**

1. First three priority categories, Plasma-derived medicinal products, Vaccine and Botulinum toxin【2017.7】
2. 50 potential counterfeited medicinal products【2018.1&7 and revised 38 items in 2019.10】
3. Ephedrine, pseudoephedrine containing products 【2019.10.1】

**E-reporting system**

(upload drug information, e.g. name, lot, shelf life)

Manufacturer → Supplier → Dealer → Hospital, clinic and pharmacies
Laboratories Listing for Laboratory Developed Test and Service (LDTS) for Precision Medicine Molecular Testing

Construct management system for LDTS for Precision Medicine Molecular Testing

Since 2018, TFDA establish LDTS guidance refer to ISO 15189

Clinical testing needs

Test with LDTS or IVD

BIOTECH COMPANY

Outsourcing

LDTS for precision medicine molecular testing

Testing with LDTS or IVD

Diagnosis、Treatment

Partially covered by Health Insurance

LDTS report

Since 2018, TFDA establish LDTS guidance refer to ISO 15189

LDTS Lab listing

Benefits:
1. Enhance quality of LDTS for Reliable and precise testing result
2. NHI insurance payment including lung cancer EGFR mutation gene testing.
Consultation Program for Medical Devices

Objectives

Providing opportunities for industry, academia, and healthcare institutes to discuss scientific and regulatory requirements for medical devices with the Food and Drug Administration during their product development and validation stages.

Flowchart

Eligibility Review
Substantial Review
Official Meeting / Correspondence
Post-consultation Follow-up
Case Close

Consulation Outcome*

August 2019

- Under Review (4)
- Post-consultation Follow-up (20)
- Certificate Issued (35)
- Clinical Trial Approved (19)
- Technology Transferred (5)
- Abandoned (40)

* 119 cases received by the end of August 2019. The statistics may not reflect this number due to the fact that some cases may have reached more than one outcome in the statistics.
International Cooperation

Member of International Organizations

International Conferences

Collaborative Study for International Standards

Collaborative Study for Testing Methods
2019 APEC GRM CoE Workshop

TARGET AUDIENCE
- Senior regulators with at least 3 years of hands-on experience in the management of regulatory reviews
- Industry managers with at least 3 years of hands-on experience in the management of regulatory submissions

PROGRAM OVERVIEW
- On-line and self-paced learning to develop knowledge base in advance of in-person training
- In person training: 3 days with plenary sessions for all attendees
  In person training is designed with lectures, group discussions and applied case studies

TRAVEL & ACCOMMODATION
Funding for travel eligible economies may be available for regulators.

COE HOSTING INSTITUTIONS
- Taiwan FDA
- RAPS Taiwan Chapter

CONTACT INFORMATION
RAPS Taiwan Chapter Secretariat  Email: GRMCOE@gmail.com
2019 APEC Medical Devices Regulatory Science CoE Workshop

- Date: Oct. 22-24, 2019
- Hosting Institution: TFDA
- Co-Organizer: APEC LSIF RHSC
- Pilot Planning Committee
  - Japan: PMDA & JIRA
  - USA: AdvaMed
  - Taiwan: TMBIA, TAMTA, ITRI
- Topics
  - Use of standards in medical device assessment
  - Challenges in standards for regulatory purposes
  - Optimizing standards for regulatory use
Collaboration with Japan

Progress for the Pharmaceutical Working Group

• Sharing and comparing review points for further cooperation, including the pilot project on product review.
• Exchanging the experience on generic drugs and OTC promotion.
• Established the Information Sharing model and Direct contact of post-marketing surveillance information.

Progress for the Medical Devices Working Group

• Prepared two separate Q&As proposed by the industries from both countries and published for the benefit of stakeholders.
• Sharing challenges faced by both sides and exchanging review experience on cutting-edge technology to improve reviewer capabilities.
  
  E.g. Cybersecurity & AI medical devices
Progress for the QMS Working Group of Medical Devices

- 2019: Abbreviated mode is accepted by Taiwan and Japan authority in review of QMS.

- 2018: Monitored audit for TUV SUD PS Japan MoC has been signed in November 30. Start of Phase III after signing of MoC.

- 2017: EoL was modified to MoC format. MoC was confirmed by relevant authorities.

- 2016: Start of Phase II for QMS Working Plan (Road Map), and monitored audit for SGS Japan, PMDA, TUV Rheinland and BSI Japan. Revising of QMS Working Plan (Road Map) 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.
Future Prospects

To Enhance International, Regional and Cross-strait Regulatory Collaboration

To Establish Training Programs and Scientific Workshop
- GTP, GMP, and Specificity of cell production process, animal model, clinical trial design

To Accelerate Review Efficiency

To accomplish legislation of the Act
- To establish category and define the regenerative medicine, cell therapy product, gene therapy product, tissue engineering product

To continue establishing specific guidance
- Risk management and long-term traceability system

Better Products
Better Life

To establish an electronic-platform
Thank You