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Reinforce Management of Medicinal Products





Enhance Regulatory Environment for Medicinal Product Management

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- Implement the Patent Linkage system of Drugs
- Facilitate on new drug approvals and shorten the average review time



Reinforce Medicinal Product Digital Management and Risk Control

- Implement electronic submission system for drug registration
- Improve drug safety surveillance and analysis
- Increase critical pharmaceuticals domestic production



Actively Participate in International Pharmaceutical Organizations

- Expand participation in ICH related meetings
- Host the 2021 APEC International Conference
- Hold the 9th Joint Conference of Taiwan and Japan on Medical Products Regulation
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Reinforce Management of Medicinal Products

In order to implement the product life-cycle management and effectively ensure the safety, efficacy, and quality of medicinal products, TFDA actively participates in international organizations which constructs a robust regulatory environment and harmonizes with international standards to improve regulations of medicinal products management. We continue working on various aspects, such as the regulations of medicinal product distribution, digital management, the supervision of quality and safety, and the inspection technology for quality, in order to further strengthen the risk management and thus provide a safe environment for medicinal products usages as well as facilitate the development of the domestic pharmaceutical industry. In addition, TFDA works on medical information exchange with New Southbound countries to expand the visibility and influence of Taiwan within the New Southbound countries.

■ Section 1

Enhance Regulatory Environment for Medicinal Product Management

■ Introduction of the Policy

In order to cope with the development

trends around the world, TFDA not only increases the accessibility of medicinal products, expedites the drug approval process, but also encourages the drug development to fulfill the medical needs to the public. At the same time, we continue improving the relevant regulations and the patent linkage system of drugs, as well as cooperating with the current development status of the domestic pharmaceutical industry, to provide a better medicinal product regulatory environment.

■ Implementation Strategy

I. Promote the legislation of “*Regenerative Medicinal Products Act*”

In order to promote the sustainable development of regenerative medicine, the Ministry of Health and Welfare has been promoting the formulation of the “*Three Laws of Regenerative Medicine*” since 2021, using the “*Regenerative Medicine Development Act*” (*Draft*) as the supreme law to establish the overall goal and direction of regenerative medicine development in Taiwan. The “*Regenerative Medicine Implementation Act*” (*Draft*) and the “*Regenerative Medicinal Products Act*”



(Draft) were then formulated based on the regenerative medicine implementation management and regenerative medicinal products. Among above, TFDA is in charge of the “*Regenerative Medicinal Products Act*” (Draft). In addition, TFDA continues to announce the stipulation of relevant review guidance on regenerative medicinal products as reference for the industry developing regenerative medicinal products, and further improving the regulatory environment for regenerative medicinal products.

II. Implement the Patent Linkage of Drugs

In order to improve the intellectual property protection environment in medicinal products, an amendment to the Chapter 4-1 of the *Pharmaceutical Affairs Act*, Patent Linkage of Drugs was announced under the Presidential Decree on January 31, 2018. In addition, TFDA announced the sub-regulation and implemented the Registration System for Patent Linkage of Drugs to provide new drug owner list and to publish patent information. The implementation of the Patent Linkage of Drugs has been launched since August 20, 2019.

III. Improve the review mechanism for new drug registration

TFDA has announced a series of specific measures in recent years, including the announcements of the “*Points to Consider on Drugs for Pediatric or Rare Disease Designation*”, the revision of the “*Abbreviated Review Mechanism for New Drug Ap-*

plications”, “*Priority Review Mechanism for New Drug Applications*”, “*Accelerated Approval Mechanism for New Drug Applications*”, “*Points to Consider for Breakthrough Therapy Designation*” to improve the efficiency of drug review and accelerate the approval of new drugs.

▪ Achievements and Benefits

I. Draft the “*Regenerative Medicinal Products Act*” (Draft)

In line with the promotion plan of the “*Three Laws on Regenerative Medicine*”, TFDA has been drafting the “*Regenerative Medicinal Products Act*” (Draft) since 2021, which covers the management of registration of regenerative medicinal products, the relevant regulations on conditional approval, the protection of the rights of the providers, and the regulations on the manufacture, sale and post-marketing management of regenerative medicinal products.

II. Implementation of the Patent Linkage of Drugs

TFDA implemented the Patent Linkage of Drugs to achieve the legislative intent of the patent law to protect patentees, affirm the research and development efforts of new drug license holders; and provide generic drug industry with transparent patent information and firsthand patent status, so as to encourage generic pharmaceutical companies to engage in design around of patent. In addition, we clarify infringement-related concerns before going on the market, so that the launched generic drugs

will not be subjected to the risk of suspension of sales at any time due to infringement issues, which can further affect the rights and interests of patients. As of the end of 2021, there were 22 cases of drug patent linkage challenging design around and 9 drug licenses were issued.

III. Facilitation on New Drug Approvals

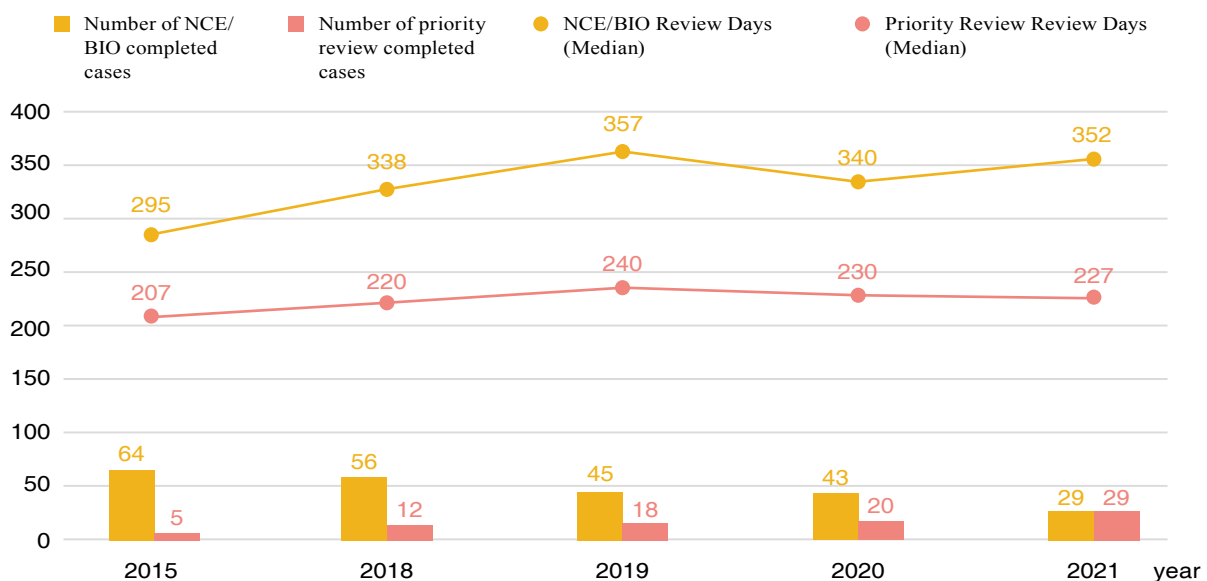
Among the 134 new drugs approved in 2021, 61 were new drugs with new chemical entities (NCE) and 42 were biological products. In order to accelerate the launch of drugs to fulfill the medical needs in our country, TFDA significantly adopted more cases of new drugs with NCE and biological products under the priority review mechanism. There were 29 cases were reviewed under the priority review mechanism in 2021, and the average review time was shortened to 227 days (Figure 3-1).

■ Section 2

Reinforce Medicinal Product Digital Management and Risk Control

■ Introduction of the Policy

With the advancement of international pharmaceutical regulations and electronic drug policy administration, the development of electronic submission for drug registration has become the current international trend. TFDA continues to enhance and expand the functions of the online submission system for drug registration, in order to accelerate operations and improve submission quality, and also to strengthen the active and passive drug monitoring mechanism for better risk management and quality control. In addition, TFDA enhances the domestic production capacity of critical pharmaceuticals and Active Pharmaceutical Ingredients (APIs) in Tai-



* RTF cases are not included in the calculation

Figure 3-1

Comparison of the Registration Review Days between the Standard Review and the Priority Review for New Drugs of NCE/Biological Products



wan and provide domestic pharmaceutical manufacturers with consultation and fast review process to gradually strengthen and consolidate the supply chain of APIs.

▪ **Implementation Strategy**

I. Strengthen Taiwan's electronic management of drug administration

In order to implement electronic drug administration, and comply with the regulations of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) and other international standards, TFDA continues to expand the functions of the electronic submission system for the application side, review side and document management, improve the quality of the submission and the digital integration of the electronic review task, further improving the drug registration and review environment. TFDA has announced the launch of the electronic Common Technical Document (eCTD) system since January 1, 2022.

II. Reinforce drug safety surveillance and analysis

In addition to the reporting system, TFDA also actively monitors domestic and international drug safety and quality information, conducts quality surveillance of commercial products and manufacturers audits. TFDA shall initiate safety re-assessment or quality investigations if new safety issues or major quality abnormalities are found. At the same time, in order to

understand the clinical use of medicines in Taiwan, TFDA also uses the national health insurance database to analyze the drug usage in Taiwan as reference for the evaluation of the effectiveness of risk control measures and future policy making.

III. Strengthen critical pharmaceuticals and increase domestic production capacity

TFDA completed the item evaluation of critical pharmaceuticals, which based on the domestic list of essential drugs, national health insurance data, current status of drug license applications and sources of API supply; TFDA also drafted a list of the “critical pharmaceuticals” and convened domestic pharmaceutical manufacturers to jointly discuss R&D strategies to enhance R&D willingness with regulatory guidance and efficient review. The relevant items shall be adjusted annually in accordance with the status of drug supply on a rolling evaluation base.

▪ **Achievements and Benefits**

I. Implement electronic submission system for drug registration

Through the integration of pharmaceutical regulations and information management, TFDA has been promoting the electronic registration of drugs since 2021. A total of 31 companies have been assisted to complete the eCTD submission test and pass the system verification. In addition, a number of new online application items were added in 2021, such as new clinical

trial applications, changes clinical trial amendments and clinical trial study report applications, to provide a wide range of online applications.

II. Drug safety surveillance and analysis

In 2021, there were 13,615 domestic adverse drug reaction reports, 75 domestic and foreign drug safety alerts, 220 COVID-19 vaccine safety alerts, 32 drug safety assessments, 5 drug risk communication forms and 4 drug safety quarterly newsletters were issued; TFDA received 893 reports of suspected product quality defects and actively monitored 1,470 foreign drug quality alerts. These measures were taken to raise the health care professionals' and the public awareness to ensure the safety of the public medication.

III. Increase critical pharmaceuticals domestic production

TFDA selected 259 "critical pharmaceuticals" to communicate with the domestic pharmaceutical manufacturers about the willingness to produce. In 2021, 1 case of domestic critical API development was identified, and TFDA assisted in evaluating and providing project counseling on compliance with the relevant regulations and reviews for marketing applications. In addition, TFDA provided consulting services on the R&D process and marketing regulations for 5 critical pharmaceuticals development cases.

■ Section 3

Complete the Regulations for the Distribution of Medicinal Products

■ Introduction of the Policy

The Good Distribution Practice (GDP) is a measure to extend the rigorous quality management spirit of Good Manufacturing Practice (GMP), covering the overall pharmaceutical supply chain to ensure the quality and integrity of medicinal products can be maintained during the process of delivering to the pharmaceutical companies, medical institutions, and pharmacies from the pharmaceutical manufacturers.

Many organizations and countries around the globe have implemented the GDP for Medicinal Products. The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) had also officially announced the Good Distribution Practice for Medicinal Products in June 2014. Therefore, TFDA has been promoting yearly the GDP system that meets the international standards, to complete the drug distribution quality management, ensure medicine work safely for publics and increase international competitiveness.

■ Implementation Strategy

I. Revise GDP-related regulations

To actively improve the related laws and regulations, TFDA issued an amendment to Article 53-1 of the *Pharmaceutical Affairs Act* under the Presidential Decree



on June 14, 2017. The regulations specify that businesses engaged in the wholesaling, importing and exporting of western medicines should meet the requirements of the GDP, and their businesses can only be implemented after passing the inspection and obtaining the western pharmaceuticals distribution license by the central health competent authority.

In conjunction with the amendments to the *Pharmaceutical Affairs Act*, relevant management regulations were formulated on December 28, 2017, and May 28, 2018, respectively, specifying regulations on the application for inspection and issuance of licenses.

II. Implementation timeline of GDP

- (I) On February 18, 2016, Ministry of Health and Welfare (MOHW) announced that pharmaceutical manufacturers and pharmaceutical companies holding the Western Pharmaceutical Product licenses shall comply with the GDP for Medicinal Products starting January 1, 2019.
- (II) On May 10, 2019, it was announced that pharmaceutical companies of the western pharmaceutical products that require cold chain storage and transportation shall comply with the

GDP for Medicinal Products starting January 1, 2022.

- (III) On July 27, 2020, it was announced that pharmaceutical companies that handle the distribution, import, and export of active pharmaceutical ingredients of western medicine shall comply with the GDP for Medicinal Products starting January 1, 2023.

III. Implement the GDP related supplementary measures

TFDA has progressively promoted the distribution management system of western medicines since 2011 and provided consultation and educational training to the industry, including continuing to conduct topic forums, technical seminars, and teaching observation of pharmaceutical companies. TFDA also invited GDP experts to provide on-site counseling. TFDA actively communicates with the industry to disseminate related management policies and timelines; moreover, TFDA and the industry reach a consensus; We created a PIC/S GDP area on TFDA official website for announcement of the relevant GDP regulations to be used as references for the business operators.



▪ Achievements and Benefits

By the end of 2021, a total of 827 western pharmaceutical manufacturers and companies have fulfilled the GDP standard to ensure the quality of drug storage and transportation as well as the quality and safety of drug use.

■ Section 4

Actively Participate in International Pharmaceutical Organizations

▪ Introduction of the Policy

In order to deepen and promote international collaboration, TFDA continues to participate in important international organization events, such as Asia-Pacific Economic Cooperation (APEC), ICH, and PIC/S, etc., and also strengthen bilateral and multilateral cooperation through exchange and experience sharing with various international regulatory institutions, further enhance our international participation and influence of Taiwan's pharmaceutical administration.

▪ Implementation Strategy

I. Expand participation in ICH related meetings

After officially becoming a member of the ICH, TFDA has continuously expanded its participation in the ICH Assembly Meeting and worked with expert working groups to formulate global drug technical guidelines to keep up with international standards and improve international reg-

ulatory environment. In addition, TFDA organized relevant training to support the domestic pharmaceutical industry to implement ICH-related regulations.

II. Host the 2021 APEC International Conference

TFDA hosted the “2021 APEC Good Registration Management Regulatory Science Center of Excellence Workshop (GRM CoE)” from August 24 to September 16, 2021. TFDA collaborated with teams of experts from industries, regulatory authorities and academia across countries and institutions to provide trainings for regulatory science professionals among APEC economies. We also invited experts among over the world to share and exchange their experiences in the pharmaceutical administration.

III. Conduct the 9th Joint Conference of Taiwan and Japan on Medical Products Regulation

TFDA hosted the “9th Joint Conference of Taiwan and Japan on Medical Products Regulation” on October 14, 2021, via video conference with Japan. Both Taiwan and Japan shared the latest information of medical products regulations, as well as other important topics such as COVID-19 measures, orphan drugs regulations, implementation for new medical devices regulations and emerging topics of medical devices.

IV. Continue to participate in the PIC/S activities

As a Participating Authority of PIC/S, TFDA sent representatives to sev-



eral sub-committees to participate in the organization affairs; also, to participate in the expert circles and working groups discussing the revision of GMDP regulations and standards with international experts. In 2021, the participated meetings include the first and second “Virtual Committee Meeting”, “Inspectors Training on ICH Q12 Webinar”, “PIC/S-IES Joint Webinar on Distant Assessment/Remote Virtual Inspection”, “2021 PIC/S Virtual Seminar” on “GMP Assessment Approaches in Post COVID-19 Era” organized by MFDS of Korea, and “The 2nd PIC/S Expert Circle Meeting on Controlling Cross Contamination in Shared Facilities” organized by WHO.

▪ Achievements and Benefits

I. Contribution to ICH-related meetings

TFDA attended the ICH Assembly Meeting as a full member in June and November, 2021. Towards the end of 2021, 44 experts were nominated to participate in 28 ICH expert working groups and participated in the formulation of ICH guidelines with

other international experts to make an active contribution. In 2021, TFDA completed two drug guidelines, and also conducted ICH guidelines training in Taiwan to enhance the familiarity within the industry, so that emerging regulations of pharmaceuticals can be more effectively implemented in Taiwan’s pharmaceutical industry.

II. Promote cooperation and interaction of pharmaceutical management in the Asia-Pacific region

Through organizing APEC workshops, TFDA actively maintains good relations with various economies and seeks opportunities for close cooperation. TFDA also provides a platform for communication and dialogue between industries, regulatory authorities, and the academia, which helps strengthen Taiwan’s overall capacity. In 2021, 69 seed participants from 12 member economies completed the training. In addition, TFDA has been reporting periodically on the results of promoting regulatory harmonization to APEC, which further expands and accumulates our international impacts.





Figure 3-2 2021 9th Joint Conference of Taiwan and Japan on Medical Products Regulation

III. Reinforce bilateral medical product interaction between Taiwan and Japan

Apart from the official representatives of Taiwan and Japan, more than 800 participants from industries joined the conference. Through the Joint Conference of Taiwan and Japan, business operators from both sides were able to have a better understanding of pharmaceutical and medical device regulations, and to enhance mutual understandings and collaborations between the officials and the industries, creating a blueprint for Taiwan-Japan collaboration in medical product regulations (Figure 3-2).

IV. Continue to strengthen GMP inspection through the PIC/S platform

(I) Assign representatives to participate in PIC/S affairs and activities, TFDA could express opinions directly, keep

abreast of the latest international regulatory trends, ensure the quality of Taiwan’s pharmaceuticals, strengthen our participation in international affairs, and enhance the TFDA’s visibility and influence.

(II) TFDA participated in several meetings held by PIC/S in 2021, which included the introduction and updating of latest GMP regulations and interacted with Regulatory Authorities in the field of GMP from various countries to share information as well as the experiences and mechanisms of remote assessment of pharmaceutical manufacturers; in order to understand the change of management system of pharmaceutical manufacturers in the world, and the future status of GMP assessment approaches in post COVID-19, to align the GMP management system of Taiwan to harmonize with international standards.

■ Section 5

Improvement of Drug Quality Analysis Technology

■ Introduction of the Policy

In response to the international incidents of the possible presence of the mutagenic azido impurities such as AZBT and 5-AMBBT in sartan medicines, an analytical method is required for detecting the contaminants in pharmaceuticals to ensure the medication safety for the public. Further, in response to the international development trend in the field of regenerative medicine and to meet the large demand for quality control testing of pharmaceutical R&D in Taiwan, it is also necessary to introduce innovative preparation methods and new testing technologies of international standards and establish human cytomegalovirus nucleic acid national standards to support the industry's testing needs and to meet the quality regulations of related products.

■ Implementation Strategy

I. Introduction of multi-analytical technologies to detect drug impurity

Based on the characteristics of the compounds, TFDA developed a new method to detect the azido impurity AZBT in five sartan drugs, using HPLC-MS/MS with simple sample preparation along with addition of internal standards for calibration. Besides, TFDA conducted quantitative analysis of 5-AMBBT azide impurity in Losartan with HPLC-DAD.

II. Introduction of international innovative technology for producing national standards

For the first time, TFDA produced and established credible human cytomegalovirus nucleic acid national standards in Taiwan. We introduced WHO's virus culture method by using cell line; then the General European Official Medicines Control Laboratory compiled Digital Polymerase Chain Reaction (DPCR) detection technology was used to quantify the candidate standard. Three foreign official control laboratories and two domestic biotechnology-related laboratories have been invited to join the collaborative study organized by TFDA to ensure the prepared standard credible as a standard control of raw materials for cell therapy products.

■ Achievements and Benefits

Two fast, sensitive and accurate analytical methods have been established and published as recommended methods, which can be adopted by private laboratories, for testing azido impurities in sartan APIs. TFDA's work will help increase the testing capacity in Taiwan. The established analytical methods have been applied to 78 API sample testing, and the affected drug products have been recalled from the market according to the test results to ensure drug safety. The methods were also published on the General European OMCL Network website. TFDA makes effort in promoting international cooperation through the continuous exchange of pharmaceutical information to enhance international visibility. TFDA not only has been recognized interna-

tionally for production of biological standards through the innovative preparation methods and quantitative techniques, but also supplies to domestic industry for quality control of raw material testing, hence enhances self-sufficiency of Taiwan's testing capacity.

■ Section 6

Deepen the Medical Information Exchange of the New Southbound Policy

■ Introduction of the Policy

To implement Taiwan's New Southbound Policy, TFDA acts in concert with the Ministry of Health and Welfare to promote the "New Southbound Medical and Public Health Collaboration and Industrial Chain Development" flagship project, which aims to deeply cultivate the medical and health network and expand Taiwan's influence in the New Southbound countries through Taiwan's medical and health care soft power, and to promote Taiwan's medical and health care industry development while linking the comprehensive medical and health care industry chains. In the post-epidemic era, TFDA not only strengthens the medical exchange and cooperation with New Southbound countries through our experience gained through long-term commitment in establishing an international pharmaceutical regulations environment, border pandemic control concept, and the relevant industry advantages; but also reinforces health industry partnership with New Southbound countries to assist our

health industry to enter the New Southbound market and to accelerate the development economy and trade of the regional networks.

■ Implementation Strategy

I. Collect and analyze healthcare product regulations information in new southbound countries

In order to conduct in-depth research on the new southbound national pharmaceutical-related regulation information and exchange of medical management information technology to establish long-term and stable partnerships, TFDA has been collecting information on regulations and industrial trends through the related seminars held by the New Southbound countries, including 3 online seminars on medical and health-related topics held by Singapore, Australia and Thailand. In addition, the Director General of TFDA was invited as a lecturer at the "2nd APEC Virtual Workshop on Facilitated Regulatory Pathways" on September 16, 2021. By sharing the review, approval of drugs for rare diseases and related regulations and management system and exchanging the experience of regulatory decision-making with health authority representatives of many countries, not only the multilateral interactive partnership was strengthened, but information on relevant national laws and regulations was also collected.



II. Conduct courses on new southbound countries medical and health policies and regulations

On September 30, 2021, TFDA conducted courses on the pharmaceutical regulations system and application practices of the new Southbound countries. Experts and scholars in the medical and health fields and representatives of the pharmaceutical industry were invited to share information on the regulatory strategies, regulation updates and changes in trends in New Zealand, Australia and Singapore. These courses would help to strengthen authorities' regulatory attainment and benefit the international harmonization of pharmaceutical regulations in Taiwan.

▪ Achievements and Benefits

In the post-epidemic era, digital technology is used to actively understand international pharmaceutical regulations and trends, including completing attendance reports of medical and health-related seminars and sharing regulatory practice management courses, which benefits the exchange of information, the establishment of communication channels, as well as the promotion of bilateral or multi-lateral cooperation. TFDA expects to use this model to strengthen practical exchanges with new southbound countries and other countries to optimize medicinal product management and expand international cooperation opportunities.

