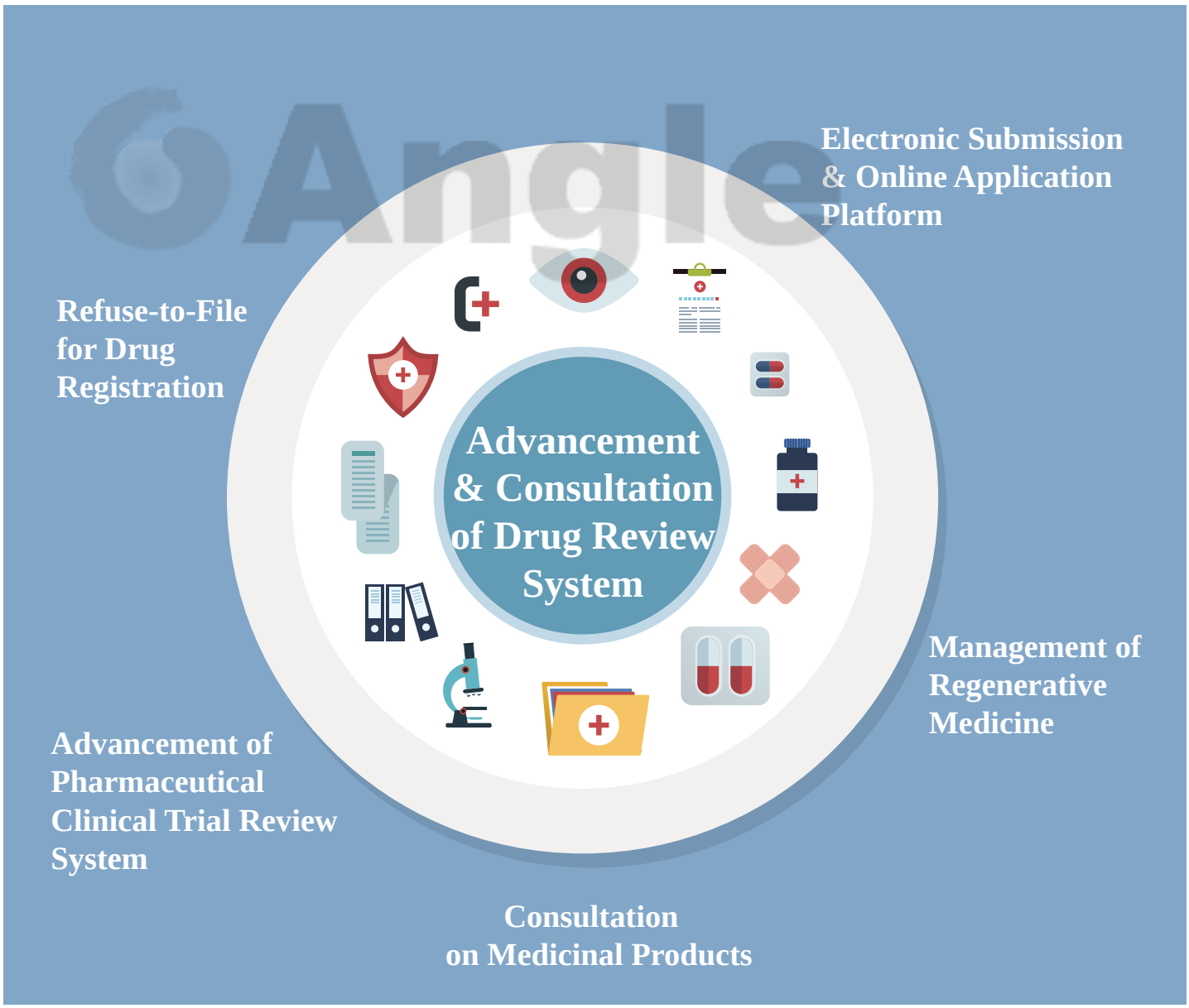
Refinement and Improvement of Drug Safety



APEC Regulatory Science Training Center of Excellence

TFDA Organized the “2017 APEC Good Registration Management (GRM) Regulatory Science Center of Excellence Workshop.”

- Policy on Orphan Drug Management
- Management Policy on Medicinal Product Trace and Track System
- Establish Drug Patent Linkage System
- Good Distribution Practice (GDP)
- Advancement of testing technology on illegal drugs
- PIC/S Meeting

03 Refinement and Improvement of Drug Safety

To complete the national drug management system and promote drug administration that in line with international provisions, TFDA has established corresponding regulations in accordance with International Conference on Harmonization (ICH) and World Health Organization (WHO) to gradually perfect the management system in Taiwan. As the quality requirements of post-marketing medicinal products by international laws and regulations are becoming more stringent every year, corresponding provisions in Taiwan are in need of keeping up with the updates. TFDA thereby reviews existing regulations and revises accordingly and establishes novel rules for drug management following the global trends in advance therapeutic products regulations. Moreover, to ensure the consistency of quality, safety and effectiveness of drugs, TFDA optimized the drug review system and set up registration/post-approval management scheme for medicinal products with high-risks or targeting specific populations. Meanwhile, TFDA actively works on international collaboration and participate and international activities to reach regulatory convergence and take part in global standard harmonization.

Section 1 Advancement and Consultation of Drug Review System

Origin of Policy

To facilitate the accessibility of new drugs and support the development of domestic biomedical/biotechnology industry, TFDA has optimized measures for clinical trial protocol reviews, which include established the expedited review track for regenerative medicinal products clinical trials, refined the review process of clinical trial protocol amendments and created a comprehensive regulatory consultation network/project counseling system to help applicants to prepare complete submission package, and thus accelerate new drug development as well as reducing relevant costs. In addition, TFDA continues advancing the review process of drug registration, implementing the refuse-to-file (RTF) policy for new drug registration, and promoting the online review and application platform (ExPRESS) to facilitate correct document submission and shorten the review/approval process.

To keep up with the emerging biotechnologies and ensure product safety and efficacy of regenerative medicines, TFDA actively develop regulations for the management of advanced biotechnology, and construct a specified regulatory framework for regenerative medicines based on the heterogeneity of regenerative medicinal products and its complexity in clinical applications and specialty in manufacturing processes. This regulatory framework is expected to achieve an independent and straight forward management on regenerative medicinal products.

Implementation Measures

1. Advancement of pharmaceutical clinical trial review process

The TFDA released three "Advancement Measures for Pharmaceutical Clinical Trial Protocol Review Process" on August 10, 2017. The details are as follows:

(1) Simplify the review process of "First-in-human medicinal products" clinical trials review process, i.e. change the review process from "consult with external experts case-by-case and forward to advisory committee meeting for further discussion if needed" to "reviewed by Center for Drug Evaluation (CDE) and consult with external experts if needed; forward to advisory committee meeting for further discussion if any further issue exists," to shorten the case-by-case consultation period.

(2) Establish the "Expedited Review Track for Regenerative Medicinal Product Clinical Trials," introduce a 30-day expedited review track for multinational (must be carried out at least in one of the 10 medically advanced countries, multicenter, non-first in human trials, and for investigator-initiated clinical trials which the regenerative medicinal product has been used in other clinical trials conducted in Taiwan and manufactured by the same laboratory with identical manufacturing processes for academic purposes, to encourage the development of emerging regenerative medicinal products in Taiwan.

(3) Refine the review process of clinical trial protocol amendments based on the risk levels and implement diverse review flows (i.e. technical review, administrative review, and retained by the applicant for future inspection) to enhance the review efficiency.

2. Refuse-to-file for the application of drug registration

The refuse-to-file (RTF) scheme for the application of drug registration was initiated since 2017 in order to strengthen the review efficiency. Upon submission for registration, the submission will be rejected if the applicant (1) fails to provide complete administrative documents in accordance with the Regulations for Registration of Medicinal Products; or (2) fails to provide complete technical documents in accordance with the format stipulated in the Common Technical Documents (CTD); or (3) fails to pay the submission fee based on the Fee Charging Standards for Registration of Western Medicinal Products and Medical Devices.

3. Electronic submission and online application platform for review of medicinal products

In order to harmonized with international standards, the paper-less application and review system of medicinal products procedure has been step wisely implemented since 2015, while submissions using paper-based copies and CDs are gradually reduced with the establishment of e-submission platform. The paper-less pharmaceutical management system was refined in 2018 and firstly implemented on the applications of license extension and cancellation, and the on-line submission system is design to be gradually integrated with the official documentation system. The comprehensive E-service system is expected to be fully implemented in 2020 and further enhance the review efficiency and to help the subsequent real-time data inquiries and updates.

4. Management of regenerative medicinal products

TFDA stipulated a draft of "Regenerative Medicinal Product Ordinance" in 2017, which clearly defines the regulatory scope as regenerative medicinal products that are "commercialized, manufacturing standardized and normalized for the purpose of batch production and marketing sales." This regulatory scope is distinguished from the regulation for regenerative medicinal therapies, which is defined as medical technologies that are "practices clinically performed to treat certain patient in certain medical institute." The contents of the draft Ordinance involves assessment of donor eligibility and informs consents, the management of conditional approval, post-marketing surveillance and tracking system. The regulatory framework is designed to ensure the quality, safety, and effectiveness of regenerative medicinal products and protect donor/patient's rights for proper treatments. By reinforcing the management policies and escalating the law hierarchy, it is expected to create a standard for the biomedical/biotechnology industry to comply with and support the development of regenerative medicine in Taiwan. Legislation of the Ordinance is expected to be finalized in the end of 2018.

5. Consultation and counseling on medicinal product projects

To facilitate pharmaceutical industry development, encourage novel drug research and development and provide consultations/counseling on new drugs, biologics, biosimilars, regenerative medicinal products that are under development or filing for registration, TFDA specifically stipulates the "Point for Project Consultation for Medicinal Products" to help applicants prepare documents adequately, and thus accelerate the approval new drugs and reduces corresponding costs.

Applications for the Project Consultation approach are assessed based on 4 indicators, including "innovation," "contribution," "early achievement" and "regulatory compliance." For applications qualified to the above criteria, TFDA organizes a project team to provide consultation

services and delineate potential defects, allowing the applicants to prepare complete submission package that fulfill review requirements, and thus facilitate review efficiency. TFDA also announced review points of all types of new drug registration, which provides references for the preparation of technical documents and helps increasing transparency of review, facilitating submissions and expediting new drug approval.

Outcomes and Benefits

In total, TFDA processed 298 new applications for pharmaceutical clinical trials in 2017; among them, 72% were multi-reginal and multi-center clinical trials (Figure 3-1). In addition, the ratios of Phase I and Phase II clinical trial applications have shown increasing trends for the past few years (Figure 3-2), indicating that the ability of related institutions in our country to conduct clinical trials and their quality level are recognized internationally.

In order to continue enhancing our country's competitive advantages in clinical trials and to advance the research and development of new drugs, the Administration streamlined the review procedure and review time efficiency for pharmaceutical clinical trial protocols. Three "Advancement Measures for Pharmaceutical Clinical Trial Protocol Review Process" were announced and enforced on August 10, 2017. The number of days required for processing the applications and the overdue rate has both significantly dropped (Table 3-1).

Regarding the review of drug registration, TFDA announced the refuse-to-file mechanism for applications of drug registration on January 1, 2017. Except for some applications that are rejected due to incomplete submission package, rest of the other applications have been able to enter the review process successfully. Ratio for the reviewed applications to total applications are 84.3% in new drug registration and 68.3% in generic drug registration. The time needed for repeated modifications of cases has been reduced and the time efficiency in the review of cases by TFDA has been improved.

To facilitate the development of the pharmaceutical industry in Taiwan, TFDA provides project consultation/counseling approach on medicinal products. As of the end of 2017, TFDA has successfully assisted the registration of 5 new drug by providing consultation services. Two of these new drugs, which are domestically developed new drugs, set new records as been first approved new drug for certain indication in the world: one of the two "Global No. 1" product with ferric citrate was approved for CKD patients receiving hemodialysis to control hyperphosphatemia; the other with liposomal irinotecan was approved for patients with metastatic pancreatic cancer treated with chemotherapy (gemcitabine).

Table3-1 Outcomes of "Advancement Measures for Pharmaceutical Clinical Trial Review System"

Implementation Measures	Outcomes
Simplify the review process of first-in-human medicinal products clinical trials	Shorten the average period from 68 days to 47 days
Establish the expedited review track for regenerative medicinal product clinical trials	Shorten the average period from 94 days to 26 days
Refine the review process of clinical trial protocol amendments	Reduce the overdue rate from 15% to 4%

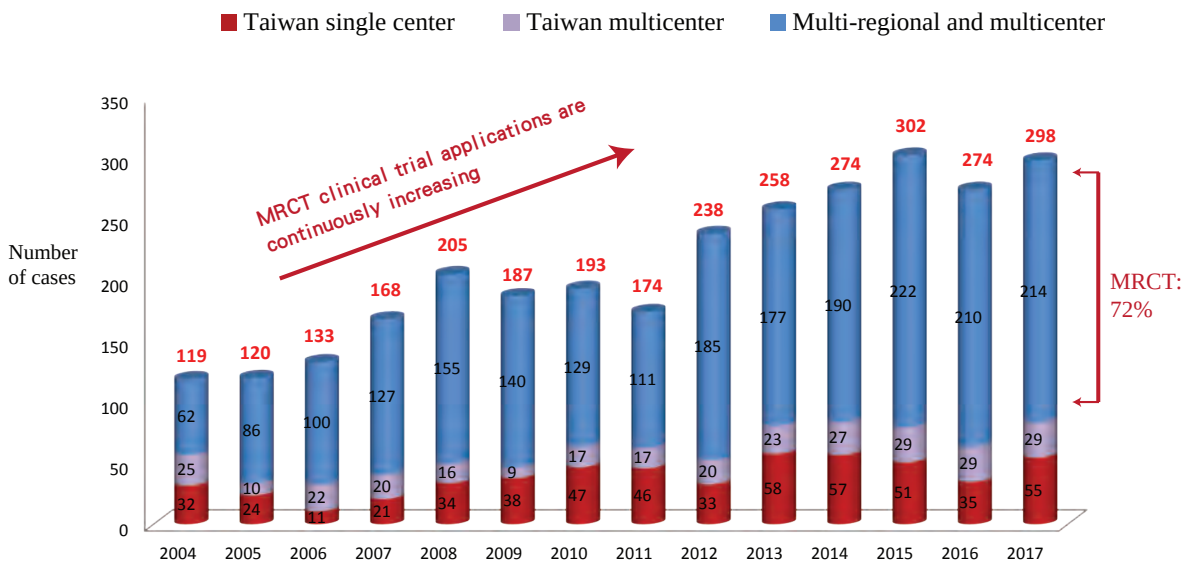


Figure3-1 The Applications for Clinical Trials of Medicinal Products (By Trial Scale)

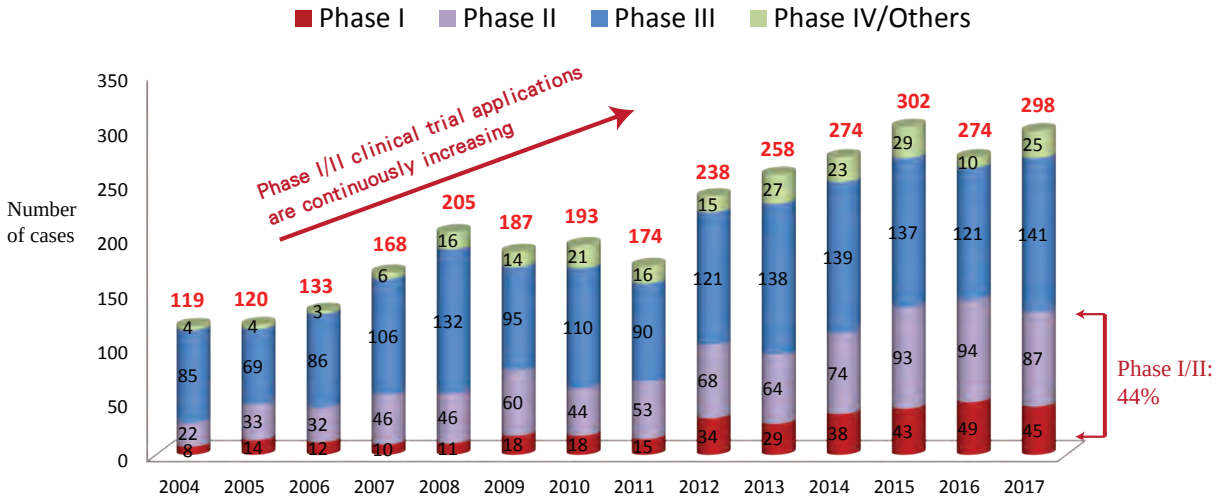


Figure3-2 The Applications for Clinical Trials of Medicinal Products (By Study Phase)

Section 2 Establish Drug Patent Linkage System

Origin of Policy

The focused topics of intelligence protection among international medicinal products lately consist of the linkage system ("patent linkage system") between exclusive protection, drug patent and listing approval in terms of drug permit applications.

Patent linkage system refers to the linkage between new drug listings and disclosure of patent information and the linkage between the review process of generic drug listings and the possibility of infringing new drug patents which allows pharmaceutical companies to resolve disputes (patent infringement issues) over patent-related issues within a certain time frame (before the listing of generic drugs). It is also a reference for central competent health authorities to approve/reject the listing of generic drugs.

Implementation Measures

By referencing regulations of the US, Canada and South Korea, and the current status of the pharmaceutical industry development in Taiwan, the TFDA added Chapter 4-1 "Patent Linkage of Drugs" in the *Pharmaceutical Affair Act*, and promulgated this section in the Government Official (Presidential Order) on January 31, 2018. The contents included that the holder of a new drug permit permit to submit patent information regarding substance, composition or formulation and medical use within the statutory limitation. The applicant for a generic drug permit must provide a statement describing the patent status of the approved new drugs. The applicant for a generic drug permit must notify the holder of the new drug permit, the Central Competent Health Authority, patentee or the exclusive licensee, in advance to allow the person of interest to clarify the validity of a patent or the possibility of patent infringement. After that, the Central Competent Health Authorities may continue reviewing the application of the generic drug permit application. However, the issuance of a drug permit may be temporarily suspended under special circumstances within 12 months. The first successful application of a generic drug permit without the fact of a patent infringement or patent around will be granted a 12-month period of marketing exclusivity.

Outcomes and Benefits

By implementing the patent linkage system and issuing patent rights to the inventor, it is expected to advocate the idea of patent right protection and affirm the great contribution of the drug permit holder, encouraging them to devote themselves to the development of medical/pharmaceutical research. It is also helpful to allow the holder of a new drug permit to control relevant patents before listing and to encourage and urge pharmaceutical companies devoted to novel drug development or patent around designs, in order to increase the volume of generic drug development, facilitate industrial potential and international competitiveness, and achieve the governmental goals of promoting emerging industries (e.g. biomedicine/pharmaceuticals/biotechnology).

Section 3 Management Policy on Medicinal Product Trace and Track

Origin of Policy

To strengthen the management of medicinal products distribution, TFDA stipulated the "*Regulations governing the trace and track system for medicinal products" based on Pharmaceutical Affairs Act* Article 6.1, paragraph 3 on September 6, 2016. The regulations specifically require vendors and manufacturers to establish a trace and track system based on the quality, efficacy, safety and risk levels to connect the source and distribution of medicinal products. The establishment of trace and track system is expedited in a faster manner due to the counterfeit CRESTOR incident on March 2, 2017.

Implementation Measures

Starting on July 1, 2017, the Administration has prioritized three classes of drugs, namely blood preparations, vaccines, and Botulinum toxins for Stage 1 trace and track system. Throughout 2017, a total of 351 businesses were helped to complete their declaration process. For the 116 items, the fulfillment rate of the declaration by the businesses exceeded 90%. In addition, in order to maximize the categories and items available for traceability reports, the Administration, on January 1, 2018 and July 1, 2018, respectively, based on the risk assessment and screening principles of high use volume and high value of NHI-covered drugs and with items such as orphan drugs, controlled drugs, and those with high technical thresholds and low counterfeiting risk excluded, announced in phases inclusion of 20 and 30 items of high interest in the traceability reporting system. Holders of permits for such drugs and distributors engaged in the wholesale of such preparations shall upload information such as sources and whereabouts of drugs from the previous month by the 10th day of the current month to the drug trace and track system.

Outcomes and Benefits

The drug trace and track reporting system became operational in May 2017 and is user-friendly with diversified interfaces; users can report by submitting Excel files (Comma Separated Values, CSV files), Web API and by completing an online form. In addition, to boost the familiarity of businesses and local health authorities with the drug trace and track system, the Administration added the trace and track section on its website, created the page promoting the exclusive zone for businesses in the reporting system, and set up the system consultation window. Throughout 2017, a headcount of up to 1,700 people received consultations. In addition, the Administration organized a total of 8 workshops and educational training sessions in 2017 for businesses and public health centers, which were participated in by a headcount of 375 people in total. The cooperation among businesses in reporting the required information and the reporting efficiency was improved to consolidate the drug tracking or follow-up reporting system.

To collect feedback from local applicants and health bureaus and optimize application platform and user's interface, TFDA establishes a back-stage management and statistical analysis area in 2018 to strengthen the management of drug supply chain, comply with local health bureau's inspections and ensure safe drug use.

Section 4 Good Distribution Practice (GDP)

Origin of Policy

The goal of implementing GDP is to extend the requirements on medicinal products quality control from GMP (in terms of manufacturing) to GDP (in terms of distribution), to ensure the quality and the integrity of medicinal products during storage and transportation, to effectively respond to emerging drug recall incidents, to properly distribute to the consumer within a reasonable time frame and to prevent falsified medicinal products from entering the supply chain. The ultimate goal is to ensure drug quality and safety of the public.

The Pharmaceutical Inspection Co-operation Scheme (PIC/S) officially released GDP in June 2014, which has then become a well-recognized GDP in the world. GDP is now well practiced in many international organizations and countries, including WHO, EU, Singapore, Malaysia, UK, Germany, Switzerland, USA, and Australia. To implement quality management of drug distribution, ensure drug safety, upgrade international competitiveness, the TFDA promotes global well-recognized GDP policy accordingly.

Implementation Measures

1. GDP-associated measures

Starting from 2011, the TFDA has initiated GDP policy by providing consultation and educational training sessions (e.g. focused forum, technology seminar, observation tour in pharmaceutical companies, etc.), organizing 710 sessions of on-site GDP experts/consultants counseling, and awarding 107 manufacturers with excellent performance. The TFDA also actively participates in communications and promotion activities, organizes several orientation meetings, convenes negotiation meetings and public hearing and reaches consensus on management policies and schedules with the industry. In addition, the TFDA not only convenes an advisory board meeting composed of industrial/official/academic experts to discuss about management system and technology regulations and summarize a frequent Q&A for the applicant's reference, but also establishes a PIC/S GDP zone (including approval lists, counseling programs, Q&A and educational

training programs) on the official webpage to promulgate policies and official directions as references for applicants.

2. Schedule and related laws of GDP implementation

On February 18, 2016, the TFDA promulgated the implementation details, and schedules of "*Good Manufacturing Practice (GMP) Part III: Distribution.*" Manufacturers and permit holders of Western medications are expected to meet all regulations starting from 2019. To achieve full-GDP implementation, the MOHW actively revises corresponding laws by promulgating the drafts of *Pharmaceutical Affair Act* Article 53-1 and Article 92 amendments. Such amendments have been promulgated under official Presidential Order on June 14, 2017. The "*Western Pharmaceuticals Good Distribution Practice Regulations*" were then released on December 28, 2017, as the GDP standard for Western drug dealers. Furthermore, to form a well-established management system, the MOHW also stipulated the "*Regulations for the Issuance and Management of Western Pharmaceuticals Distribution Licenses and Certificates*" to meet the requirements for a subsequent application and approval issuance.

Outcomes and Benefits

By promoting and implementing global well-recognized GDP, ensuring drug safety and improving drug distribution quality, 275 manufacturers and dealers of Western pharmaceuticals have met the criteria of GDP as of the end of 2017. (Figure 3-3)

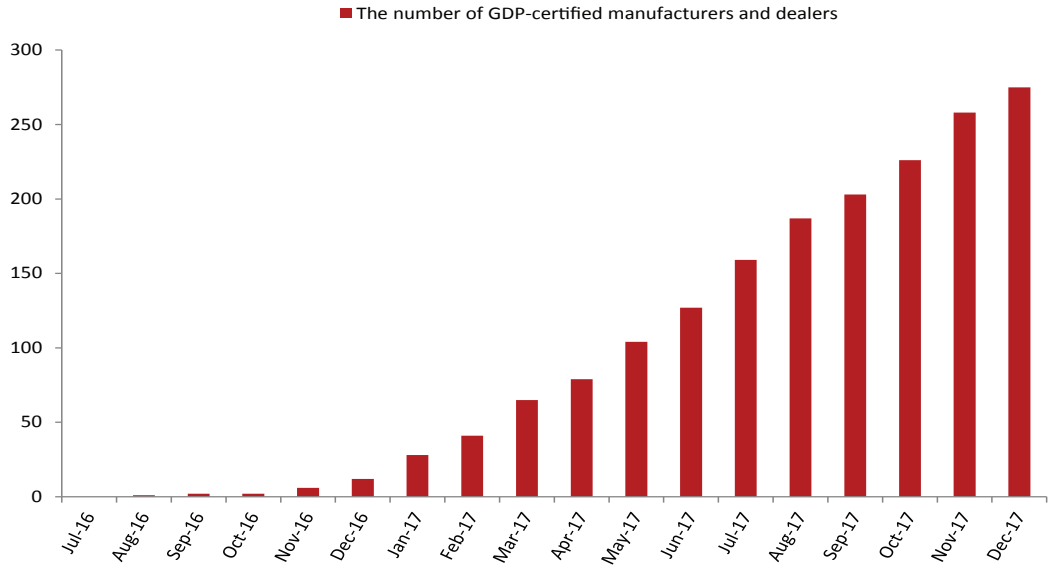


Figure3-3 The number of GDP-certified business undertakings as of the end of 2017

Section 5 Policy on Orphan Drug Management

Origin of Policy

The "*Rare Disease and Orphan Drug Act*" was finalized on January 14, 2000, and became effective from August 9 the same year. Since then, Taiwan has become the 5th region which had passed rare disorder-related acts in the world (after the US (1983), Japan (1993), Australia (1997) and EU (2000)), indicating that Taiwan keeps in step with global trends regarding the fulfilment of patient needs.

Although the US is the first country in the world stipulating regulatory systems regarding rare disorder and orphan drugs, whereby promulgated the "*Orphan Drug Acts*" long ago in 1983, Taiwan displays a more inclusive attitude toward such topic by combining the "*Rare Disorder Act*" and "*Orphan Drug Act*". The "Rare Disease and Orphan Drug Act" covers topics such as preventive eugenic health, health education, patient welfare, international collaboration and medical team staffing. The comprehensive scope of the Act suggesting that the management of rare diseases in Taiwan is not limit to orphan drug regulation, but has been referred to multidisciplinary teamwork (including disease prevention, medical assistance public health, etc.).

Implementation Measures

To encourage pharmaceutical companies to manufacture or importing orphan drugs, "*Rare Disease and Orphan Drug Act*" specifies that the valid duration of orphan drug licenses has been extended up to 10 years. During the 10-year period, no other drug registration of similar classifications will be approved to protect the interest of the thereof pharmaceutical company. In addition, under the premises of quality, efficacy and safety of medicinal products, the required application documents for orphan drug registration could be simplified (e.g. cancelling the requirement of certification of approval issued by one of the top 10 advanced countries, exemptions from sample testing, lower registration fee, etc.) to facilitate the manufacturs and importation of orphan drugs, therefore extend the lifespan of patients with rare diseases.

Outcomes and Benefits

As of the end of December 2017, a total of 99 drugs are launched to be subject to "*Rare Disease and Orphan Drug Act*" and a total of 85 orphan drug licenses have been issued.

According to Article 21 of the "*Rare Disease and Orphan Drug Act*", the central competence authorities are required to publish a list of approved orphan drugs on the annual report, indicating information such as the number of uses, number of indicated patients, adverse events and other relevant reports. Starting from the 1st issue of the "Annual Report on Drugs for Rare Disease"

published in 2002, all drugs of rare disease-related information is summarized and collected from paper-based information reported by medical institutes or pharmaceutical companies. In 2017, TFDA initiated the online reporting system for drugs of rare disease to encourage and facilitate relevant reports.

Section 6 APEC Good Registration Management Regulatory Science Training Center of Excellence (CoE)

Origin of Policy

To facilitate international collaboration and regulatory convergence for medicinal product management, the TFDA has become a regular participant in APEC Life Science Innovation Forum and is actively involved in the work promoted under the Regulatory Harmonization Steering Committee (RHSC). The TFDA has been serving as the co-champion of Good Registration Management priority work area (PWA) with the Ministry of Health, Labour and Welfare (MHLW) and the Pharmaceuticals and Medical Devices Agency (PMDA) of Japan. By promoting training and implementation of "good review practice" and "good submission practice" under the collaboration of regulatory authorities and industry, this work advocates the concept of "good registration management," promotes mutual trust between regulatory authorities and the pharmaceutical industry, and expedite regulatory convergence between APEC member economies by 2020.

Implementation Measures

In cooperation with RHSC to implement the platform of the APEC Regulatory Science Training Center of Excellence (CoE), each CoE hosting institution is responsible for developing and hosting training programs following the core curriculum developed by the PWA champions. The CoE serves as a platform to promote capacity, cooperation and regulatory convergence among different APEC member economies.

The TFDA hosted an APEC Good Registration Management Regulatory Science Training Center of Excellence Pilot Workshop in Taiwan in November 2016 and submitted an application to RHSC together with RAPS Taiwan Chapter for recognition as a formal CoE in February 2017. The application was endorsed without any objections in the RHSC Meeting on February 21, 2017.

TFDA, RAPS Taiwan Chapter, and APEC Life Science Innovation Forum have signed

a memorandum of understanding (MOU) in CoE operations in July 2017 based on the CoE Operating Model stipulated by RHSC. This achievement is credited as a milestone for TFDA because the capability in organizing regulatory science training has been well-recognized by a regional harmonization initiative, and is attributed to our long-term involvement of APEC activities.

Outcomes and Benefits

The TFDA hosted the "2017 APEC Good Registration Management Regulatory Science Center of Excellence (CoE) Workshop" in Taipei between October 31 and November 2, 2017. PMDA (Japan), RAPS Taiwan Chapter and Asia Partnership Conference of Pharmaceutical Associations (APAC), Ching-Kang Foundation for Pharmacy Promotion (CKF) and National Yang-Ming University were the co-organizers of this training event (Figure 3-4).

The training event lasted for 3 days, including common sessions, reviewer-specific sessions and applicant-specific sessions. A total of 70 (industry, academy, and official) participants from 10 APEC member economies took part in this training event, including Hong Kong (China),

Figure3-4 Group photo of the "2017 APEC Good Registration Management (GRM) Regulatory Science Center of Excellence Workshop"

Indonesia, South Korea, Malaysia, Papua New Guinea, the Philippines, Singapore, Thailand, Vietnam and Taiwan. The trainees should take part in organizing training sessions at their respective institutions, associations or companies to promote the concept of Good Registration Management to more APEC member economies. In addition, experts from Canada, Japan, the Philippines, Singapore, and UK were invited as speakers at the meeting to share their opinions and practical experience about Good Registration Management principles.

The event was well-recognized and obtained positive feedbacks from participants of different APEC member economies. After the event, the TFDA received requests from several APEC member economies for providing training materials and lecturers to help their organization of local training sessions. Serving as a hosting institution of the APEC Good Registration Management Regulatory Science Training Center of Excellence (CoE) not only increases the international visibility of TFDA but also facilitates our opportunities in international collaboration.

Section 7 Participation in PIC/S

Origin of Policy

The Pharmaceutical Inspection Co-operation Scheme ("PIC/S") refers to the official international organization composed of regulatory authorities in the field of Good Manufacturing Practice (GMP) of medicinal products from all over the world. The organization devoted to the international development, implementation and maintenance of harmonized GMP standards and quality systems of inspectorates and facilitating the co-operation and networking of competent authorities. Every year, the PIC/S Committee Meeting and annual seminar will be hosted by different PIC/S Participating Authority, as the largest PIC/S event, the seminar will focus on a particular aspect of GMP topic and open to inspectors from PIC/S Participating Authorities and other interested Medicine Regulatory Authorities.

Implementation Measures

1. PIC/S Committee Meeting

A 2-day PIC/S Committee Meeting was convened between September 11-12, 2017, discussing long-term developing road map (e.g. strategies and projects for harmonizing the GMP regulations and enhancing the international collaboration, including reviewing the progress of work plans on revising the standard, global inspector training, etc.) and short- to mid-term assignments and progress. During this meeting, the Chairperson, Deputy Chairperson, and Chairs of Sub-Committees of PIC/S in 2018-2019 were also elected. The representatives of TFDA were also candidates of positions of PIC/S Sub-Committee, to actively participate in PIC/S affairs and events, consolidate Taiwan's membership, increase our international visibility and explore more substantial collaboration opportunities with other competent authorities from other countries through PIC/S platform.

2. PIC/S annual seminar

PIC/S Annual Seminar was then hosted between September 13-15, 2017 (Figure 3-5), which was the grandest annual gathering of PIC/S that brings together global GMP inspectors to discuss pharmaceutical GMP-related topics every year. The theme of 2017 was "Quality Control Laboratories: How to Inspect." Quality Control is part of GMP which is concerned with sampling procedures, specifications, testing methods and release to ensuring that the necessary and relevant tests are actually carried out and materials and products will only be released for use and supply until their quality has been judged to be satisfactory. Discussions involve "the latest GMP requirements," "out-of-specification (OOS) and out-of-trend (OOT) investigation," "data integrity," "technical transfer of test methods," and "inspection skill of quality control laboratories at pharmaceutical manufacturers." Through keynote speeches given by experts from the US, UK, France, Australia, Canada, Japan and Taiwan and workshops discussions with participants, a more complete quality standard, improving inspection regulations and skills to ensure the integrity, authenticity, reliability and traceability of the data, effectively supervise quality control laboratories of pharmaceutical manufacturers, and eventually achieve the goal of public benefit.

Outcomes and Benefits

1. Become a member of PIC/S

After becoming a PIC/S participating authority since 2013, the TFDA actively participates in PIC/S events and has organized PIC/S meetings and activities in Taiwan several times. All events/activities went very successfully and helped the TFDA win the opportunity to host “2017 PIC/S Committee Meeting and Annual Seminar” in Taiwan.

2. PIC/S handover ceremony

The finale of 2017 PIC/S Annual Seminar is the handover ceremony. By receiving the walking stick of PIC/S from the previous Organizer (MHRA, UK, 2016) and passing it to the next Organizer (US TFDA, 2018) (Figure 3-6), Director-General (TFDA) Shou-Mei Wu declared the event conclude successfully. A total of 170 official inspectors of 60 regulatory authorities and international organizations from 50 countries participated in the event. As the event was well-recognized by both the PIC/S and the participants, the international visibility of Taiwan and professionalism of TFDA is greatly acknowledged.

Figure3-5 PIC/S annual seminar between September 13-15, 2017

Figure3-6 PIC/S handover ceremony

Section 8 Advancement of Testing Technology on Illegal Drugs

Origin of Policy

The TFDA uses evidence-based method to uncover high-risk and high-violation rate products, prevent illegal drugs from being distributed. The TFDA has also actively improved its testing volume and capacity by participating in international meetings and experience exchange/sharing.

Implementation Measures

1. Suspicious counterfeit drugs

As the counterfeit “CRESTOR” incident in March 2017 (Figure 3-7) severely compromised safe drug use in Taiwan, the TFDA completed 79 CRESTOR sample testing within a week. Non-conforming samples derived from lot MV503, MK479 and MF414 contained the counterfeit substance Atorvastatin.

During sampling and testing, 28 samples derived from illegal factories and warehouses, the TFDA also seized suspicious evidence of a counterfeit drug, including ingredients for “Januvia,” Januvia tablets and packaging materials. For these reasons, the TFDA immediately activated audition/inspection on a total of 462 commercialized products, i.e. 184 Januvia samples (ingredient: sitagliptin), 150 VYTORIN samples (ingredient: Simvastatin/Ezetimibe), 117 LIVALO (ingredient: Pitavastatin), 11 ZYTHROCIN (ingredient: Azithromycin). After inspecting the appearances, components and amounts, all of the above products met the manufacturer’s specifications and thus all doubts have been cleared.

The TFDA responds very quickly to prevent counterfeit drugs from being distributed. A total of 569 samples were tested in 2017. By adopting evidence-based science, the TFDA is able

Figure3-7 Samples of blood lipid lowering agent

to provide prosecution and justice department real-time audition and inspection results/analysis as the foundation for administrative procedures. Besides that, the TFDA is also keen to develop short-acting testing methods, in order to prevent illegal drugs from being distributed and to maintain safe drug use.

2. Successfully prevent illegal BTX preparations from being distributed into Taiwan

Under the assistance of TFDA, MOF seized unapproved BTX preparations imported from South Korea (Figure3-8). The test results showed that the illegal preparations contained Botulinum Toxin Type A, indicating that the importer has violated the *Pharmaceutical Affair Act* Article 22-1, Paragraph 2: Self-import medicinal products without approval. Such information then was launched on the TFDA website to suggest to the public how to choose legal products rather than use medicinal products without approved sources; and to help custom officers be aware of similar incidents. In 2017, with the assistance of TFDA, MOF successfully stopped 5 batches of similar BTX preparations (either through posted packages or tourists) from entering Taiwan and thus preventing illegal drugs from being distributed into the Taiwan market.

Figure3-8 BTX preparation samples

3. TFDA hosted the “2017 APEC Conference on Management and Related Scientific Detection Technology for Adulteration of Dietary Supplements with Drug and Drug Analogs”

TFDA hosted the “2017 APEC Conference on Management and Related Scientific Detection Technology for Adulteration of Dietary Supplements with Drug and Drug Analogs” at NTUH International Convention center between June 28-29, 2017 (Figure 3-9), more than 200 industry, academy and official prestigious guests from the US, Europe, Japan, Singapore, South Korea and

Malaysia participated in the event.

Many international experts were invited to deliver speeches sharing testing technology or management experiences in their countries. Speakers from Taiwan (e.g. Deputy Director-General Dr. Hui-Fang Cheng, Prosecutor Hsin-Pei Shen from Taipei District Prosecutors Office and Officer Wen-I Liao from MOF) also gave talks regarding topics such as “Experiences of Illegal Drugs in Taiwan,” “Experiences of Counterfeit Drugs Investigations in Taiwan” and “Custom Boarder Measures of Drugs in Taiwan,” and the participants can understand and discuss about current challenges on seizing illegal drugs through communication and sharing.

Figure3-9 2017 APEC Conference on Management and Related Scientific Detection Technology for Adulteration of Dietary Supplements with Drug and Drug Analogs

Outcomes and Benefits

Testing methods are energetic developing in usual, and can be quickly mobilized upon occurrence of emergencies (such as incidents involving illicit drugs) to successfully intercept unknown drugs and prevent illicit drugs from entering the market. TFDA will continue to participate in related conferences, exchange and discuss the experiences with international experts, as well as further improve our analytical techniques in order to protect public health.