PROFESSION
SERVICE
QUALITY
INNOVATION

2019

Taiwan Food and Drug Administration
Annual Report

CONTENTS

2019 Taiwan Food and Drug Administration Annual Report: Foreword

Protecting public health and establishing a safe living environment are important principles for our government administration. Taiwan Food and Drug Administration (TFDA) aims to regulate the quality and safety of food, drugs, medical devices, and cosmetics that are daily used by the public. In order to document the important policies and implementation of TFDA, an annual report that summarizes various important policies, plans, and achievements in the previous year is prepared every year and published domestically and internationally for reference.

In 2018, TFDA continued to improve its work in various aspects and achieved excellent results. For food safety management, we conducted the “Five-point Food Safety Policy reform plan” to improve the farm-to-table management system. We strengthened border inspection effectiveness as well as stipulated and amended 46 relevant regulations and standards regarding the Act Governing Food Safety and Sanitation, to enhance the management capability in the food industry, and ensured a “Safe and Healthy Food” environment for consumers. At the same time, we were committed to continuously integrating inter-departmental resources and using big data identification data to build automated risk identification modules in order to further improve risk management and the efficiency of early warning detection.

As for the management of drugs, we refined new drug review management system to accelerate new drug approval process. In order to reinforce the drug risk control, high-profile category items were added in phased into the trace and track system of drugs in 2018 and finished drug safety reassessment of 47 items to ensure the quality of medicines. Moreover, 647 western pharmaceuticals manufacturers and dealers have met GDP standards to fulfill the quality management of the distribution practice for medicines. Also, new pharmaceutical factory for controlled drugs has completed and been in compliance with the PIC/S GMP to enhance the manufacturing quality and production capacity of schedule 1 and 2 controlled drugs.

Regarding cosmetics, after years of evaluation, communicating with stakholders and reviewing by relevant government organizations, the "Cosmetic Hygiene and Safety Act" was officially put into place in 2018, for the future management of cosmetics will be more effective. Moreover, regulations on the Residue Limit for several kinds of heavy metal contained in cosmetics were also amended, to ensure the consumers’ safety and foster the development of the cosmetics industry.

In 2018, we finally joined and became a member of ICH (International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use), which is a

major achievement in the international field of medicinal product management regulations. In addition, we signed a cooperation agreement on pharmaceutical management with Malaysia; and the Memorandum of cooperation on the Quality Management System of Medical devices with Japan. Furthermore, we also hosted several workshops and forums, which greatly enhanced Taiwan's international reputation and international influence of domestic medicinal products.

TFDA continuously improves the domestic inspection capability and develops testing methods, the number of compounds which can be identified by high-throughput screening of agricultural products was increased to 373 in year 2018, with an increase number of 172 pesticides in 10 years; the multi-inspection methods for pesticide residue in livestock products have increased the number of inspection items from 60 to 126. Therefore, we are able to rapidly conduct lab testing in response to illegal incidents to maintain people's safety of food and medicinal products.

In addition, TFDA also created a "food and drug misleading advertisement area" on its official website, to monitor exaggerated and misleading advertisements, or which claims of medical efficacy; in order to protect the public health and consumer rights, we remind the public not to believe in advertisements with exaggerated or false claims of medical efficacy by publishing the information on advertisements suspected of violating regulations from foreign websites. A total of 59 cases have been posted as of 2019, with a total of over 565 thousand clicks!

TFDA's mission is to advance public health by helping them to have "safe and effective medicinal products, safe and healthy Food". Under the vision of "Being a reliable guardian on food and medicinal product safety" and "Creating a safe food and medicinal consumer environment", TFDA will continuously construct a well-established system of management and regulation to be in line with the international standards and promote the Special Law for the Management of Regenerative Medicine Products, and vigorously promotes the legislation of the Medical Device Act. TFDA is dedicated to regulating Total product life cycle management for food, medicinal products and cosmetics; through the big data analysis of food and medicinal products, we will promote information transparency, and continue to devote in establishing a comprehensive safety management system for food and medicinal products.

Director-General, Taiwan Food and Drug Administration, Ministry of Health and Welfare Shou-Mei Wu

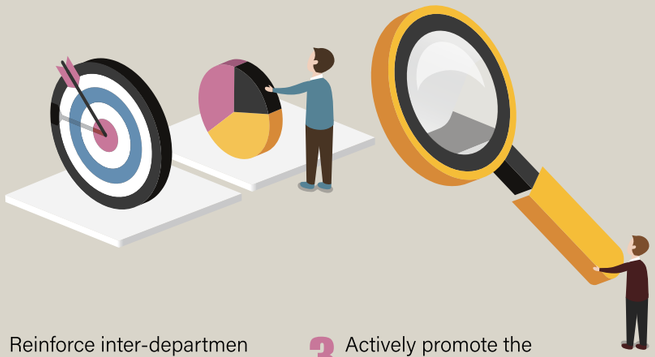
01 Organization and Policies

Vision

"Being a reliable guardian on food and medical product safety," and "Creating a safe food and medicinal consumer environment"

Mission

Safe and effective medicinal products, safe and healthy food



2018 Administrative goals

1 Implement total product life cycle management of food, medicinal products and cosmetics, and maintain the reputation of MIT

2 Reinforce inter-departmen-tal collaboration, and combine the big data analysis of food and medicinal products, to construct a comprehensive safety and protection network of food and drugs

3 Actively promote the transparency of information, fulfill consumer right to know more, and strengthen the communication and promotion of food, medicinal products and cosmetics safety

01 Organization and Policies

Taiwan Food and Drug Administration of Ministry of Health and Welfare (TFDA) was founded on July 23, 2013, as part of the organizational reform in the Executive Yuan. To fulfill Ministry of Health and Welfare's commitment of promoting the health and wellbeing of the public, TFDA takes "Safe and effective medicinal products, safe and healthy food" as its mission, under the vision of "Being a reliable guardian on food and medicinal product safety, creating a safe food and medicinal consumer environment"(Figure 1-1). Upholding the core value of "total product life cycle management" of food, medicinal products and cosmetics, through source, production and distribution management, TFDA continues to devote in establishing a comprehensive safety management system for food and drugs.

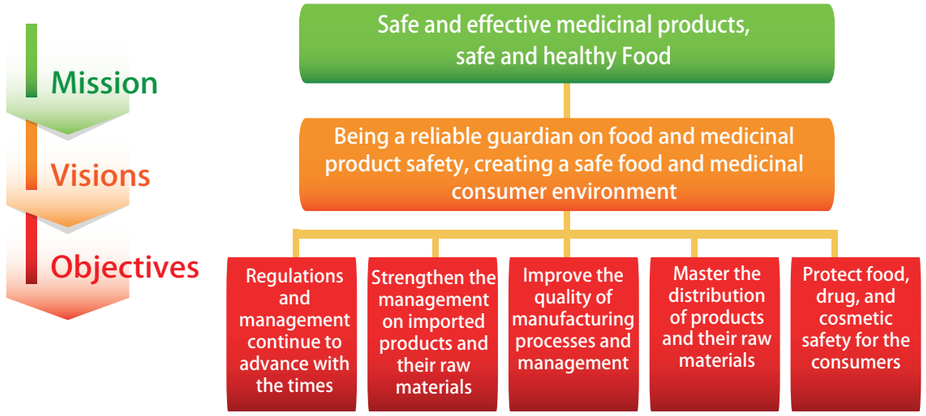


Figure1-1 TFDA visions and mission

Section 1 Organization Framework

Led by the Director-General, TFDA is composed of two Deputy Director-Generals, one Chief Secretary and seven business units, including: Division of Planning and Research Development, which is responsible for planning and management, technical planning management, international cooperation, legal system and consumer protection etc.; Division of Food Safety, Division of Medicinal Products, Division of Medical Devices and Cosmetics, as well as Division of Controlled Drugs are responsible for products management, policies, and relevant regulations of their managed products; Division of Risk Management (renamed as Division of Quality Compliance and Management from June 8, 2008) is responsible for laboratory management and authentication, manufacturers management and inspection of pharmaceutical and cosmetic products, and inspection of human organ bank; Division of Research and Analysis is responsible for the testing of food, medicinal products and cosmetics, methodological development and evaluation, pharmacopeia editing and compilation; TFDA also sets 3 District Centers (North, Central and South) which are responsible for laboratory testing of imported food, medicinal products and cosmetics; as well as distribution examinations and inspections. In addition, TFDA also composed of 5 Administrative Units (Office of Secretariat, Office of Personnel, Office of Accounting, and Office of Information management) to support administrative/management matters. (Figure 1-2). Also, TFDA has two Task Forces (i.e. Manufacturing facility for controlled drug and Decision Support Center) to provide professional information and assistance through professional consultation units such as Center for Drug Evaluation, Taiwan and Taiwan Drug Relief Foundation.

Section 2 Administrative Goals

TFDA sets the administrative goals and focuses based on the administrative policies of Executive Yuan and administrative programs of MOHW along with the budget plans, current development highlights and social needs on food, medicinal products and cosmetics management in 2018.

1. Implement total product life cycle management of food, medicinal products and cosmetics, and maintain the reputation of MIT (Made in Taiwan) food, medicinal products and cosmetics on the premise of quality and safety assurance.
2. Reinforce vertical integration and horizontal inter-departmental collaboration, and combine the big data analysis of food and medicinal products, to construct a comprehensive safety and protection network of food and drugs.
3. Actively promote the transparency of information, fulfill consumer right to know more, and strengthen the communication and promotion of food, medicinal products and cosmetics safety, to ensure the safety of food and medicinal products.

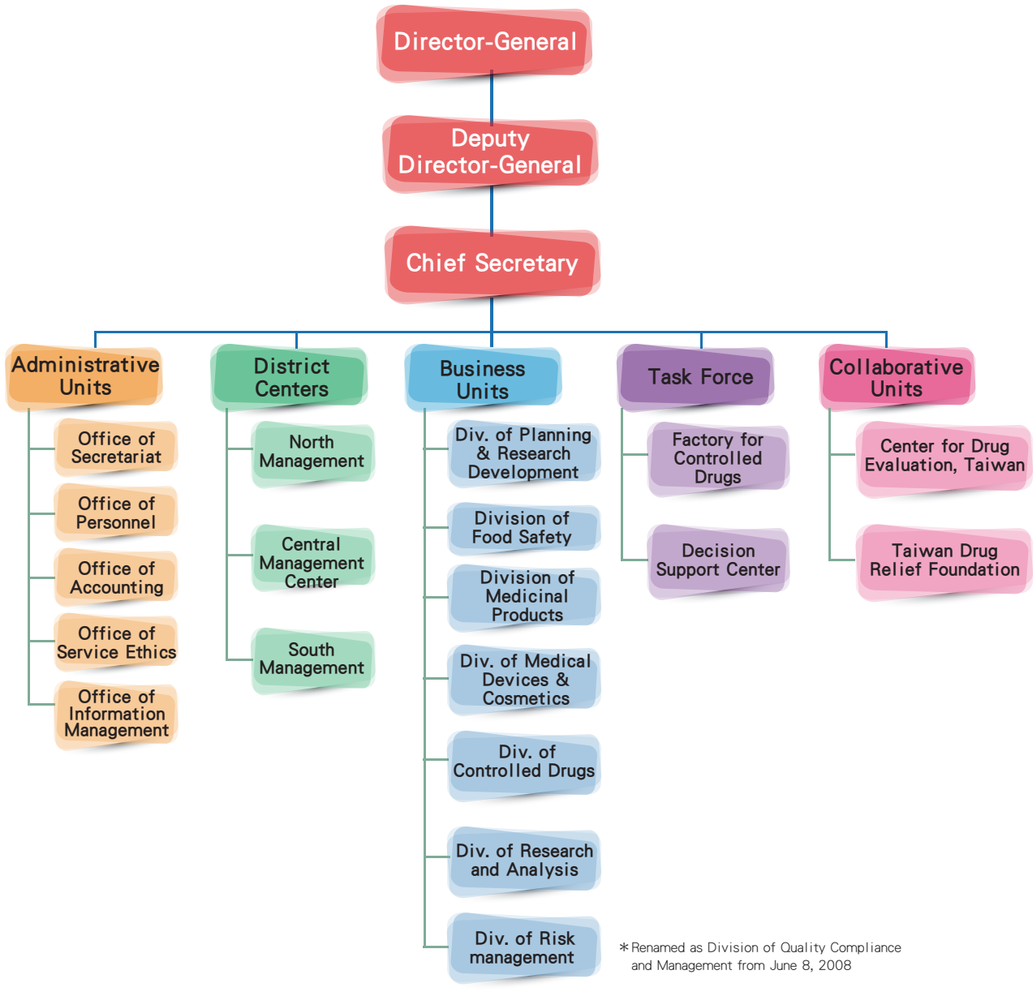


Figure 1-2 Organization framework

Section 3 Food Management Overview

The structure of food management system is based on “farm-to-table” management. Only by ensuring the safety of products from raw materials to consumers at all stages, we can provide a stable cornerstone for public health and social stability. We carried out the "Five-point Food Safety Policy" reform plan (Figure 1-3) that integrates the strength of the government, industry and the general public, to improve the farm-to-table management system, enhance the management capability in the food industry, enhance consumer protection and communication, and ensure a “Safe and Healthy Food” environment (Figure 1-4).

To assure the public of wholesome and safe food, TFDA collected and referred to international standards and technologies for the stipulation and amendment of the “Act Governing Food Safety and Sanitation,” to enhance the inspection capacity and capabilities, as well as to develop inspection methods. We will be continuously reinforcing the source control, enhancing the self-management ability of food business operators in the industry, establishing a dedicated personnel system, practically carrying out the supervision of food production and marketing chain, and applying systems to enhance efficiency and information disclosure, etc. TFDA and the health bureau of local government work together to carry out the food inspection project and post-marketing surveillance, to stop the sales of low quality food products and ensure the sanitation, safety and quality of food.

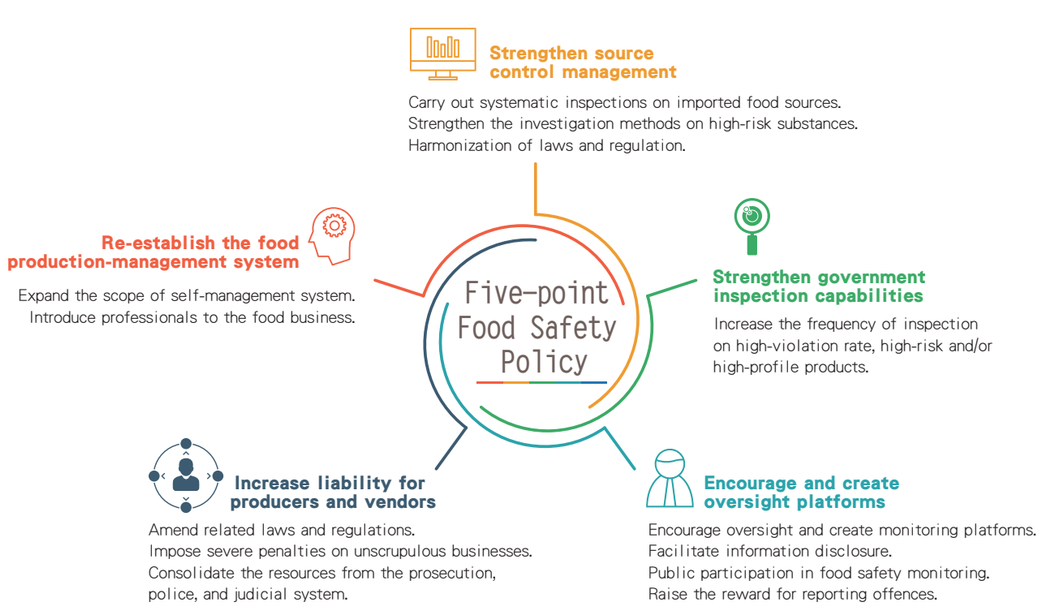


Figure 1-3 Five-point Food Safety Policy

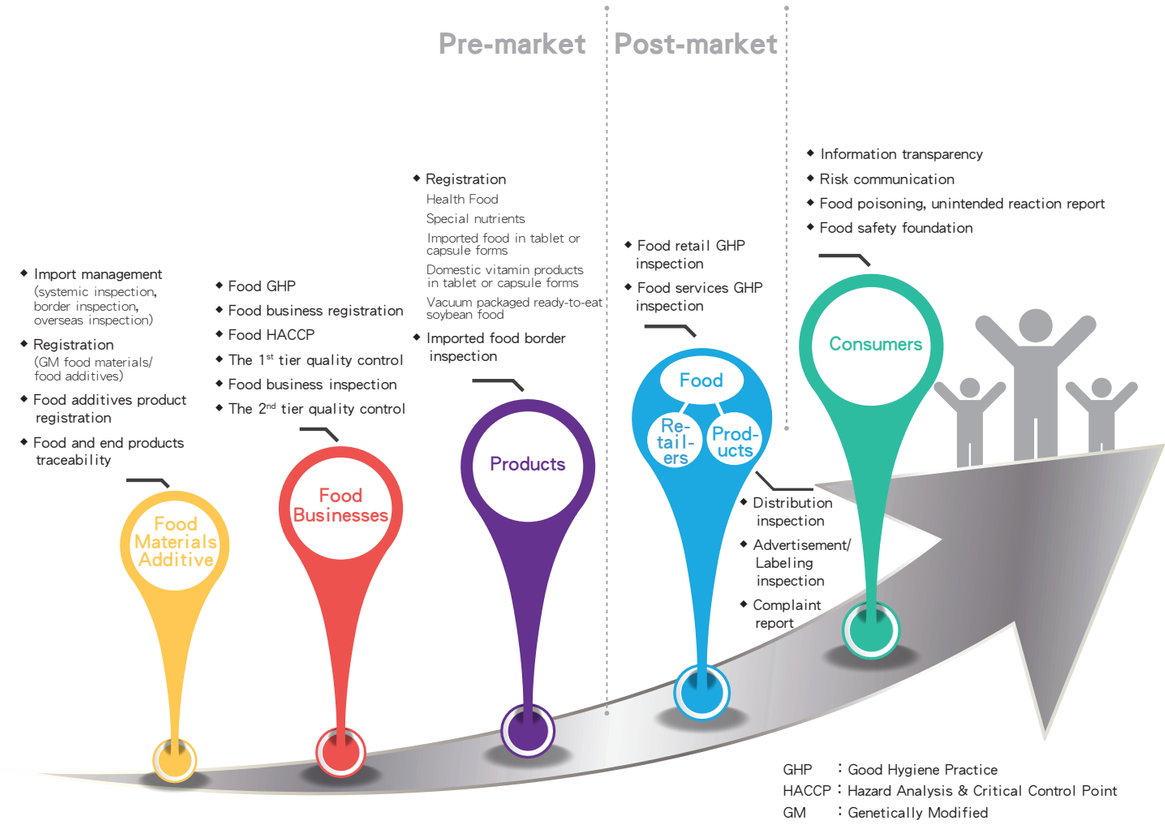


Figure 1-4 Food management framework

Section 4 Overview of Drugs and Cosmetics Management

1. Medicinal products management framework

Medicinal products are different from ordinary consumer products as they are vital to the public's lives. Medicine industry is highly regulated and it requires drug license from the central governing health authority before its products can be on the market for sale. Therefore, TFDA is able to control and reinforce the monitoring mechanism for medicinal product safety by amending drug regulations to be in line with international standards, establishing a simplified review mechanism, creating a system for the source manufacturers and management, standardizing the monitoring of drug distribution and quality, eliminating illegal medicinal products, and strictly controlling the inspections of medicinal products, to ensure the safety for the public.

The life cycle of medicinal products from R&D to marketing, including preclinical validation, clinical trial, pre-market application, production and post-market surveillance shall be in compliance with various good operating practices. Therefore, TFDA has established a comprehensive medicinal product life cycle management by the internationalization of regulatory management, control and manage for production source, pre-market control, post-marketing surveillance, and distribution management of pharmaceutical business operators and products (Figure 1-5), to effectively control the safety, efficacy and quality of medical devices while facilitating the development of domestic biotechnology and pharmaceutical industry, so to create a win-win situation for consumers, business operators and the government.

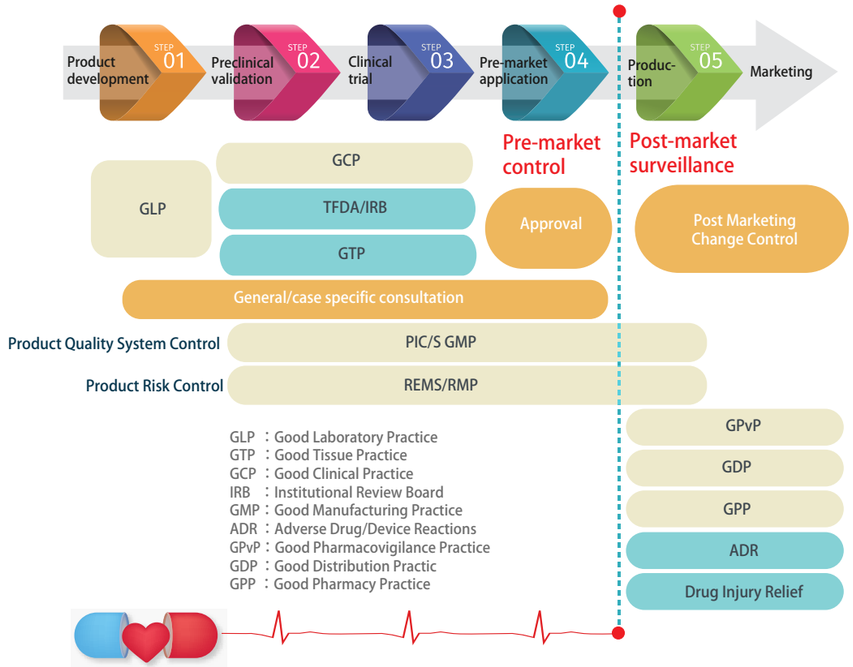


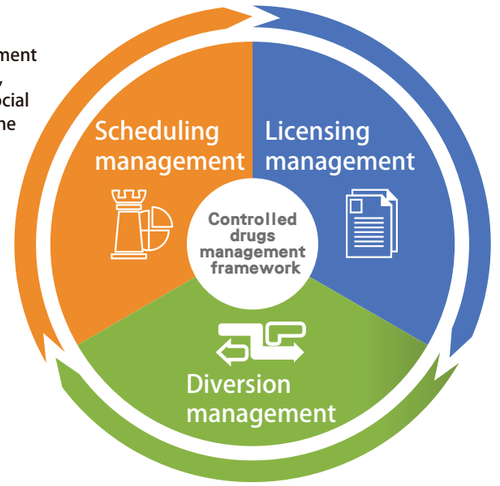
Figure 1-5 Product life cycle management framework for medicinal products

2. Controlled drugs management framework

All countries value the importance of drug abuse issue nowadays, especially the addictive controlled drugs, as they will be likely to harm the citizens' health due to improper or illegal use. Therefore, the management of addictive controlled drugs and prevention of drug abuse are important issues to the society and the public health nowadays.

According to "Single Convention on Narcotic Drugs (1961)," "Convention on Psychoactive Substances (1971)" and "Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of the United Nations (1988)," Taiwan has imposed controls on narcotics, psychotropic substances and their preparations through the "Narcotics Hazard Prevention Act." However, due to the necessity of controlled drugs in medical or scientific application, the "Controlled Drugs Act" has been established to give a control framework, which is composed of licensing, scheduling, and diversion management (Figure 1-6) to complete the management of controlled drugs.

Four schedules of management according to addictiveness, dependence, abuse, and social risks. The first schedule is the highest relative risk.



- Controlled drugs registration license (institutions and business operators)
- Controlled drugs prescription license (dentists, physicians, and veterinarians)
- Permit for exporting, importing and manufacturing (Source management)
- Relevant licenses: Transportation permit, letter of approval for medical education, research and trial purpose

Registration → Reporting → Inspection
Institutions — Health authorities

Figure 1-6 Controlled drugs management framework

3. Medical devices management framework

The medical device industry is poised to become Taiwan's leading biotech industry in terms of development potential, given its rapid developments in technology and growing demands for healthcare technologies. In response to the growing prospects of the medical device industry in Taiwan, TFDA has established a Total Product Life Cycle (TPLC) management policy for medical devices (Figure 1-7) that includes harmonization with international standards and regulations, production source control, pre-market control, post-market surveillance, management of pharmaceutical companies and product distribution channels, and provision of professional counseling services. The purpose of the TPLC policy is to effectively control the safety, performance, and quality of medical devices, and to promote the developments of Taiwan's biotech and pharmaceutical industry, in order to create an environment beneficial for consumers, industry, and government.

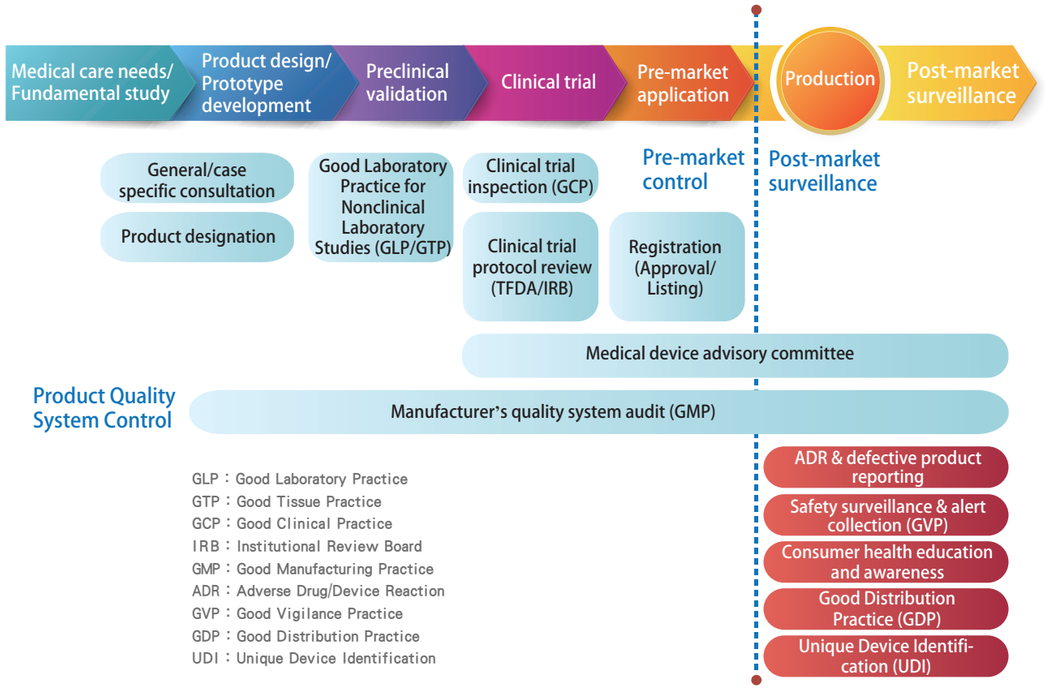


Figure 1-7 Total product life cycle management policy for medical devices

4. Cosmetics management framework

The current cosmetics management system is divided into production source control, pre-market management, and post-market surveillance. (Figure 1-8) Source control management includes ensuring that manufacturers comply with Establishment Standards for Cosmetics Manufactory and promoting voluntary Good Manufacturing Practice (GMP) for cosmetics. Pre-market management includes registrations of specific purpose cosmetics, and post-market surveillance focuses on implementing cosmetics quality surveillance programs, joint audits spanning multiple counties and cities, establishing a product adverse event reporting system for cosmetics, monitoring of domestic and global cosmetic safety alerts regularly, and strengthening consumer awareness of safe cosmetics use to create a comprehensive cosmetics quality and safety protection network.

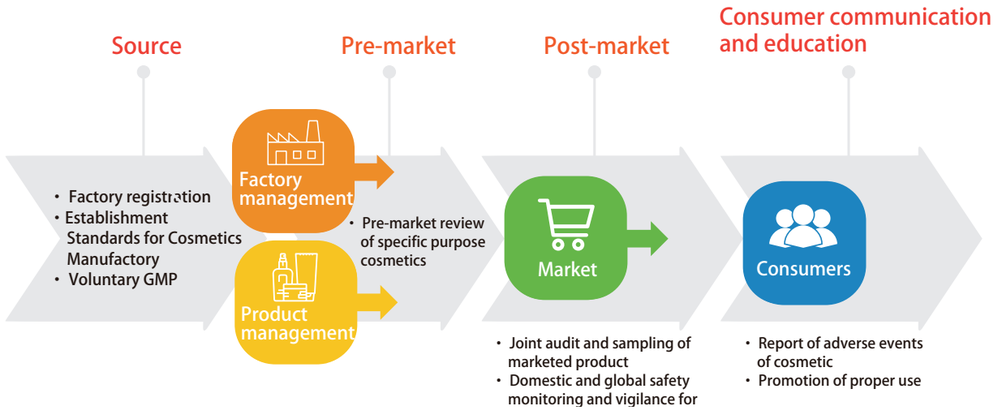


Figure 1-8 Cosmetics Management Framework

Note: The President announced the “Cosmetic Hygiene and Safety Act” on May 2, 2018. The Executive Yuan announced the enforcement date. Except for the relevant provisions of the information that shall be labeled on outer packaging or containers of cosmetics would be implemented on July 1, 2021, the remaining provisions would be implemented on July 1, 2019. The term "medicated cosmetics" revised to "specific purpose cosmetics.” The current inspection and registration system for medicated cosmetics will be replaced by the product notification and product information file. The transition period for the new and old registration system is five years

Section 5 Future Perspectives

With the trends of global trade and the development of technology, the discovery of novel substances and the impact of emerging technologies and new chemicals, the safety and sanitary issues of food and medicinal products gradually become critical. In view of the importance of food and drug safety and the expectations from the public, TFDA integrates different departments and businesses, and expand the participation of the public to construct a safe protection network for agriculture and food industry. Future important administrative plans include:

1. Adopt the Forward-looking infrastructure Development Program (infrastructure to ensure food safety) to respond to future challenges, and execute 4 sub-programs, i.e. “The construction plan of modern national food and drug laboratory and educational training buildings,” “Efficiency improvement program to expedite border inspection system,” “Program to strengthen health department’s food safety audition and inspection capacity” and “Program to strengthen central competent authority’s food safety, safe drug use and illegal drug inspection capacity.”
2. Enhance the food safety management, implement “Five-Point Food Safety Policy,” continue to expand the food safety management resources, and enhance citizen participation by the integration of inter-departmental organizations, business operators and the public, to maximize the effectiveness of limited resources. Moreover, we hope to practically carry out the three-tier product quality management, so that the goal of ten times market inspections can be achieved, and the domestic food management capacity will be enhanced.
3. Improve the drug regulatory management, continuously strengthen the control of drug supply chain, and promote the regulation of the Management of Regenerative Medicine Preparations to ensure the safety of drugs for the citizens in Taiwan.
4. Actively promote the legislation of the Medical Device Act and announced the relevant sub-regulations such as the Cosmetic Hygiene and Safety Act to meet the international standards, enhance consumer protection, and facilitate the development of medical devices and cosmetics industry.

02 Reinforced Food Safety Management

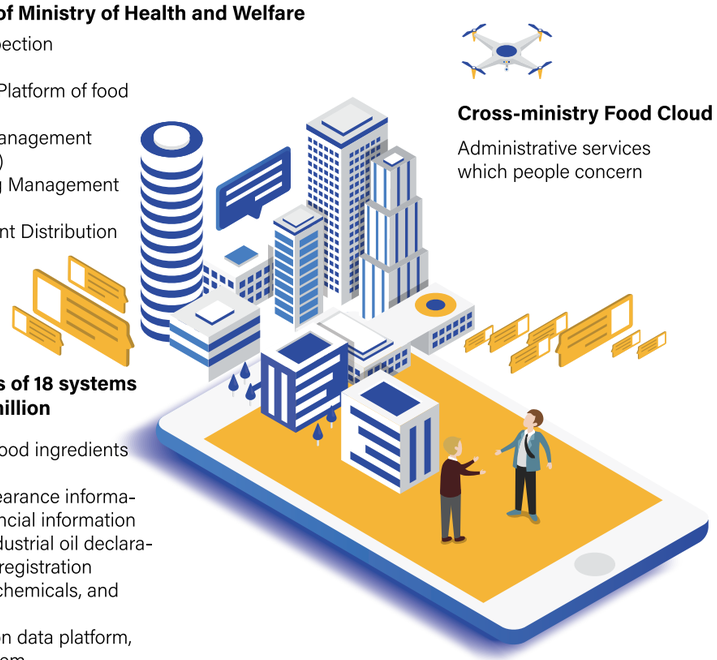
Food Safety Information Network

Core Food Cloud
Five Musts system of TFDA of Ministry of Health and Welfare

Must apply: Imported Food Inspection System(IFI)
Must register: The Registration Platform of food businesses (Fadenbook)
Must trace: Food Traceability Management Information System(Ftracebook)
Must test: Sampling and Testing Management System
Must audit: Product Management Distribution System (PMDS)

Cross-ministry Food Cloud

Administrative services which people concern



Cross-ministry Food Cloud
Total number of submissions of 18 systems of 6 ministries is about 110 million

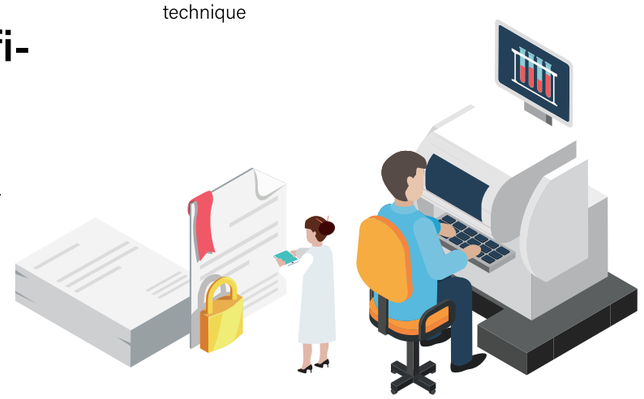
Ministry of Education: campus food ingredients registration system
Ministry of Finance: customs clearance information, electronic invoice, and financial information
Ministry of Economic Affairs: industrial oil declaration management, imported fat registration system, production of selected chemicals, and business registration system
Council of Agriculture: inspection data platform, and feed oil trace and track system
Environmental Protection Administration: Chemic cloud, and waste oil declaration management system
Ministry of Health and Welfare: usage amount of medicine

Certification for "2nd tier quality control" and "food expansion verification system"

- There were 489 business operators that should be certified in 2018, and about 91% of these applications successfully obtained the certifications
- There were 9 business operators passed the third-party certification of 2nd tier quality control, received the approval letter from TFDA and submitted the application of inspection to Malaysia

New Food Test Technology

- Hold the "2018 Annual Food Safety and Analytical Techniques Symposium"
- Establishment of multi-inspection technology for cross-category additives
- Development of high-throughput inspection technique



02 Reinforced Food Safety Management

To ensure food safety from the farm to table, it requires joint efforts of the respective government agencies devoting to the total food management, which helps shaping and assuring quality dietary environment. In 2018, we strengthened management measure of the import source control, improved food management regulations, carried out the supervision of food production and marketing chains, implemented 2nd tier food quality control, built a food safety information network and have improvement and innovation in the IT system of food safety management and the development of food inspection technology.

Section 1 Reinforced Food Safety Management

Origin of Policy

In order to strengthen the control of the high risk imported food, "Regulations for Systematic Inspection of Imported Food" has come into force since 2014, first implemented in the imported meat, and was amended to expand the scope of applicable products of animal origin. In order to meet the practical management, TFDA amended the requirements of certification for imported edible oils and fats in order to respond to the international new transportation and storage grease containers and technologies.

Furthermore, following the government's digital service transformation policy and simplified the work flow. The English version of sanitary certificates of processed food for export and related certificates have been gradually processed online since 2016.

Implementation Measures

1. Expand the scope of systematic inspections

The specific imported aquatic and dairy products are included in the systematic inspection and the implemented on January 1, 2018.

2. Implementation of the attached health certificate for the imported edible shellfish products

Due to the occurrence of some food poisoning events of imported oyster from Korea, TFDA implemented an import management measures of imported shellfish from Korea attaching official health certificate in 2016. As a result of risk factors such as shellfish poisoning and norovirus, a requirement had been expanded that all shellfish products (Figure2-1) exported to Taiwan for human consumption should be accompanied by an official health certificate containing information on the catching/ harvesting area since January 1, 2018.

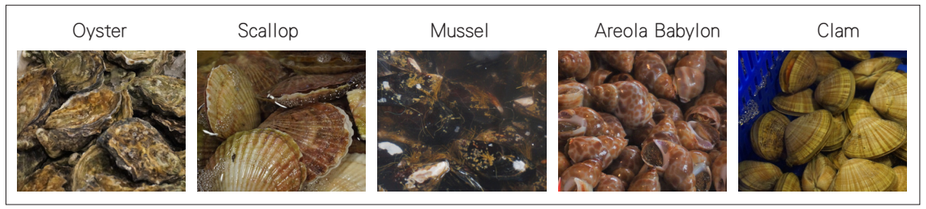


Figure2-1 Photos of edible shellfish

3. Amendment to the "The obligatory inspection applicants import edible oil, special dietary foods, food in tablet or capsule form and products which are approved by the central competent authority should attached related documents"

Added the specification of the storage and transportation in other reusable and non-reusable containers, and amended the regulation of official certificate.

4. Simplified the application process of the English version of sanitary certificates of processed food for export

Since October 1, 2017, the applicants applied for the English version of sanitary certificates of processed food for export if they pass 2nd tier quality control on manufacturers and the relevant certificate is issued and on the record, are able to exempt the on-site inspection while applying for sanitary certificate of products from the very manufacturer 15 days before the expiration of the approved certificate. Besides, “the free sales certificates” of the English version of sanitary certificates are changed to online application since March 1, 2018.

Outcomes and Benefits

1. Strengthen the management of imported food and enhance sanitation and safety of products:

(1) The systematic inspection management measure is adopted by most countries in the world for animal-derived products before they were approve the market access, and it can be confirmed that the exporting countries’ management system and the supervision measures of government agency for food sanitary and safety are equivalent to Taiwan. With this management measures, the high risk overseas source management of food can be practically implemented to strengthen the management of imported food products.

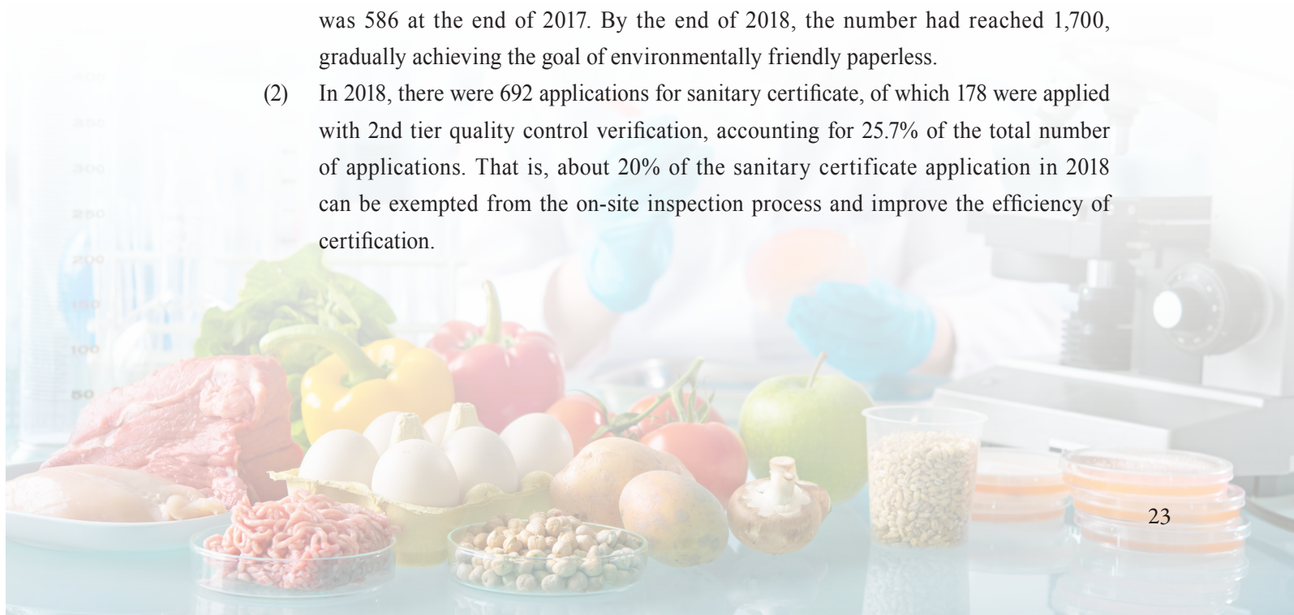
(2) The inspection control of the imported edible shellfish products is for the implementation of source management for shellfish products. In the case of pollution incidents occurred in specific region, all products in the area or fishing grounds can be controlled in time without having to control all the products from the exporting country or region, so to reduce the impact of trade due to the incidents regarding safety and health of food.

(3) In accordance with practical operations, TFDA strengthened the sources management of imported oil and fat, which can improve the hygiene and safety management and maintain smooth trade.

2. Convenient exporters apply for the English version of sanitary certificates of processed food and related certificates

(1) The online application system was launched in 2016, the total number of applications was 586 at the end of 2017. By the end of 2018, the number had reached 1,700, gradually achieving the goal of environmentally friendly paperless.

(2) In 2018, there were 692 applications for sanitary certificate, of which 178 were applied with 2nd tier quality control verification, accounting for 25.7% of the total number of applications. That is, about 20% of the sanitary certificate application in 2018 can be exempted from the on-site inspection process and improve the efficiency of certification.



Section 2 Improve the regulations of food management

Origin of Policy

In order to improve Taiwan's food-related regulations, the Act Governing Food Safety and Sanitation and Health Food Control Act were actively reviewed in 2018, and a total of 46 related regulations have been promulgated and amended. Furthermore, to enhance the self-management ability of business operators, a number of measures have been implemented and developed to comprehensively improve the hygiene and safety management of food production process.

Implementation Measures

1. Comprehensively governing the registration of food businesses

According to Article 3, Subparagraph 7 of the Act Governing Food Safety and Sanitation, the food businesses include the business operators engaged in the manufacture, processing, preparation, packaging, transportation, storage, sale, import or export of foods or food additives. It has been successively announced that registration is required for food manufacture and processing, importing, food service, and retail business operators. Moreover, in order to improve the understanding of basic information of food businesses, the amendment to Article 4 of "Regulations Governing the Registration of Feood Businesses," was announced that the logistics industry is included in registration regulations, and "Basic information of the storage" registration is required for each type of business operators .

2. Improve the trace and track management system

(1) Promote food businesses retain the source documents

TFDA announced "Food businesses shall retain the related source documents of the raw materials, semi-products and end products, including the types of documents to be retained and the period of retention" on September 27, 2018, requiring the food businesses shall retain the related source documents or the supplier's signature records of the raw materials, semi-products and end products for at least five years by written or electronic record, from January 1, 2020.

(2) Expand the scope of food business operators that shall establish their own trace and track system of foods

22 types of industry of "food business operators that shall establish their own trace and track system of foods and related products" were announced in phased since 2014. "Importers of frozen, refrigerated, dehydrated, pickled, gelled, plant protein and stuffed products of plants, mushrooms and algae," "manufacturers of other food products" and "meal box vendors" were added on June 26, 2018. Electronic declaration and electronic invoice system have been established in various phases since 2019.

3. The first tier quality control includes all of the food manufacturers industries with the designated scale.

17 types of industry of "food businesses that shall enact the food safety monitoring plan and food inspection, minimum testing cycle, and other related matters" were announced continuously since 2014. On September 20, 2018, 16 types of industry including "agricultural plants, mushrooms and algae products" were added, and the food safety monitoring plan should be enacted and the mandatory inspections shall be conducted in various phases since October, 2018.

4. Implement and introduce HACCP to food industry

On April 17, 2018, "meal box supply business for the railway transportation passengers shall meet the Regulations on Food Safety Control System" was announced and stipulated, regulating the food industry of Railway Corporation own - (affiliated) kitchen or other subcontracted meal box shall implement Hazard Analysis and Critical Control Point (HACCP) since 2019. On May 1, 2019, stipulated the "edible oil and fat factory", "canned food factories" and "egg production factory" should be in compliance with the Regulations on Food Safety Control System, regulating factory registration and the food factories that have more than 5 employees shall enact the HACCP in stages since July 1, 2018. By requiring food industries to introduce preventive concepts of HACCP in process management, the level of food safety management is aimed to be comprehensively improved

5. Set up professionals with vocational certification

On May 1, 2018, the regulation of "Food businesses belonging to a designated category and scale shall have professionals with vocational or technical certification" was announced, and 15 categories of food industry: the processed meat products, processed aquatic products, processed dairy products, meal box service, international tourist hotels and five-star hotels with catering service, meal box supply business for the railway transportation passengers, edible oil and fat industry, canned food industry, egg products industry, noodle and flour industry, soy sauce industry, edible vinegar industry, seasoning sauce industry, and non-alcoholic beverage industry were regulated and required to hire professionals with vocational certification to enhance the capability and quality of food industries, ensuring the hygiene and safety of food process.

Outcomes and Benefits

1. Enhance the comprehensive registration of food businesses

The logistics industry was included in registration regulations in 2018, and "Basic information of the storage" registration is required, to better understand the storage and logistics information in the food industry, implement counseling and inspection management for the industry and improve the efficiency of inspection by Health authority.

2. Improve the trace and track management system

As of the end of 2018, a total of 25 categories in the announcements of "food business operators that shall establish their own trace and track system of foods" had been made successively in various phases, including all food manufacturers with a factory registration and capital of more than NTD 30 million. At the same time, TFDA promotes food business operators to retain the source documents. By requiring the food business operators to retain the related source documents of the products, including business operators with different category and scale in the industry, to manage the upstream suppliers of the products and improve the food trace and track system through practical implementation.

3. The first tier quality control includes all of the food manufacturers industries with the designated scale.

As of the end of 2018, a total of 33 categories in the announcements of the "food businesses that shall enact the food safety monitoring plan and food inspection, minimum testing cycle, and other related matters" had been made successively in various phases, including all food manufacturers with a factory registration and capital of more than NTD 30 million to improve the management system of the first tier quality control and ensure the hygiene and safety of foods.

4. Implement and introduce HACCP to food industry

For food categories that were of high risk, high concern and essential for people's livelihood, such as edible oil and fat, canned food, egg products and railway meal boxes etc., TFDA continuously introduce preventive concepts for food safety management to enhance the hygiene and safety control in the production process.

5. Set up professionals with vocational certification

By 2018, 15 categories of food industry shall have professionals with vocational certification. With the implementation of specialized professionals such as food technologist, the professionals were responsible for food safety control system, traceability, emergency response measures for incidents regarding food hygiene and safety, hygiene and safety of raw materials, quality control, risk assessment and control, laboratory quality assurance, and educational training, to strengthen the production management and self-discipline ability of business operators in the industry.

Section 3 Reinforced Supervision of food production chain

Origin of Policy

Provide a reliable food safety environment for the public is the responsibility of the government. According to the Act Governing Food Safety and Sanitation, the competent authority is responsible for supervision and inspection through overseas source inspection, imported product inspection at borders, post-market inspection, and cooperation with police to enhance the inspection of food and drugs, to ensure the food supply safety and identify potential risks, as well as to adopt the warning and control measures in advance. Governing of food safety and sanitation.

Implementation Measures

1. Overseas on-site inspection

According to the needs for source control and the recently imported records, the central competent authority sent personnel abroad to conduct on-site inspection for the sanitation and safety management of the imported foods.

2. Inspection of imported products at borders

The annual inspection plan will be stipulated every year in order to ensure the safety of imported food products, and we will review and adjust the inspection methods and items with the rolling approach according to the criteria such as inspection records, characteristics of products, and domestic and foreign information, etc. The foods that do not pass the customs clearance inspection at borders will be returned or destroyed according to the regulations, furthermore, the information of these products such as company name, address, product name and illegal status may be revealed to the public. At the same time, TFDA will increase the product sampling rate up to inspection batch by batch if necessary.

3. Domestic manufacturing processing and circulation supervision

TFDA is responsible for supervising and assisting the health bureau of local government in implementing food inspection and supervision, and planning food inspection management guidance and strategies to coordinate and conduct matters regarding national food inspections.

Every year, 40-50 projects are planned and the diverse inspection strategies are applied, including the two-way inspection of manufacturers' source, strengthening the inspection of higher risk business operators, and the cross-industry cooperation between the central and local governments. With the big data analysis technology of Food Cloud, we are devoted to reinforcing the inspection of high-attention, high-violation, and high-risk product items, including domestic manufacturers, catering service, distribution service, sales, food business importers and their products.

4. Cooperative investigation between prosecutors and police

The additional regulation of Article 42-1 was added to the Act Governing Food Safety and Sanitation in 2014, stipulating that the police should send personnel to assist the health management agencies to conduct inspections to remove obstacles and protect the personal safety of inspectors, as well as the dedicated contacts between the health authorities, prosecutors and police are created. Besides, in order to enhance the handling efficiency of food and medicinal products crime cases, we will further establish a communication platform for food and drug related crime cases, and jointly enact an "implementation plan for the inspection of food and drug crime cases by prosecutorial authorities" with Taiwan High Prosecutors Office to integrate the professional and resources of various agencies.

Every year, we conduct the "Strengthen the Food and Drug Crime Study Seminar" with the Ministry of Justice, to create good communication channels with the prosecutorial authorities, reinforce the mutual assistance in judicature, and enhance the efficiency of food and drug investigation.

Outcomes and Benefits

1. Overseas on-site inspection

In 2018, TFDA conducted overseas inspection on 33 factories in 6 countries. The overall assessment of inspection complies with the relevant regulations of Taiwan.

2. Inspection of imported products at borders

A total of 682,580 batches of food related products were inspected at the customs clearance in 2018, including 115,507 batches were inspected on site and 58,915 batches were inspected by random sampling. A total of 820 batches failed to meet the inspection requirements, accounting for 1.4% of the sampling batches, and the rate of passing the inspection is 98.6%.

3. Domestic manufacturing processing and circulation supervision

In 2018, the inspected number of domestic business operators in the industry is 175,000, and the number of inspected products is 593,000. The qualified rate of GHP food business operators for initial inspection reached 80%, and the pass rate for second inspection was higher than 90%. The qualified sampling rates for the imported and domestic foods were 98% and 96%, respectively.

Countries and items of overseas factories inspection in 2018

1 Spain/pork/6 factories
2 New Zealand/veggies juice/5 factories
3 USA/poultry/5 factories
4 USA/beef/6 factories
5 Canada/beef and canola oil/4 factories
6 Japan/beef/7 factories

Figure2-2 Countries and items of overseas factories inspection in 2018

4. Cooperative investigation between prosecutors and police

TFDA held "Strengthen the Food and Drug Crime Study Seminar" with Ministry of Justice on March 14 to 16 in 2018 to improve the cooperation and exchange. A total of 194 joint inspections were conducted with the police in 2018, and seized the incidents of overdue food and aquatic products, use of expired raw materials for food production, etc., with total fines amounting to more than NTD 99 million dollars of punishment, fines and confiscation of illegal gains in accordance with the law.

TFDA will continue to improve the supervision mechanism of food production and marketing chain and enhance the efficiency of food management, to establish a reliable food safety environment the government has high capability, business operators respect their professions, and the citizens are healthy and safe.

Section 4 Implement the 2nd Tier Quality Control Policy

Origin of Policy

The "Regulations Governing the Certification and Qualification of Food Sanitation and Safety Management System Qualifying Institutions" was announced on March 11, 2018, opening a new era for the 2nd tier third-party certification of quality control. Besides, in order to facilitate the exportation of health supplements to Malaysia, for the different regulations and product determination criteria of health supplements between Malaysia and Taiwan, the governments negotiated and approved the "2nd tier quality control" and "food expansion verification program" qualification practices.

Implementation Measures

1. The third party certification system

The following ten food manufacturing businesses: canned food manufacturers, food additives manufacturers, special nutrient manufacturers, dairy products manufacturers with factories registered, and the edible grease manufacturers, starch, flour, sugar, salt, and soy sauce manufacturers with capital more than NTD 30 million, announced must be certified. (Figure 2-3)

Figure2-3 The categories for the certifications of the 2nd tier quality control

2. Certification for "2nd tier quality control" and "food expansion verification program"

Taiwan's health supplements industry is booming. In addition to selling domestically, it is exported to many countries. However, since the exit of Taiwan's GMP certification system in 2015, Malaysia has requested official GMP certification documents before exporting health supplements to the country. Therefore, TFDA has negotiated with the Malaysia government several times to provide the substitutions for the business, which with the certifications of the 2nd tier quality control and the food expansion verification program, the businesses will receive the approval letter that meets the "Guidelines on Good Manufacturing Practice for Traditional Medicines and Health Supplements" in Malaysia, and then the application of inspection may be submitted to National Pharmaceutical Regulatory Agency (NPRA), Malaysia.

3. Study and analyze the Good Manufacturing Practice Regulations of health supplements

Considering the export demand is not limited to Malaysia, and in response to the characteristics and needs of Taiwan's health supplements industry, in 2018, after comparing the GMP regulations of health supplements manufacturers in the United States, Japan, Malaysia and ASEAN, we studied and analyzed our GMP regulations of health supplements, and will continue to recommend relevant inspection standards, verifying management system and operating procedures in the future, as well as promoting health supplements manufacturers in the nation can establish standards in line with GMP to ensure the quality and enhance the international competitiveness of the industry.

Outcomes and Benefits

1. Simplify the application process

There were 489 business operators that should be certified in 2018, and about 91% of these applications successfully obtained the certifications. With the third-party certification of 2nd tier quality control, simplified the application process for food export and reduced waiting time and cost of business operators.

2. Improve product quality and promote export

By the end of 2018, there had been 9 business operators passed the third-party certification of 2nd tier quality control and "food expansion verification program" qualification practices, received the approval letter from TFDA and submitted the application of inspection to Malaysia. Related products were successfully exported to Malaysia and there are more business operators applying for the certification continuously.

Section 5 建構食品安全資訊網

Origin of Policy

Since food safety issue has to do with the responsibilities of respective ministries and departments, the Administration applies the "Five Musts" to enhance the food safety management information system (Figure 2-4). Governing the national food industry list, product information, import declaration information, upstream and downstream relationship, inspection and audit results, and through the sharing, connection and integration of information among ministries and departments, the efficiency of risk management and early warning detection will be improved.

Figure2-4 "Five Musts" food safety management information system

Implementation Measures

1. Establish automated risk identification

In 2018, the Administration had established an automated risk identification module which can be used to quickly generate a list of industries with different risk levels through logical calculations and visual displays with the use of inter-departmental information, and provide to relevant units as follow-up inspection reference. The module has greatly improved the operation efficiencies and reduced more error of interpretation than manual review, also prevented food problems from happening.

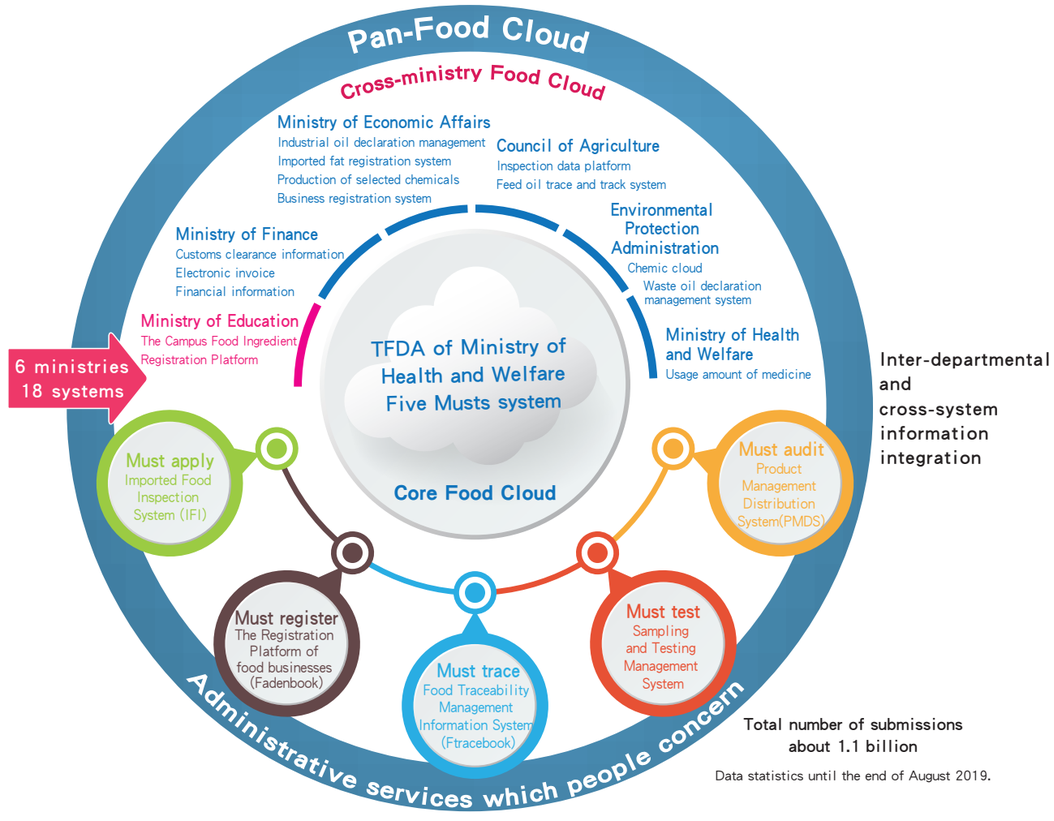


Figure2-5 Pan-Food Cloud framework

2. Integrate inter-departmental system

The Administration established the core direction according to the demands of management, 30 main categories and more than 140 visual dashboards have been created at present. For example, by integrating the customs clearance data of Customs Administration, Ministry of Finance and border inspection data of TFDA, obtaining data on the test failure rate of countries that imported food to Taiwan around the world, therefore presenting them through visual indicators such as map markers, it is clear that which country has a higher rate of food failure to effectively understand and control the lists of high-risk business operators and products, as well as to provide a dynamic analysis report as a reference for policy management and operational implementation of business divisions.

Outcomes and Benefits

1. Establish automated risk identification

We carry out the risk detection of expired food through the inter-departmental information and cross reference with TFDA's "Five Musts" system, to generate a list of potential expired risk business operators with the risk quadrant chart and it can be used as reference for inspection or research of management policies.

Through the analysis of big data, the inspectors can obtain the historical declaration information and inspection records of the business operators over the years prior to the inspection process, to effectively reduce the risk of human identification (Figure 2-6). In 2018, the "Manufacturers Aquatic Products and Meat Overdue Products" inspection plan was launched.

2. Integrate inter-departmental system

TFDA creates the core indexes according to the management requirements and presents them based on the visual charts, to quickly manage and control the business status. For example, the integration of TFDA's inspection data at borders through the customs clearance data of the Customs Administration will be able to compare the unqualified status of various products in recent years (Figure 2-3); the number of unqualified batches of products in the top five categories and the unqualified inspection rate of global imported foods are labeled in a global map, so that the countries with higher rate of unqualified foods can be seen clearly. For high-risk manufacturers, seized that the trading declaration was false on the spot, local government health bureaus have been asked to follow up and counsel in accordance with the law to strengthen improvement measures.

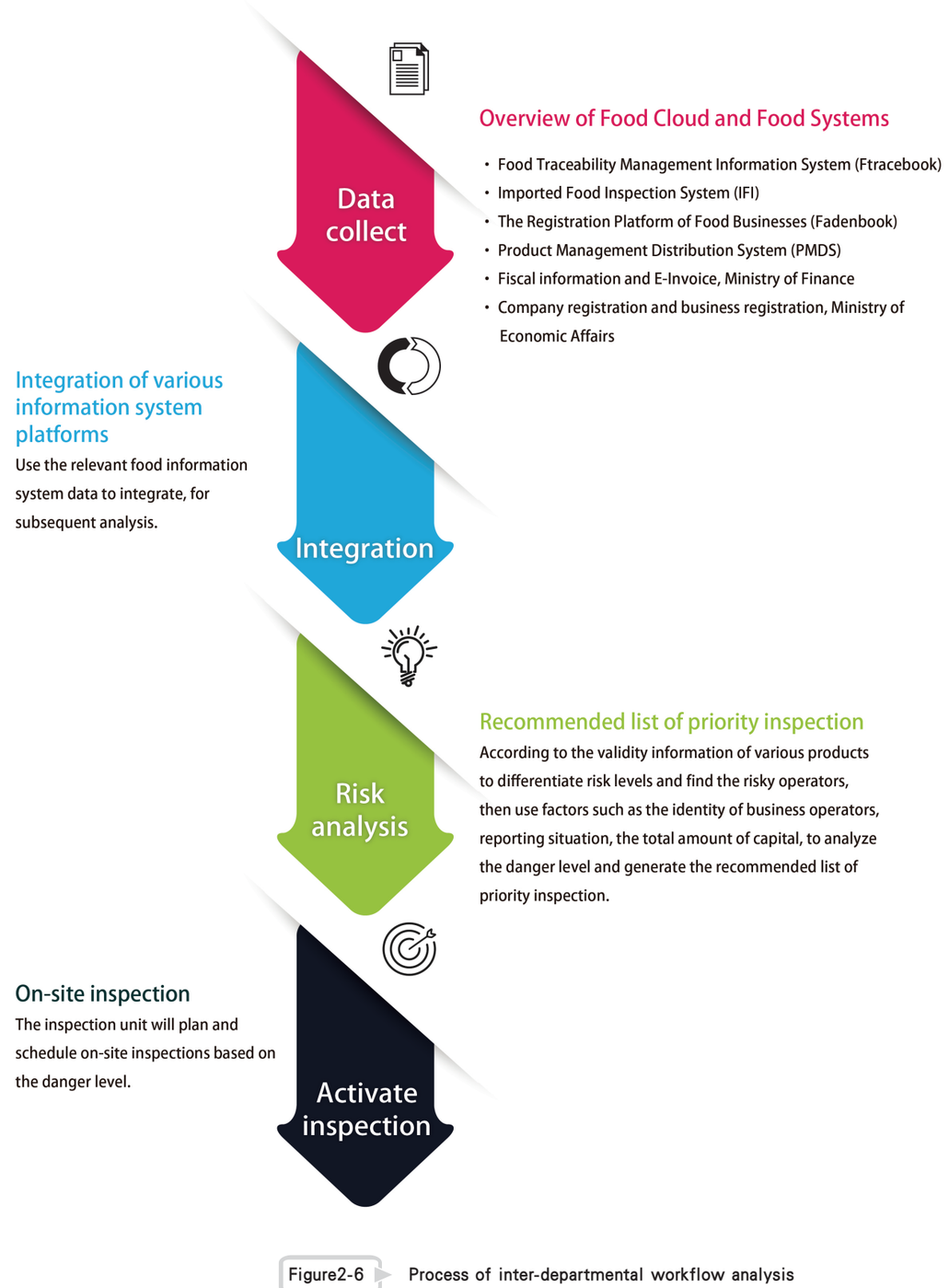


Figure2-6 Process of inter-departmental workflow analysis

Section 6 Development of New Food Test Technology

Origin of Policy

In order to meet the requirements of food-related regulations and sanitary standards such as pesticide or animal drug residues as well as to identify unpredictable, unknown or illegal additives may intentionally added and contaminants may generated from manufacturing process that may affect human health, establishing fast and accurate testing methods is required. TFDA continued improving inspection capabilities, and establishing new testing methods to react to emergency incidents, as well as to hold technical exchange and training activities to strengthen domestic testing capacity for food safety.

Implementation Measures

1. Hold the "2018 Annual Food Safety and Analytical Techniques Symposium "

TFDA held the "2018 Annual Food Safety and Analytical Techniques Symposium " on October 23 and 24, 2018, to promote inspection quality and technical exchange between inspectors (Figure 2-4). More than 250 representatives from the governments, industries, research institutes and academics participate in the symposium. Experts from the National Cheng Kung University, National Taiwan University and Academia Sinica give speeches

Figure2-7 2018 Annual Food Safety and Analytical Techniques Symposium

about mass technology in analyzing trace toxins and high-throughput screening technique development. In addition, 16 oral presentations and 68 posters are presented, and awards of excellent theses were presented at the closing ceremony of the seminar. Through this conference, the TFDA exchanges analytical techniques and experiences with experts from food-analytical field, hopes to enhance the testing ability and quality of the national laboratory and local health bureaus, and makes contribution to create a comprehensive quality and safety protection network of food in Taiwan.

2. Establishment of multiple analysis technology for cross-category additives

TFDA actively enhances the analytical technology of illegal food additives. We conduct the analysis for cross-category food additives with high-resolution mass spectrometry and the application of the newest international non-target screening technology. We also created a database of 100 legal and illegal additives such as colorants, antioxidants, sweeteners, preservatives and flavorings in foods, and include information such as retention time, molecular ions and the exact molecular weight of two ion pairs. With the information from the original database, one test can simultaneously detect 3000 compounds or more, to achieve the goal of screening cross-category additives. This technology was applied to the 101 post market surveillance cases of food additives in the beverages, snacks, sauces and processed dried meat in 2018. In the results, 1 sample is determined the non-compliant sweetener, 3 samples and 8 samples are found the colorants and sweeteners not in the label, respectively. As for the food random inspections, 8 specimens were detected non-compliant colorants and 4 specimens did not match the label from a total of 104 specimens of imported products at borders and 32 local inspection specimens. In the future, we will continuously increase the items with screening compounds in the database, in order to completely apply the multi-inspection technology for the cross-category additives and comprehensively enhance the efficiency and capacity of food inspection.

3. The contaminants in food processing and the progress of high-throughput screening techniques

(1) Development of testing methods for contaminants in food processing

Monochloropropanediol (MCPD) and Glycidyl (GD) are the contaminants be generated in the process of high-temperature deodorization of oils and fats, which may be digested in gastrointestinal tract to form Glycidol (GD) and Monochloropropanediol (MCPD). GD and MCPD are listed as Group 2A and Group 2B carcinogens by the International Agency

for Research on Cancer (IARC). The TFDA referred to a method from the American Oil Chemists' Society (AOCS), successfully developed a method for analyzing 3 globally concerned contaminants by GC-MS/MS.

(2) Development of high-throughput inspection technique

TFDA develops high-throughput inspection methods for pesticides and veterinary drug residues. “Method of test for Pesticide residues in agricultural products” was able to analyze only 201 pesticide residues in 2010 and increased to 373 in 2018, with an increase number of 172 in 10 years; “Method of test for Pesticide Residues in Livestock and Poultry Products” have increased the number of detecting targets from 60 to 126 and the methods can be applied at customs and post-marketing surveillance.

TFDA also developed small-scale multiple test methods for 2,4-D and other 15 pesticides residues and another method for 10 polar pesticides such as Glyphosate. TFDA also developed a method for 18 pesticide residues in vegetable oil such as Azoxystrobin. When it comes to veterinary drug residues, TFDA have increased the number of detecting targets for β-lactam antibiotics from 8 to 18, and can be applied to 4 matrix. TFDA also develop method for multi-residue analysis of 25 antiprotozoal drugs such as Buquinolate. These methods improve the efficiency for detecting veterinary drug residues.

Outcomes and Benefits

In response to new kind of food contaminants and illegal incidents, TFDA actively develop reliable and fast testing methods to promptly clarify the case of emergency incidents, and publish for use to all relevant interested parties to enhance the testing ability and quality of the national laboratory and local health bureaus, and makes contribution to create a comprehensive quality and safety protection network of food in Taiwan.

03 Advancement of Drug Management

Improve the drug regulatory management

- Promoting the legislation of the special law for the management of regenerative medicinal products
- Announce “Table of Checklist for Refuse to File (RTF) a New Drug Application” and “key points for the approval of drug with breakthrough medical treatment”
- Inspection and examination of imported pharmaceuticals at borders

Reinforce Drugs Risk control and digital management

- Improve the trace and track system of medicinal products
- Reinforce the drug safety reassessment
- Establish an online drug consultation database and information platform

Improve the regulations for the distribution of western medications

- Release “Western Pharmaceuticals Good Distribution Practice Regulations”
- Announce "Implementation schedule and procedures of Western Pharmaceuticals Good Distribution Practice Regulations"
- Establish PIC/S GDP area

Participate in International Conference Events

- Become the 10th regulatory member of ICH
- Participate in Asia-Pacific Economic Cooperation (APEC)
- Participate in the PIC/S Expert Circle on Quality Risk Management & Training Event
- Collaboration of medical information communication and exchange between Taiwan and Japan

03 Advancement of Drug Management

To implement total product life cycle management of drugs, effectively guarantee the quality, safety and efficacy of drugs, TFDA actively participates in international organizations, improves drug management regulations to be in line with the international standards and promote the development and competitiveness of the domestic pharmaceutical industry. In addition, TFDA continuously improves the inspection and management system for drugs, safety quality monitoring and trace and track system to strengthen drug risk management and provide a safe consumption environment for people to use drugs.

Section 1 Improve the drug regulatory management

Origin of Policy

In view of the rapid development of emerging biotechnology, and cell or gene therapy products on the international market, Taiwan listed regenerative medicine as one of the key points of the “Biomedical Industry Innovation Promotion Program” since 2016. TFDA also actively promoted regenerative medical regulations to improve the regulatory management environment. At the same time, to protect the rights of patients and facilitate the development of biotechnology industry, TFDA will continuously construct a sound drug review and management system.

Implementation Measures

1. Promoting the legislation of the special law for the management of regenerative medicinal products

In compliance with the international management trend and the current development condition in the domestic pharmaceutical industry, the management structure of regenerative medicine includes two aspects such as "products" and "medical technology." The authority units are TFDA and the Department of Medical Affairs, Ministry of Health and Welfare, respectively. In the management of regenerative medical preparations, TFDA actively promotes the legislation of the special law of the management of regenerative medicine preparations. TFDA released

the “Regenerative Medicinal Products Derivative Act (Draft)” on July 25, 2017, and it was subsequently passed by the Executive Yuan on October 18, 2018 and sent to the Legislative Yuan for consideration. It established a rigorous "pre-market review and post-market monitoring" mechanism. The applicants have to conduct clinical trials to prove the efficacy and safety of the regenerative medicine preparations, and the manufacturers also have to comply with the Good Manufacturers Practice (PIC/S GMP) with TFDA approval prior to the availability of the preparations in the market, to ensure the quality safety and efficacy of the preparations as well as to maintain the patients’ treatment rights.

2. Improvement of the inspection and management system for new drugs

A series of specific measures have been announced in the past few years, to enhance the efficiency of drug inspection and transparency of the inspections, including the announcement of “inspection key points of new drug application,” “new drug inspection process and time management,” and promotion of “refuse to file (RTF) a new drug application" etc. In addition, the “Table of Checklist for Refuse to File (RTF) a New Drug Application” was announced in 2018, to specify the information required for the registration and inspection; it is expected to enhance the inspection efficiency by improving the quality of submitted materials. The inspection and review of new drugs with urgent medical demand also has mechanism to speed up the process, including the "simplified review mechanism for the application of new drugs," "priority review mechanism for the application of new drugs," “mechanism to speed up the approval process for the application of new drugs," and "key points for the approval of drug with breakthrough medical treatment." In 2018, "key points for the approval of drug with breakthrough medical treatment" was announced, which is aimed at treating rare diseases or serious diseases and significantly improving the drug than the existing treatments. Through early legal consultation and technical issue consoling, the listing of drugs was accelerated.

3. Reinforced inspection and examination of imported pharmaceuticals at borders

TFDA enacted the amendments to the provisions of the "Regulations for the Inspection and Examination of Imported Medicaments" on August 22, 2018. The provisions clearly stipulate that inspection items at borders include the active pharmaceutical ingredients listed in Chapter 28 and Chapter 29 of the classification table for Import and export products of the R.O.C. and random inspections by batches shall be implemented. Enhance the management of imported active pharmaceutical ingredients and the accuracy of customs clearance, to prevent any illegal related activities and stop narcotics from entering the nation.

TFDA had purchased 14 Raman Spectrometers, to conduct border inspections and inspections of pharmaceutical factories. The importers must fill in information such as the active pharmaceutical ingredient’s name, manufacturer, specifications, quantity, and batch number, etc. and according to the risk judgment, the batch inspection is carried out. The chosen one will be quickly inspected with the instrument whether the imported active pharmaceutical ingredients match the purchased data, after being judged to be in compliance with the regulations, it can be released.

Outcomes and Benefits

1. Promoting the legislation of the special law for the management of regenerative medicinal products

Considering the heterogeneity of ingredients, process specificity and treatment complexity of regenerative medical preparations, the current regulations cannot be fully applied. Through the promotion of the special law of the Pharmaceutical Affairs Act, it is expected to help to facilitate effective communication and reinforce the areas that are not specifically covered in the Pharmaceutical Affairs Act, in order to improve the regulatory environment for the total product life cycle management of regenerative medical preparations. At present, Regenerative Medicinal Products Derivative Act (Draft) has been reviewed by the Legislative Yuan. We look forward to the early completion of legislation to provide more and more innovative treatment options for patients and to promote the vigorous development of Taiwan’s biotechnology industry chain.

2. Improvement of the inspection and management system for new drugs

With the core objectives of quality, consistency, clarity, efficiency and transparency in review and inspection of drugs, TFDA reinforce the inspection and two-way communication with the industries. TFDA is expected that new drugs can be quickly approved to be on the market by promoting the concept of regulatory harmonization, to improve the inspection and management system for new drugs. The number of end cases, closing cases and review days of the inspection and management system for new drugs are shown in Figure 3-1.

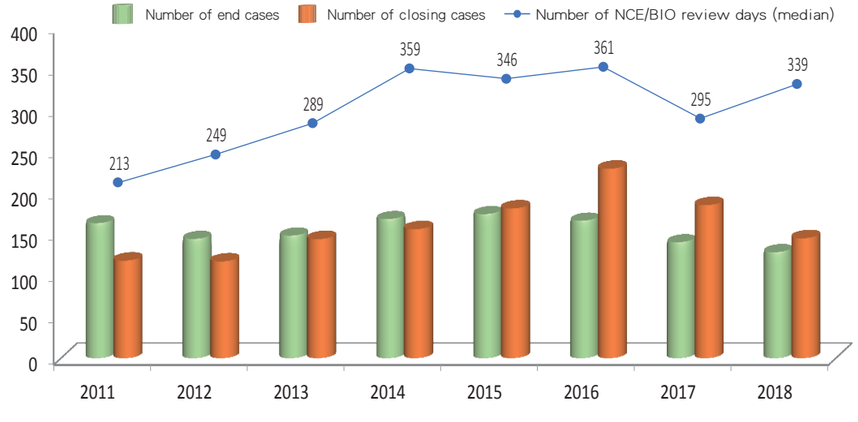


Figure3-1 Number of end cases, closing cases and review days of the inspection and management system for new drugs

3. The actual results of random inspections of imported drugs at borders

As of the end of 2018, a total of 206 batches of imported active pharmaceutical ingredients were inspected in borders and no nonconformity was found. In addition, for the purpose of strengthening the management of active pharmaceutical ingredients and inspection of the conformity of the materials in the inventory, TFDA had inspected 334 items in 119 pharmaceutical factories by batches and no nonconformity was found.

Section 2 Reinforced drugs risk control and digital management

Origin of Policy

To strengthen the management of the pharmaceutical supply chain, TFDA established the trace and track system of drugs in accordance with Article 6-1 of the Pharmaceutical Affairs Act, in order to reduce the risk of counterfeit drugs entering the legal supply chain, and for drugs with doubts about quality, the drug recall can be confirmed and effectively completed in time.

Moreover, in order to cooperate with the digital management of drugs, we establish a drug consultation database and information platform, to conveniently provide the general public with accurate drug related information. In addition, we reinforce the active and passive monitoring mechanism of drugs, to strengthen the risk control and ensure the safety of drugs for the citizens in Taiwan.

Implementation Measures

1. Improvement of the trace and track system of medicinal products

(1) Since July 1, 2017, TFDA had given priority to include three categories of medicinal products in the first phase of the trace and track system of medicinal products, including blood preparations, vaccines and botox. Based on the risk assessment criteria in national health insurance, on January 1, 2018 and July 1, 2018, we had announced and included the high concern type 20 and 30 items in the trace or track management of medicinal products in various phases.

(2) The trace and track system of medicinal products provides business operators with diverse methods of declaration, for example data import, automatic upload, or login to the web page and input data etc., and the operating interface of the declaration system was improved in 2018 to simplify the declaration for business operators.

(3) In 2018, a new cross-reference and statistical analysis function was added, which is able to provide statistics, inquiries, and output of reports. Furthermore, the authority is given to the medicinal products license holders, to conduct query and cross reference of declaration information in the national health insurance, assist in the flow control of prescription medicinal products, and strengthen the pharmaceutical firms' management of medicinal products flow.

2. Reinforce the drug safety reassessment

TFDA has established an active information monitoring mechanism for drug safety, to instantly monitor new risks of drugs, conduct analysis and safety reassessment through a notification system of adverse drug reaction, a safety monitoring system of new drugs, and proactive monitoring of domestic and internal drug safety warning information. TFDA also takes relevant risk management and control measures, such as issuance of warnings and modification of medication package insert, to ensure the safety of drugs.

3. Establishment of drug information platform

In the past few years, TFDA has established an online drug consultation database and information platform for pharmacists and assistant pharmacists in the clinics and community pharmacies to provide basic inquire about drug-related information and consultation services to patients and health professionals. The platform contains information on drug dosages, adverse reactions, recommendations for pregnancy and breastfeeding medications, and assessment of drug interactions and duplication medicine. In addition, the Chinese version of the health education leaflet is also provided by QR code. If users forget the content reminded by the pharmacist, they can scan the QR code to open leaflet and recall it at any time, that help patient take medicines safely.

Outcomes and Benefits

1. Improvement of the trace and track system of drugs

TFDA created a trace and track of drug declaration area on its official website, to provide a teaching briefing of declaration, common QA session and a dedicated phone line, as well as to provide business operators with declaration and counseling services. In 2018, we offered a total count of 1,495 counseling services; conducted six communication sessions with the industries and health education trainings in 2018, with a total of 233 participants. Besides, TFDA actively tutored 142 business operators to successfully complete the declaring operations. Through the trace and track of drug declaration, the central government cooperated with the local government health bureaus in 2018 to check the drug batch number, check the validity period, check the flow, and follow-up and arrange on-site inspection with the Health Bureau to ensure the legal supply of drugs.

2. Reinforce the drug safety reassessment

In order to strengthen the safety and quality of drugs, we carried out the safety analysis and evaluation of drugs based on the drugs with safety concerns. The drug safety reassessment for a total of 47 were conducted in 2018, and the risk control measures such as revision of medication package insert, restricted usage were adopted for 16 drugs, for example: we continued to implement the drug risk management plan for drugs that contain carbamazepine ingredient and published a risk communication form of drug safety information, to enhance the effectiveness of risk management and control as well as to ensure the safety of drugs for the public.

3. Establishment of drug information platform

In 2018, the usage amount of the platform was 13,000 person-times, among them, the drug dosage, adverse reactions and recommendations for pregnancy and breastfeeding are mainly inquired. In order to improve the query skills, TFDA held three training courses in southern, northern and central Taiwan. The courses invited pharmacists to share user experience, talk about interactions query and the use of the health education leaflets to strengthen the pharmacist service capacity in the clinics and community pharmacies.

Section 3 Improved the regulations for the distribution of medicinal products

Origin of Policy

The purpose of implementing the Good Distribution Practice (GDP) is to ensure that the drug is in compliance with the Good Manufacturers Practice (GMP) from the production stage to distribution process.

There are many global organizations and countries have started to implement drug GDP, including the World Health Organization, the European Union, Singapore, Malaysia, the U.K., Germany, Switzerland, the United States and Australia. The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Cooperation Scheme (PIC/S) also officially announced the Good Distribution Practice for Drugs in June 2014, and it has become the international implementation standard for drug GDP. Therefore, TFDA implements the distribution and quality management of drug by promoting the GDP system that meet the international standards, to ensure the safety of drugs, improve the distribution quality of drugs and create international competitiveness.

Implementation Measures

1. Amendment of GDP and related regulations

TFDA is actively improving the regulations, the amendment of Article 53-1 of the Pharmaceutical Affairs Act was enacted by the Presidential Order on June 14, 2017, regulating the business undertakings engaged in wholesaling, importing and exporting of western pharmaceuticals, their product procuring, holding and supplying related to the quality management, organization and personnel, premises and equipment, documentation, operation procedures, customer complaints, returns and recalls, outsourced activities, self-inspection, transportation and other pharmaceuticals distribution practice, shall comply with the GDP standards and pass the inspection by the central health authority, and it will obtain the western pharmaceuticals distribution license.

In compliance with the amendments of the Pharmaceutical Affairs Act, the “Western Pharmaceuticals Good Distribution Practice Regulations” were released on December 28, 2017 to be a GDP standard for drug dealers of western pharmaceuticals. The “Regulations for the Issuance and Management of Western Pharmaceuticals Distribution Licenses and Certificates” was enacted on May 28, 2018, which clearly specify the administrative regulations on license application for inspection.

2. Implementation schedule of GDP

The “Good Manufacturers Practices Part III: Distribution" was announced on February 18, 2016 and western pharmaceuticals manufacturers must fully comply with the GDP standards in 2019. In addition, the "Implementation schedule and procedures of Western Pharmaceuticals Good Distribution Practice Regulations" was announced on September 11, 2018 to regulate the drug dealers with drug permit licenses of western pharmaceuticals and they must fulfill the requirements of the Western Pharmaceuticals Good Distribution Practice Regulations starting from January 1, 2019.

3. GDP related supplementary measures

TFDA has progressively promoted the distribution and management system of western pharmaceuticals since 2011, including continuing to conduct topic forums, technical seminars, and pharmaceutical business operator’s observation learning and educational training lessons. TFDA also invited GDP experts to provide on-site counseling for a total of 740 sessions; TFDA actively communicated with the industry to promote relevant management policies and schedule to reach a consensus; The PIC/S GDP area was created on TFDA official website to announce

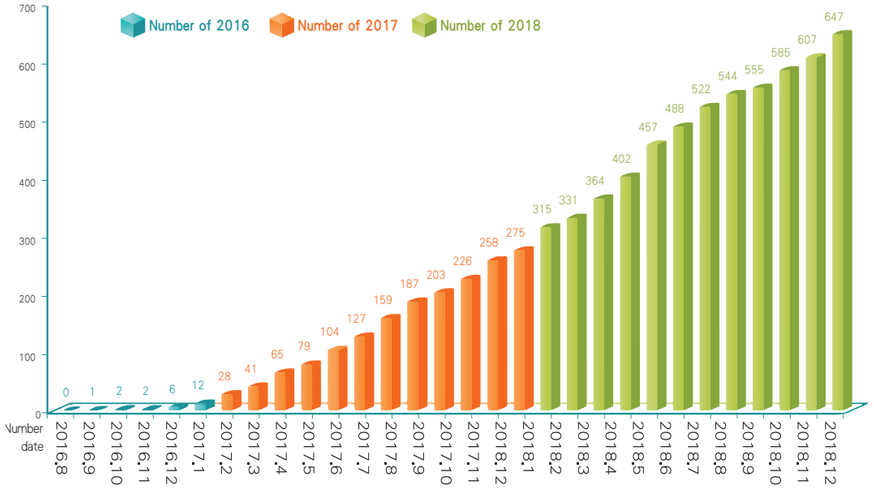


Figure3-2 至107年底已通過之藥品GDP家數

policies and letters, approved lists, messages, counseling programs, Q&As, SOP examples, promotional videos and educational training courses, to be used as a reference for the business operators while executing.

Outcomes and Benefits

As of the end of 2018, 647 western pharmaceutical manufacturers and dealers have complied with the GDP standard (Figure 3-2). TFDA implements the distribution and quality management of drug by promoting the GDP system that meet the international standards, and the quality management of drug distribution to ensure that the quality and integrity of the packaging are maintained during the storage and transportation of pharmaceuticals among drug dealers. At the same time, it effectively handles emergency drug recall events and correctly delivers them to consumers within a reasonable time, reducing falsified pharmaceuticals enter legal supply chain, etc. to ensure the safety of drugs and improve the distribution quality of drugs for the citizens in the nation.

Section 4 Create a new international pattern of pharmaceuticals

Origin of Policy

TFDA has worked hard to promote international cooperation in pharmaceutical products over the years. We actively participated in international organizations and strive to hold international conference activities to strengthen Taiwan's international participation and influence, and build an international regulatory environment of pharmaceutical products. The direction of implementations in 2018 are as follows:

1. Take the initiative to become a regulatory member of ICH

The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) is an international organization cofounded by the pharmaceutical administration and the pharmaceutical industry of the European Union, Japan and the United States in 1990. The Council aims to develop drug guidelines that can be accepted by various countries and recognized as global technical standards through international discussions in various regions. We hoped to join the ICH and participate in the stipulation of international standards, avoid the technical regulation obstacles, and create opportunity of cooperation amongst members, so that our domestic drug management regulations could meet the international standards.

2. Long-term participation in the Pacific Economic Cooperation (APEC) to promote regulatory convergence

To promote international information exchange and cooperation in drug management and regulatory harmonization, TFDA has been long-term participating in the Regulatory Harmonization Steering Committee (RHSC) of the Asia-Pacific Economic Cooperation (APEC) Life Science Innovation Forum. TFDA co-champions the "Good Registration Management (GRM)" priority work area with Ministry of Health, Labour and Welfare (MHLW) and the Pharmaceuticals and Medical Devices Agency (PMDA) of Japan. In addition, TFDA was endorsed as an APEC Regulatory Science Training Center of Excellence in the area of GRM and has been providing training each year in Taiwan. Through cooperation between the competent authorities and the pharmaceutical industry, promoting GRM has been enhancing the mutual trust between the competent authorities and the pharmaceutical industry and the regulatory convergence amongst APEC member economies by 2020.

3. Committed to participation of the PIC/S Expert Circle on Quality Risk Management & Training Event

The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Cooperation Scheme (PIC/S) is an official international co-operative arrangement composed of regulatory authorities in the field of Good Manufacturing Practice (GMP) of medical products from all over the world. It is committed 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.

Exports Circle have been set up by PIC/S to facilitate the discussions and the exchange of information among inspectors specialized in a specific area of GMP. Expert Circles meet every 1~2 years to develop draft guidance, recommendations, etc. and offer training in their respective fields of specialization.

The PIC/S Expert Circle on Quality Risk Management (QRM) was established in 2007. It has been active in developing models for QRM systems for Inspectorates as well as guidance on the assessment of QRM implementation in industry. Expert Circle meetings and training activities and held regularly to offer comprehensive training to inspectors to enable them to inspect QRM systems in a harmonized manner.

4. Expand collaboration of medical information communication and exchange between Taiwan and Japan

To enhance the bilateral collaboration relationship of medical products regulations between Taiwan of Japan, provide a platform for communication and discussion between Taiwan and Japan on pharmaceutical administration issues, regulatory science, medical products registration and clinical trials, the Taiwan-Japan Relations Association and the Japan-Taiwan Exchange Association have signed a "Framework of the Cooperation on the Medical Products Regulation between Taiwan and Japan" on November 5, 2013. TFDA, Ministry of Health, Labour and Welfare of Japan (MHLW) and the Pharmaceuticals and Medical Devices Agency (PMDA) have established the official working groups, to exchange information on medical policies and laws and regulations between Taiwan and Japan, and take turns to conduct conference every year.

Implementation Measures

1. Became the 10th regulatory ICH member

It has been 10 years since TFDA was invited to participate in the ICH conference in 1998. In addition to attending the conference, participating in the working group with more than 20 experts to stipulate global drug technical guidance, TFDA will organize relevant training to assist the domestic pharmaceutical industry to carry out the ICH related standards.

In June 2018, in the ICH conference held in Kobe City, TFDA became the 10th regulatory ICH member after the membership of European Union of Europe, Food and Drug Administration of the United States, Health Canada of Canada, Ministry of Health, Labour and Welfare of Japan (MHLW), Swissmedic of Switzerland, Health Sciences Authority (HSA) of Singapore, Ministry of Food and Drug Safety of South Korea, National Medical Products Administration (NMPA) of China, Brazilian Health Regulatory Agency(Anvisa) of Brazil. It is an important milestone for TFDA to join an international organization for pharmaceutical cooperation, and it is also a recognition of the drug regulations in Taiwan that meet the international regulatory standards.

2. Hosted "2018 APEC Good Registration Management (GRM) Regulatory Science Center of Excellence Workshop"

Cooperating with the RHSC to comprehensively promote the platform of APEC Regulatory Science Training Center of Excellence (CoE), the CoEs conduct personnel training based on the core curriculum set by each of the priority work area, to promote the capability, cooperation and regulatory convergence among the APEC member economies.

TFDA hosted the "2018 APEC Good Registration Management (GRM) Regulatory Science Center of Excellence Workshop." This training event was co-organized by the PMDA of Japan, the Asia Partnership Conference of Pharmaceutical Associations (APAC) and RAPS Taiwan Chapter.

The courses included common sessions and concurrent reviewer-specific sessions and applicant-specific sessions. A total of 62 trainees from 14 APEC member economies joined the training. The trainees were form Hong Kong, Indonesia, South Korea, Chile, Japan, Malaysia, Papua New Guinea, Philippines, Singapore, Thailand, Vietnam, Mexico, Peru, and Taiwan. Upon the completion of the training course, the participants shall be able to assist their institutions, associations or companies to deliver personnel training, to promote the concept of Good Registration Management (GRM) in individual APEC member economies.

This workshop invited 28 domestic and overseas regulatory experts to deliver training. They shared the principles of Good Registration Management (GRM) with their practical experiences.

3. Held the PIC/S quality risk management expert circle event

The PIC/S Expert Circle on Quality Risk Management (QRM) & Training Event includes a 2-day training course and a 1-day Expert Circle meeting. Internationally renowned experts, senior GMP inspectors, and experienced speakers from the industry have been invited from countries including the U.S., the U.K., Austria, Ireland, Iran, and Taiwan, and the participants are key talents nurtured by GMP inspectorates worldwide. The curriculum is designed under the QRM framework, and consists of keynote speeches and multi-theme workshops, involve the topics of principles, tools

and examples related to the implementation of QRM in industry, risk identification, data integrity etc. This event also provide a platform for participants to exchange information, share experience, revised related guidance documents and map out future plans for inspector training.

4. Conducted "the sixth Joint Conference of Taiwan and Japan on Medical Products Regulation"

"The 6th Joint Conference of Taiwan and Japan on Medical Products Regulation" was held in Tokyo on October 11, 2018. Other than TFDA, National Health Insurance Administration of Ministry of Health and Welfare, Center for Drug Evaluation, the representatives of the industries and pharmaceutical and medical device related industry and associations also attended the conference in Japan. The representatives from the official authorities and industries of both countries gave speeches on topics ranging from the development and trend of drug regulations, the practical management of Real-World Data, promotion policy of OTC, the management model for the 3D printing of medical devices and the international regulatory harmonization strategies.

Outcomes and Benefits

1. Major breakthrough in the international medical cooperation

Becoming an ICH member is a major achievement of Taiwan's efforts on stipulating international drug management regulations in the past few years, and it is also best proof that Taiwan's drug management regulations meet the international standards. TFDA has continued to expand its participation in ICH related activities (Figure 3-3). So far, more than 30 experts have been selected to participate in more than 20 expert working groups in the development of guidelines, and vigorously contributed their strength. At the same time, a working group of industry, government and academia was formed in Taiwan to understand the actual needs of industrial upgrading, and handled the guidance training and actively implements ICH guidelines, so that ICH guidelines can be implemented in Taiwan's pharmaceutical industry earlier and more effectively.

Figure3-3 A group photo of 2018 ICH event participants

2. The 2018 APEC workshop was highly recognized

A total of 62 trainees from 14 APEC member economies participated in the seminar, and the overall satisfaction score of the trainees was 4.35 (out of 5). All the participating economies valued the importance of Good Registration Management (GRM). After the workshop, many

Figure3-4 A group photo of all the participants from the "2018 APEC Good Registration Management (GRM) Regulatory Science Center and the research program of education promotion"

Figure3-5 A group photo of the 2018 PIC/S Expert Circle on Quality Risk Management & Training Event

representatives from different economies consulted TFDA for the assistance of providing training materials and lecturers in regional personnel training. The APEC Good Registration Management (GRM) Regulatory Science Center of Excellence Workshop not only enhances the international recognition of TFDA, but also substantially strengthens the communication and cooperation between TFDA and other countries (figure 3-4).

3. The PIC/S Expert Circle on Quality Risk Management & Training Event enhance international reputation

The PIC/S Expert Cirlcle Event on QRM enables inspectors worldwide to engage in intensive brainstorming and discussion, improve and strengthen their inspection skills, develop and draft related QRM technical documents that integrate knowledge and experience from around the world for use in future inspections, incorporate QRM principles into inspection systems, maximize inspection resources and produced fruitful results. This event was widely acclaimed by all participants, not only to enhance their professional knowledge through the three-day event, but also to experience the culture and passion of Taiwan. Taiwan TFDA once again accomplished its mission in international diplomacy and greatly enhanced Taiwan' s international reputation (Figure 3-5).

Figure3-6 A group photo of Joint Conference of Taiwan and Japan on Medical Products Regulation

4. Taiwan-Japan medical information communication and exchange

Through Joint Conference of Taiwan and Japan on Medical Products Regulation (Figure 3-6), promoted the exchange and understanding of laws and regulations on both sides, and strengthened cooperation and mutual trust between officials and operators on both sides. Looking forward to reaching a consensus on joint review under the cooperation framework of Taiwan and Japan's pharmaceutical regulations in the future, to benefit the pharmaceutical and medical device industries of both countries.

Section 5 Deepen the New SouthBound exchange in drug regulatory managemen

Origin of Policy

The sales of medicinal products are strictly regulated in countries around the world. The management regulations and criteria in different countries are different. Therefore, the regulatory harmonization is significantly important to the development of the market for medicinal products. To promote regulatory harmonization for medicinal products, the European Union, the United States and Japan founded the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) in 1990. The organization actively discussed topics on various technical specifications, promoting training and global cooperation. Besides, ASEAN countries have also established Pharmaceutical Product Working Group (PPWG) to promote the regulatory harmonization for medicinal products in ASEAN countries.

To cooperate with the government's promotion of the New Southbound Policy and globalization strategies and effectively enhance the consistency between Taiwan's regulatory standards and the global regulatory standards, TFDA hopes to deepen the cooperative relationship with the New Southbound countries by inventorying the drug management policies and information of the pharmaceutical industry in each of the new southbound countries and through exchanges and learning in drug regulatory framework, to expand the overseas market and export business for the industry.

Implementation Measures

1. Sign the cooperation agreement for pharmaceutical management

TFDA and National Pharmaceutical Regulatory Agency (NPRA) of Malaysia formally signed the official collaboration document over pharmaceutical regulations on March 26, 2018 in Kuala Lumpur, Malaysia. (Figure 3-7)

There are five main aspects for the signed cooperation agreement for the management of pharmaceutical products, including the exchange of related information to the management of pharmaceutical products, the exchange of management technology, experience sharing of management regulations, convention of regular meetings, and arrangement of personnel's exchange visits and seminars for the related pharmaceutical products.

2. Holding 2018 Taiwan-ASEAN drug regulatory forum

The first "2017 Taiwan-ASEAN drug regulatory forum" held by TFDA in 2017 received great feedback from domestic and overseas experts, and thus we continue to hold the second "2018 Taiwan-ASEAN drug regulatory forum".

The forum held a series of events on pharmaceutical administration issues from September

Figure3-7 TFDA and National Pharmaceutical Regulatory Agency (NPRA) of Malaysia formally signed the official collaboration document over pharmaceutical regulations.

Figure3-8 Taiwan-ASEAN drug regulatory forum workshop photo

3 to 6, 2018, inviting Malaysia, Philippines, Thailand, Vietnam, Indonesia and Regional Comprehensive Economic Partnership(RCEP) countries India and other ASEAN national authorities to come to Taiwan to share the current management status of drug administration in the participating countries.

In order to deepen the exchanges between drug regulatory authorities, the forum was held in a variety of formats such as expert meetings, workshops, information exchange meetings, on-site visits and symposiums. The topics of the workshops included “Biologics, Biosimilars and Vaccines” (Figure 3-8). The title of the symposium was “Regulation on Biologics, Biosimilars and Vaccines” (Figure 3-9). In addition, we also invited the representatives of the ASEAN drug regulatory authorities to visit the Division of Research and Analysis of TFDA and the vaccine and biopharmaceutical plants in Taiwan.

Outcomes and Benefits

1. Strengthen cooperation with Malaysian National Pharmaceutical Regulatory Agency

With the signing of the cooperation agreement on pharmaceutical management, to strengthen cooperation with Malaysian National Pharmaceutical Regulatory Agency. TFDA continues to actively facilitate the hominization of Malaysian pharmaceutical regulations, inspection technology exchange, and cooperation in the certification of laboratory management, to enhance the confidence level in Malaysia and countries of the New Southbound Policy in Taiwan’ s pharmaceutical products, so to reduce the trial testing, inspection, simplify the drug review process and shorten the time for Taiwan’ s pharmaceutical products to enter the countries of the New Southbound Policy such as Malaysia, which will facilitate the connection between regional markets, benefit the related industries in Taiwan.

Figure3-9 A group photo of official participants in the Taiwan-ASEAN drug regulatory forum

2. Promoting the development of domestic biotechnology pharmaceutical industry

TFDA plans to create contacts for long-term communication and information exchanges with other country's drug regulatory authorities or industry associations through information exchanges with representatives of various countries, sharing experiences and understanding the needs of other countries, and to increase the opportunities for information exchanges and international cooperation with other countries.

Through the researches in information such as RCEP Pharmaceutical Product Working Group (PPWG), RCEP national drug inspection, status of pharmaceutical manufacturers, regulations for entering the market, medical insurance business, understanding the latest information on the regional policy of integration in drug regulation in Asia, TFDA assisted domestic pharmaceutical industry to understand the Asian market, and to enhance the cooperation opportunity with international pharmaceutical industry. In addition, we increased the opportunity of further training for different drug regulatory authorities to enhance their capability and knowledge in drug regulation, strengthen the mechanism of the regulatory harmonization, and enhance the opportunity for international cooperation.

The 4-day 2018 Taiwan-ASEAN Drug Regulatory Forum organized 2 expert meetings, 3 workshops, 3 information exchange meetings and held 1 symposium, collecting information or suggestions for different topics, so that the mentioned

activities could be more comprehensive. Furthermore, we also conducted research on RCEP national drug management, new drug R & D regulations and policies, analyzed and wrote drug review procedures, health care business policies, and international new drug regulations in various countries. A total of 4 research reports were produced, which assisted competent authorities to stipulate strategies and promote the implementation of policies to promote the global development of Taiwan' s biotechnology and pharmaceutical industry.

Section 6 Improvement of drug quality inspection technology

Origin of Policy

Drugs must pass rigorous clinical testing for the verification of its efficacy and safety before entering into market. However, TFDA actively implements scientific proofs to monitor products with high risk, in order to reduce unpredictable risks after entering into market and ensure the quality of drugs. We also enhance our inspection capabilities through the feedbacks from the notification system, manage product warnings and cooperate with international organizations.

Implementation Measures

1. Establish a testing method for sartan drugs that may contain nitrosamine impurities.

The sartan drugs may contain nitrosamine impurities was continuously issued because of an pharmaceutical ingredient called Valsartan may contain N-Nitrosodimethylamine (NDMA) since the end of June, 2018.

TFDA actively started to develop a method for detecting NDMA by liquid chromatography tandem mass spectrometer (LC-MS/MS) and applied the method to other active pharmaceutical ingredient of Valsartan and found some of them also contains NDMA. In addition, TFDA also enlarged testing scope to other sartan drugs, including Candesartan, Irbesartan, Losartan, Olmesartan, Telmisartan, and Azilsartan. In response to the U.S. FDA's safety alert, TFDA simultaneously bring "N-Nitrosodiethylamine (NDEA)" and "N-nitroso-N-methyl-4-aminobutyric acid, (NMBA)" into our detecting targets. TFDA have announced three testing methods for 5 nitrosamine impurities in active pharmaceutical ingredient of sartan drugs. TFDA tested at least 600 products and 96 products were recalled because of detecting with NDMA, NDEA or NMBA. TFDA required the manufacturers and drug dealers to strictly fulfill self-management, evaluate the carcinogens that may be generated in the manufacturing process.

2. Handling of abnormal finding in influenza vaccine

To ensure the quality of the influenza vaccines, Taiwan's management strategy is in line with the World Health Organization (WHO). On the basis of Article 74 of the "Pharmaceutical Affairs Act" and the "Regulations of the Lot Release Procedures for Biologics," every batch is required to provide relevant information for review and TFDA will check the condition of transportation, storage and random sampling before the vaccines entering into market. According to the Chinese Pharmacopoeia, 11 tests items need to be carried out to ensure the efficacy and safety of the vaccines. The "Lot Release Certificate" will be issued only if the batch of vaccines compliant with the acceptable quality level and will be labeled on the package.

TFDA received 2 reports issued about vaccines with abnormalities in color and foreign materials inside respectively on October 26 and 29, 2018. TFDA Immediately performed the safety test and the rubber stopper leach test to the same batch of retained sample vaccines with abnormal appearance, and the results were all acceptable. TFDA also strengthen risk control mechanisms to ensure the quality and safety of vaccines

Figure3-10 Liquid Chromatography Tandem Mass Spectrometer

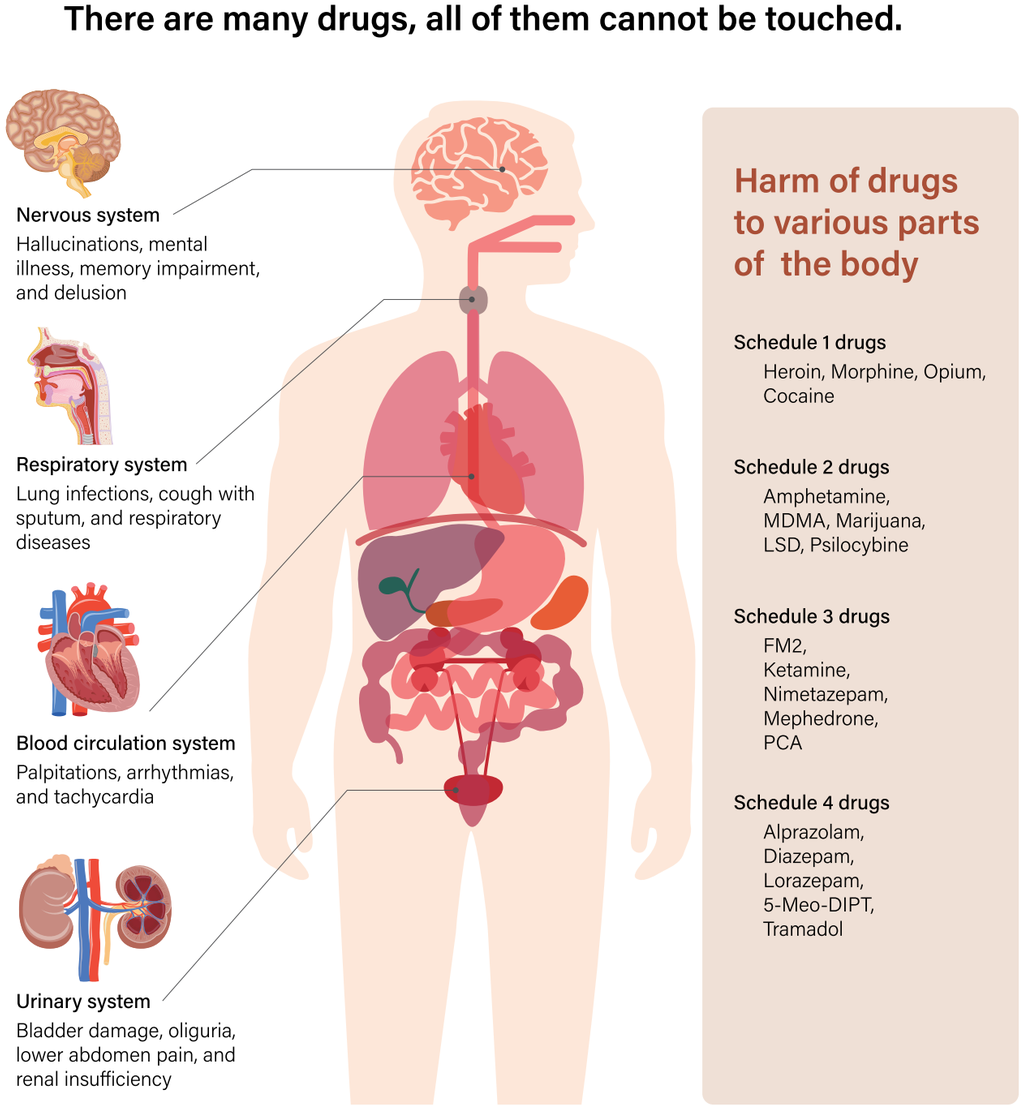
Figure3-11 FTIR (Fourier Transform Infrared spectroscopy)

Outcomes and Benefits

TFDA promptly and successfully verify the non-compliant pharmaceutical products through rapid response and teamwork:

1. TFDA found that other active pharmaceutical ingredients of Valsartan also contained NDMA and published recommended testing methods we developed to OMCLs network, shared relative information to EDQM and MFDS to jointly maintain medication safety with other administrative agencies worldwide. TFDA also required the manufacturers to strictly fulfill self-management to ensure every batch of active pharmaceutical ingredient of sartan drugs without NDMA and NDEA residues before used in manufacturing process and incorporates the strategy into the GMP audit focus to maintain medication safety.
2. TFDA successfully blocked two batches, totally 518,405 vials of noncompliant influenza vaccines from entering into Taiwan and shared abnormalities information to OMCLs and GEON, actively demonstrate our determination to secure the quality and safety of vaccines. In addition, TFDA also strengthen risk control mechanisms and required manufacturers to strengthen fulfill self-management to jointly maintain medication safety.

04 Reinforced Management of Controlled Drugs and Prevention of Drug Abuse



04 Reinforced Management of Controlled Drugs and Prevention of Drug Abuse

TFDA has established a drug abuse monitoring mechanism, to effectively manage the controlled drugs and prevent drug abuse, as well as to understand the domestic trend and investigate the international information on the emerging substances of drug abuse, to be used as a reference for the illegal drugs management of Ministry of Justice. In addition, Ministry of Justice places added the emerging drugs with scientific use into the "Controlled Drugs Act," to avoid drug leakage and endanger the health of the citizens in the nation.

Since 2017, TFDA has actively cooperated with the Executive Yuan for the promotion of "New-generation Anti-drug Strategy" and implemented various new anti-drug monitoring measures. TFDA also strengthened the advocacy to educate the public to stay away from drugs which demonstrates the government's anti-drug determination and actions to against drugs.

Section 1 Promote amendment to the regulations on controlled drugs

Origin of Policy

According to the "Controlled Drugs Act" and its related sub-regulations, the government had amended the rules on controlled drugs to fulfill the requirements, to prevent the abuse or illegal use of controlled drugs. In addition, the guidelines and regulations precaution for narcotic analgesics have been progressively established since 1993, to be the foundation of prescription and management of addictive narcotic drugs.

Implementation Measures

The “Controlled Drugs Review Committee of the Ministry of Health and Welfare” is held every six months to strengthen the management of controlled drugs. As for the emerging drugs that have needs for scientific usage, it will conduct a management assessment and review relevant regulations for discussion and amendment.

The narcotic analgesics play an important role in pain management. In response to the implementation of relevant laws and regulations, we plan to add or amend of related guidelines

and regulations for the reference in the medical profession, to ensure the safety of medications and facilitate the enhancement of medical quality.

Outcomes and Benefits

The "Controlled Drugs Review Committee of the Ministry of Health and Welfare" convened the 37th and 38th meeting in 2018 and added two emerging drugs as the controlled drugs (Table 4-1). The Article 2 of the attached table of "Regulations Governing the Allocation and Purchase Limitation of Schedule 1 and 2 Controlled Drugs" and Article 20 of the "Enforcement Rules for the Controlled Drugs Act" were amended (Table 4-2).

Seven guidelines and regulations such as "Guidelines and Regulations for Clinicians Long-Term Prescribing Narcotic Analgesics To Patients With Non-cancer Chronic Intractable Pain" were amended in 2018 (Appendix 2-12) and the "Cancer Pain Treatment Manual" and "Specification for Clinical Use of Narcotic Analgesics" were abolished.

Table4-1 2018 Addendum to Classification of Controlled Drugs

Date of amendment	Schedule	Promulgate the names of the controlled drugs	Descriptions
May 11	Schedule 3	1-(Thiophen-2-yl) -2-methylaminopropane [1-(Thiophen-2-yl)-2-methylaminopropane, Methiopropamine, MPA]	CNS stimulant, a type of Amphetamine chemical synthetics.
		Methylbenzyl N-benzylcathinone, Benzedrone and MBC, including 2-MBC, 3-MBC and 4-MBC similar structural materials.	CNS stimulant, a type of Cathinone chemical synthetics.

Table4-2 107年管制藥品相關法規修正事項

Date of amendment	Name of the regulation	Descriptions
February 13	An amendment to the Article 2 of the attached table of "Regulations Governing the Allocation and Purchase Limitation of Schedule 1 and 2 Controlled Drugs" was amended	Review the revised the usage limits of Schedule 1 and 2 Controlled Drugs by medical institutions, pharmacies, veterinary clinics and veterinary institutions to meet the actual needs of each organization.
April 24	Amendment to the Article 20 of the "Enforcement Rules for the Controlled Drugs Act"	In response to the special delivery condition for the Schedule 1 and 2 Controlled Drugs or the supplementary measures for unable to deliver or sent by the post office due to thee factor of force majeure.

Section 2 Improved pharmaceutical quality of the schedule 1 and 2 controlled drugs

Origin of Policy

TFDA pharmaceutical plant of controlled drugs (hereinafter referred to as the pharmaceutical plant) has been in compliance with the GMP in 1988, the cGMP in 2004, and the PIC/S GMP in 2014 (Figure 4-1). However, due to the factors such as the aging factory, insufficient production space, and the increasing demand for various types of controlled drugs by the general public, thus the Plan for the construction and renovation of pharmaceutical plant of controlled drugs was carried out to increase the production capacity and space for research and development, and the construction period is from 2012 to December 2019.

Figure4-1 製藥工廠簡要沿革

Implementation Measures

The new pharmaceutical building is a seven-story building, which is designed based on the modern pharmaceutical factories and it is compliance with the international GMP regulations. The ingredients and raw materials are shipped from the dock on the first floor of the new plant to passing the double door room and placed in the inspection area, to prevent external dirt, mosquitoes and bugs from entering the plant. The second floor is a place for water for injection (WFI) and purified water installation, and it provides water for manufacturers use in the manufacturing areas on the third to fifth floor. The manufacturing area is for producing injections, tablets, liquid preparations, film coated tablets and patches; the semi-finished products or finished products will be sampled and sent to the microbiology laboratory on the 6th floor and the chemical laboratory on the 7th floor for testing (Figure 4-2).

Figure4-2 The new pharmaceutical building for controlled drugs

At present, the pharmaceutical plant continues to carry out the construction and renovation plan of the GMP pharmaceutical building established in 1988, to reinforce its structure and earthquake resistance to comply with the current regulations. In the future, the pharmaceutical building will be used as the packaging area for injections, warehouse of finished products and administrative office area. The building will be connected to the new pharmaceutical building from the first to the third floor, and the logistics flow from raw materials to finished products will be in clockwise direction and is separated from the human flow, to reduce the risk of cross-contamination and product mix-up.

Outcomes and Benefits

The new pharmaceutical building will produce injections and tablets with two production lines to increase the production capacity. It also received the green building mark and the intelligent building mark. The plan for the future is to gradually increase the self-produced products and capability for research and development, and gradually achieve the goal of fully domestic production for the Schedule 1 and 2 Controlled Drugs.

Section 3 Improve drug abuse warning and monitoring mechanism of drug abuse

Origin of Policy

The endless drug abuse problems that endanger the health of the citizens. To prevent against the problem of drug abuse, TFDA collects drug abuse incident reported through healthcare facilities and other statistics such as drug abuse urine sample tests, tests performed with non-urine specimens in suspicious drug and controlled drug cases, drug seized, etc., and monthly compiled into the “Drug Abuse Case and Testing Statistics” to provide to TFDA and relevant units (Figure 4-3). In addition, TFDA conducts the “National Survey of Substance Use” every four years since 2005 to learn the domestic prevalence of illegal drugs and the drug abuse factors in the society, to understand the current status of drug abuse in Taiwan and provide reference to relevant government authorities for stipulating the anti-drug strategy to prevent the harm of illegal drugs.

Implementation Measures

1. Reporting mechanism for healthcare facilities on drug abuse

TFDA has established a Drug Abuse Reporting System (DARS) to receive information through drug abuse cases reported by domestic health facilities, to obtain the epidemiological information of drug abuse cases in the nation.

2. Management and reporting of approved institutions for drug abuse urine tests

In 2018, one new approved institution for drug abuse urine tests and one designated health institution were added. As of the end of December, there were totally 16 approved urine inspection institutions for drug abuse urine tests and designated health institutions in the country. The approved testing institutions will regularly submit the inspection results to the TFDA Urine Test for Drug Abuse Reporting System (UDARS) on a monthly basis. The routine performance monitoring for the approved institutions will be conducted every season, and of 58 times combined for the approved institutions in 2018.

3. Non-urine (drugs) testing and reporting upon drug abuse

According to the division of labor in drug testing of the Ministry of Justice, there are 10 institutions in Taiwan at present to help prosecution, police, and investigation authorities test non-urine specimens for drug abuse. In accordance with Article 9-3 of the "Enforcement Rules of Narcotics Hazard Prevention Act," each of the testing institutions shall regularly report the illegal drugs testing results to TFDA UDARS system, then TFDA collect the statistical data on a monthly basis, including the positive results of non-urine specimens in suspicious drug and controlled drug cases; the statistical data can be used as a reference for TFDA and all departments to stipulate illegal drug prevention strategy.

4. The 2018 National Survey of Substance Use

The fourth National Survey of Substance Use was conducted in 2018. The main sampled group is the citizens with household registration in Taiwan and between the ages of 12-64 years old. The survey includes 20 counties and cities in Taiwan, in addition to investigating the use of common addictive substances such as cigarette, alcohol and areca, also aims to discuss in depth the behavior, motivation, use frequency and obtained source of drug abusers in depth.

Outcomes and Benefits

1. Reporting status of drug abuse at healthcare facilities

The analysis data of DARS, showed a headcount of 34,371 users in total reported for drug abuse by healthcare facilities in 2018. The headcount of people for the first three types of drugs abused was 16,565 for heroin (48.2%), 13,618 for methamphetamine (39.6%), and 1,796 for ketamine (5.2%). Compare with the data of drug abuse reporting in 2017, the percentage of heroin reporting decreased from 52.9% in 2017 to 48.2% in 2018. It shows that the government has achieved results in heroin control.

2. Reporting status of approved institutions for drug abuse urine tests

In 2018, there was a total of 249,618 urine tests performed throughout Taiwan, among them, 68,302 were positive, and the positive rate was 27.4%. The headcount of positive cases for the first three types of drugs abused was 47,592 for methamphetamine, 15,699 for ketamine and 11,464 for morphine. Compare with the data of urine tests in 2017, the percentage of methamphetamine cases decreased 8.5% and the percentage of morphine cases decreased 21.9%.

3. Reporting status of drug abuse non-urine (Drug) tests

In 2018, there was a total number of 135,618 cases with positive test results in non-urine specimens in suspicious drug and controlled drug cases in Taiwan, of which 28,323 were methamphetamine cases, 21,044 were ketamine cases, and 20,663 were heroin cases. Compare to the data in 2017, the numbers of cases with positive test results in non-urine tests of (methyl) amphetamine, ketamine, heroin all decreased compared to 2017, and the largest reduction was heroin cases, 17.2%.

4. Results of 2018 National Survey of Substance Use

The 2018 National Survey of Substance Use had a total of 28,840 respondents, of which 18,626 people completed the survey. Using the same benchmarks surveyed in 2005, 2009, and 2014 (analyzed only for individual types of drugs), the lifelong prevalence of illegal drugs usage was 1.15%, a slight decrease compared to the survey conducted in 2014 (1.29%). However, in order to obtain more comprehensive data on illegal drugs usage in 2018, new topics were added, such as "using modified mixed type of drugs, for example drug coffee bags, drug plum powder bags and drug rainbow cigarettes, etc." and "involuntary use of illegal drugs." If contains the data from the newly added questions, the lifelong prevalence rate is 1.46%, of which the top three drugs are amphetamine, ketamine and ecstasy. As for the first time users of the illegal drugs, most of them used illegal drugs at their classmates or friends' houses.

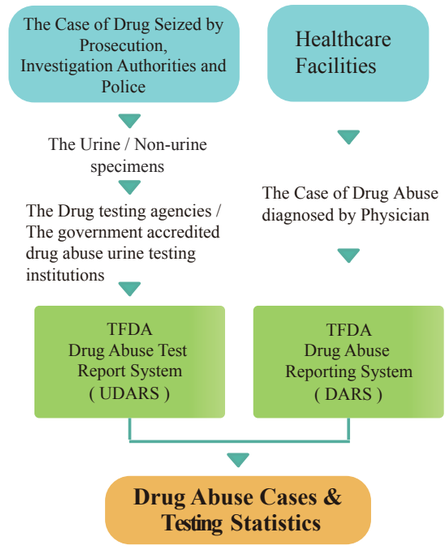


Figure4-3 Drug Abuse Case and Testing Statistics

Section 4 Implement New-generation Anti-drug Strategy

Origin of Policy

On May 11, 2017, the Executive Yuan initiated the "New-generation Anti-drug Strategy" that focuses on five aspects, namely drug monitoring, drug prevention, drug sweeps, drug rehabilitation treatment and strategies for amending laws and regulations. The "New-generation Anti-drug Strategy Action Plan" was determined on July 21, 2017 and was amended on November 21, 2018. It is expected to assist in illegal drug control and safeguard the health of new generations.

Implementation Measures

As the authority in charge of the anti-drug strategies, TFDA introduced, in terms of drug monitoring, the two core sub-strategies, namely "prevention against the importation of illegal drug raw materials in the name of the active pharmaceutical ingredient (API)" and "expand inspection capabilities to detect illegal drugs." Border checks and control are performed on active pharmaceutical ingredients and the capabilities in testing of illegal drugs are reinforced through inter-departmental collaboration in order to block illegal drugs so that they cannot spread in the country.

Outcomes and Benefits

TFDA enacted the amendments to the provisions of the "Regulations for the Inspection and Examination of Imported Medicaments" on August 22, 2018, and added the inspection items of active pharmaceutical ingredients; the "Portable Raman Spectrometer" is implemented for batch testing (Figure 4-4), and the active pharmaceutical ingredients can be detect on the site; at the same time, we will also inspect the pharmaceutical factory for active pharmaceutical ingredients warehouse in the field at a pharmaceutical company were inspected, in order to prevent any illegal circumstances.

Figure4-4 Demonstration of Raman inspection for the active pharmaceutical ingredients

We had created the "Portable Raman Spectrometer" spectra database, to continually expand the inspection capabilities at borders. In 2018, a total of 750 Raman spectra database of active pharmaceutical ingredients, illegal drugs, controlled drugs, and New Psychoactive Substances (NPS) were created, and the information has been shared with various anti-drug agencies to prevent illegal drugs from import.

The illegal drugs are constantly changing for past few years to make testing more and more difficult. In order to detect illegal drugs in real time, TFDA integrated domestic testing resources since 2017 and established a inter-department communication platform for the "method for new substances in urine testing" to improve the Nuclear Magnetic Resonance (NMR) testing mechanism of new substances. TFDA had purchased 176 standards of illegal drugs and new substances and created 251 standard items in the mass spectrogram databases, as well as actively developed the recommended test methods " Method of Test for Synthetic Cathinones in urine (1) & (2)" and published on the TFDA website to enhance the inspection capabilities of private testing institutions.

However, the prevention of illegal drugs requires cooperation between the government and private institutions. At the same time, TFDA also organizes the recommended laboratories to perform urine tests for new illegal drugs which targets at the private approved institutions for drug abuse urine tests for promotion. On September 7, 2018, TFDA announced the recommended laboratories for testing methcathinone in urine. In the future, proactive efforts will be devoted to extending the developed illegal drugs urine testing items and methods to private testing institutions to comprehensively enhance the testing capabilities throughout the country.

Section 5 Reinforced Propaganda of NPS prevention

Origin of Policy

TFDA has planned a series of programs for drug abuse prevention, to create a diverse environment for the prevention of drug abuse and strengthen the anti-drug promotion strategies, so to enable the public to be more involved in the promotion programs.

Implementation Measures

1. Drug abuse prevention in diverse workplaces

We established an anti-drug educational model for workplace in 2018 and encouraged enterprises to join the anti-drug promotion. We assisted the enterprises to conduct anti-drug education as part of the employee education and training in workplace, to create a drug free, health and safety work environment, as well as to build a local network to prevent drug abuse.

Figure4-5 The signature and flash mob activity by anti-drug alliance

2. The anti-drug alliance of Internet celebrities

TFDA takes a different approach compared to the past and promotes anti-drug via new media propaganda for young people such as inviting Internet celebrities to propagandize through their social media, to expand the scope of promotion.

3. Taiwan anti-drug squadron "Swinhoe's Pheasant"

For the propose of anti-drug prevention, the Executive Yuan has set up Taiwan anti-drug squadron, which was organized by Ministry of Health and Welfare, Ministry of Education, Ministry of Justice and Ministry of the Interior, to promote anti-drug health education with anti-drug mobile van from November 12, 2017 to December 8, 2018. The anti-drug mobile van "Swinhoe's Pheasant", which in charge of TFDA has toured southern Taiwan including Kaohsiung City, Tainan City, Chiayi County, Pingtung County, and Chiayi City, and spread anti-drug knowledge to campuses, communities and rural areas, as well as provided the public with multi-drug prevention knowledge and help information.

Outcomes and Benefits

1. The promote results of drug abuse prevention in diverse fields

Since 2015, TFDA has not only established eight anti-drug resource centers, cooperating with 85 NGOs for providing the consulting services for about 20,000 people in 2018, but also trained 880 seed instructors to conduct anti-drug education campaigns at the workplaces, schools and communities. TFDA had conducted a total of 309 educational sessions for drug abuse prevention and correct usage of the sedative sleeping pills, with a total of about 43,000 participants.

2. The anti-drug propaganda with Internet celebrities

In 2018, the "Anti-Drug Promotion Program with Internet Celebrities" invited five groups of popular Internet celebrities, to demonstrate the harm of drugs to young people by the special makeup effect of using the drugs. Through the flash mob activities (Figure 4-5), short films, and exposure on Internet celebrities' online social media like FB, IG etc., we hope to remind young people to say no to drugs, stay away from drugs, with a total of 3.96 million reaches.

3. " Swinhoe's Pheasant" promotion tour in the southern region

The "Swinhoe's Pheasant" promotion tour started from Kaohsiung City from November 12 to December 31, 2018. Through the instructions by lecturers, videos of celebrity interview, emerging drugs simulation and scent display box, expecting to enhance the anti-drug knowledge for the public, so that they will stay away from drugs to prevent the harm of drugs (Figure 4-6, Figure 4-7).

Figure4-6、7 The anti-drug squadron "Swinhoe's Pheasant" and the promotion activity

Section 6 Testing results of emerging narcotics of drug abuse

Origin of Policy

The NPS abuse problems are emerging. Delinquents modified the structure of known illegal drugs to produce new chemicals in order to avoid seizing and inspection, which has caused an increasing trend of new NPS discovered year after year. According to UNODC, There were at least 888 NPSs was found until the end of 2017 and 150 have been detected in Taiwan including Mephedrone and Bath salts. The problem causes negative effects to health and our society that can not be neglected and has been considered as an important issue need to solved.

Implementation Measures

1. Host international conferences

The "2018 APEC Workshop on the Analytical Technology of New Psychoactive Substances," was held on June 27, 2018. TFDA invited experts and scholars from the United States, Japan, South Korea, Malaysia, Thailand, Indonesia and Taiwan (Figure 4-6) to introduce the current status of NPS abuse in various countries, testing technology and future challenges in Asia-Pacific region. More than 200 scholars and experts had participated the meeting. We also discussed about "management strategy of GHB (Gammahydroxybutyrate) precursors from different countries" and other topics about NPS management strategies with experts in the closed meeting.

Figure4-8 A photo of participants in the "2018 APEC Workshop on the Analytical Technology ofNew Psychoactive Substances "

2. Improvement of testing techniques

TFDA have detected Bromomethcathinone, Chloromethcathinone, 25B-NBOMe and Desoxy-D2PM in cases from the prosecution, police and investigation authorities over the years and we also detected 2C-E, MPHP and 6-Methoxy methylone for the first time. In 2018, TFDA detected not only Methamphetamine and N-Ethylamphetamine but also N-Acetylmethamphetamine, was a compound newly detected in a tooth filling powder sample (Figure 4-8, the specimen labeled "zinc polycarboxylate cement") submitted by the District Court.

In addition, Mitragyna speciose, native in Southeast Asia, caused dozens of death in the United States. It may cause tachycardia and confusion. TFDA have successfully detected Mitragynine in two bags of unknown brownish green powder (Figure 4-9) submitted by the customs. TFDA also identified the powders were Mitragyna speciosa by DNA plant species identification technique and NCBI GenBank database.

Figure4-9 Tooth filling powder

Figure4-10 The brownish green powder in bag

05 Institutional Reforms in Medical Devices and Cosmetics Management

Outcomes and Benefits

In recent years, the number of new psychoactive substances and drug abuse is increasing. Many of them exist in the form of food commonly used in daily life, such as coffee bags and candies and may contain multiple illegal ingredients simultaneously. TFDA promote international collaboration by collecting information about current status of emerging psychotropic substances abuse in various countries and sharing testing techniques and discussing future challenges with experts worldwide.

TFDA continues to develop new testing methods for new psychoactive substances, providing scientific evidence for a variety of illegal compounds detected for the first time in Taiwan, also as a basis for law enforcement for police, justice and other administrative agencies.

05 Institutional Reforms in Medical Devices and Cosmetics Management

To strengthen the domestic medical device and cosmetics management system and meet the international standards, TFDA had drafted the "Medical Device Act", which was passed in the Legislative Yuan on 2018/12/14 through parliamentary group consultation. Meanwhile, TFDA also started to amend the "Statute for control of cosmetics Hygiene" in 2011, which was renamed as "Cosmetic Hygiene and Safety Act" on 2018/5/2, to strengthen the quality and safety management of medical device and cosmetics in our country. Furthermore, TFDA had mad an important breakthrough in international cooperation on medical device management. In 2008, Taiwan and Japan signed the "Memorandum of cooperation on the Medical devices factory inspection and Reporting" and implemented the system of on-site inspection in overseas medical device manufacturers.

Moreover, in order to improve the quality of laboratory developed tests and services for precision medicine molecular testing in the precision medicine molecular testing Laboratory, the "Guidance on Laboratory Developed Tests and Services (LDTS) for precision medicine molecular testing" was announced in 2018 to enhance protection of the health and safety of the citizens and speed up the development of precision medical industry.

Section 1 Promotion of the Medical Device Act

Origin of Policy

The regulations for medical device management in Taiwan were originally stipulated in the Pharmaceutical Affairs Act. As the characteristics of medical device management and the relevant business model in the industry are clearly different from those of pharmaceutical products, in order to strengthen the domestic medical device management system and make it in line with the international standards, TFDA has initiated the assessment on the institution of a legal framework for the medical devices, and developed the "Draft Medical Device Act" that met the needs in international and domestic environments.

Medical Device Act (draft)

1. Promote technological research and development as well as product innovation in the industry
2. Strengthen product circulation and distribution quality management
3. Strengthen the safety monitoring and management of post-market medical devices
4. Construct institutions for management of clinical trials for medical devices
5. Implement the risk grading system for management of medical devices
6. Improve the diversified approaches to management of medical devices in the industry

Cosmetic Hygiene and Safety Act

1. Amend the definition of cosmetics
   Regulate the use of non-medical toothpaste and mouthwash
2. Add product notification
   Establish PIF, GMP
3. Abolish registration of colorants
4. Registration of specific purpose products (5-year transition period)
5. Add SAE & hazards reporting
   Border inspection
   Regulation of recall and withdrawal
6. Abolition of criminal punishment
   Added whistle blowing terms

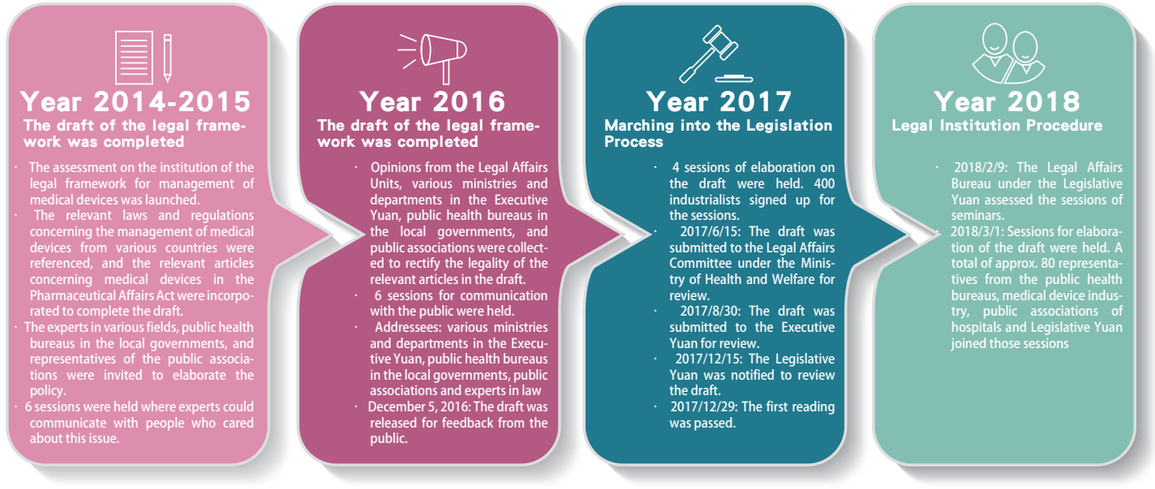


Figure5-1 The Process of the Promoting the "Draft Medical Device Act"

Implementation Measures

The "Draft Medical Device Act" was released to the public for feedback on December 5, 2016 and submitted to the WTO on January 31, 2017 for preview to avoid technical barriers to trade (TBT). The Legislative Yuan was served with the "Draft Medical Device Management Act" on December 15, 2017 for review and resolution, and the first reading procedure was completed on December 29, 2017. On October 25, 2018, the articles have been reviewed one by one. On December 14, 2018, the parliamentary group consultations were completed (Figure 5-1). It is hoped the domestic medical device management system can be improved through the establishment of the Medical Device Act.

Relevant Focuses in the Draft

In the whole-new “Draft Medical Device Act,” the most important part includes adopting the electronic online registration system for some low-risk medical devices, simplifying the pre-market application process and implementing product risk management. Professionals engaged in medical device design, such as academic researchers and software developers, can apply for a license in their own names. This will increase the willingness of the industry/academy/research communities to develop advanced medical devices. A flexible approval mechanism for new medical devices will be introduced to accelerate the market launch of new medical devices. In addition, for clinical trials of medical devices without significant risks, administrative procedures will be simplified and can be performed without the approval of the Food and Drug Administration. This will accelerate the research and development process of domestic emerging medical materials and inject new energy into our country’s medical equipment industry.

Outcomes and Benefits

The separate legislation of the Medical Device Act can help enhance compliance with the law among medical device industrialists, so that the management system of medical devices can be in line with the trends of international regulations, and the difficulty of exporting domestic medical devices can be reduced to facilitate the development of medical device industry in Taiwan. The expected outcomes and benefits of the Draft Medical Device Act are as shown in Figure 5-2.

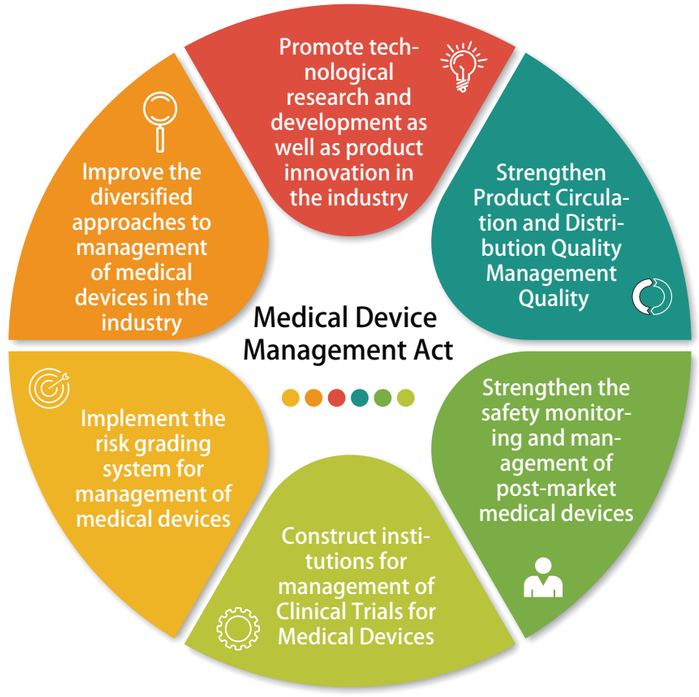


Figure5-2 The outcomes and benefits of the Medical Device Act (Draft)

Section 2 Reform of management system in medical device manufacturers

Origin of Policy

To enhance the manufacturer's quality of imported medical devices products, reduce the risk of medical devices on the market, promote the on-site inspection on overseas manufacturers of medical devices, reinforce the supervision responsibility in the pre-market and post-market stage for the imported medical devices, and establish a management model of medical device manufacturers for risk management.

Besides, on November 5, 2013, the Taiwan-Japan Relations Association (formerly known as the East Asia Relations Association) and the Japan-Taiwan Exchange Association (formerly known as the Japan Exchange Association Taipei Office) signed the "framework agreement on the cooperation of laws and regulations in drugs between Taiwan and Japan." After signing the agreement, TFDA and the Ministry of Health, Labor and Welfare of Japan (MHLW) and the Pharmaceuticals and Medical Devices Agency (PMDA) had established a working group for the Quality Management System (QMS) of medical devices, to reinforce the cooperation between the two countries.

Implementation Measures

1. On-site inspection on overseas manufacturers of medical devices

To establish a risk management mechanism for on-site inspection on overseas manufacturers of imported medical devices, TFDA announced the priority items and schedules of implementation for the on-site inspection on overseas manufacturers of imported medical devices. The regulations stipulate that the medical device manufacturers with the following products shall apply for on-site inspection due to the establishment, relocation, expansion and reinstatement of overseas manufacturers of the imported medical devices.

Table5-1 The priority items and schedules of implementation for the on-site inspection on overseas manufacturers of imported medical devices

items	Implementation date
Replacement heart valve (E.3925)	January 1, 2018
Vascular graft prosthesis (E.3450), Keratoprosthesis (M.3400), passive tendon prostheses (N.3025)	January 1, 2019
Implantable pacemaker pulse generator (E.3610)	January 1, 2020

2. Memorandum of cooperation for mutual recognition of medical device inspection reports between Taiwan and Japan

The working group continued to plan for observing regular auditing between the inspection agencies, to verify a mutually recognized QMS certification body. TFDA assessed that the risk management of the Japanese medical device manufacturers and then signed a draft Memorandum of cooperation (MOC) with Japan in 2017, and the draft was revised several times by both parties. The "Memorandum of cooperation on the Quality Management System of Medical devices" (referred to as the Taiwan-Japan MOC) was signed in Taiwan at the end of 2018. On November 30, 2018, our representative from the Taiwan-Japan Relations Association and the Japan representative from the Japan-Taiwan Exchange Association signed the Taiwan-Japan MOC at the 43rd Taiwan-Japan Economic and Trade Conference, and the MOC was announced and took effect on December 11, 2018.

The memorandum, which certified four QMS certification bodies (TUV Rheinland Japan, TUV SUD Japan, SGS Japan, BSI Group Japan), and PMDA by MHLW authorizing, was conducted by TFDA. Both of the two parties recognize the contents of the audit reports issued by the abovementioned units within three years, and they have a mutual trust based on the risk management system for overseas medical device manufacturers. The report from Japan clearly follows the standard audits of JQMS. It was translated into English and Chinese without notarization. The documents can be simplified in the QSD procedures for importing medical devices; in addition, the domestic manufacturers in Taiwan may also translate the TFDA audit report into an English or Japanese version as a document for entering the Japanese market.

Outcomes and Benefits

1. On-site inspection on importing manufacturers

In 2018, we had completed the on-site practical inspection with high priority and mandatory items for two factories and it is expected that the inspection will be conducted for 7 factories in 2019. We started the inspection from the manufacturers that produce high-risk cell tissue devices to the manufacturers that produce products with large impacts and used by a large amount of users, and the manufacturers that have more defective products notified after the product entering the market, to protect the health and well-being of the citizens with the quality and risk management in manufacturers.

2. Implement memorandum of cooperation for speeding up the review process

Both of the two parties have mutually agreement on cooperation and

implementation based on the signing of the Taiwan-Japan MOC. Since Taiwan-Japan MOC signed, there are more than ten Japanese manufacturers and one Taiwanese manufacturer have applied through this method. In the future, the Japanese inspection agencies will inform the TFDA for on-site auditing in Taiwan, which will assist the medical device manufacturers of both parties to speed up the document review process, facilitate the outstanding medical devices to enter the market, and provide a quality medical environment for the citizens in the country.

Section 3 Implementation of Cosmetic Hygiene and Safety Act

Origin of policy

The Office of the President officially enacted the "Cosmetic Hygiene and Safety Act" on May 2, 2018. This Act was formerly known as the "Statute for Control of Cosmetic Hygiene." The main purpose of law amendment is to respond to the development of the globalization market, reinforce the source and circulation management of cosmetics, and construct a high-quality cosmetics environment for the citizen in the nation. In this amended version, the implementation date is set to be on July 1, 2019, except for the relevant provisions of the information that shall be labeled on outer packaging or containers of cosmetics is set to be on July 1, 2021. The key points of the Cosmetic Hygiene and Safety Act are shown in Figure 5-3.

Implementation Measures

1. In response to the development of the globalization market and the trend of regulation harmonization, the new act was stipulated in accordance with international regulations and included the toothpaste and mouthwash in the cosmetics management, to further ensure the safety of consumers. On the basis of the announced schedule by the Ministry of Health and Welfare, the business operators must complete the product notification and establish the product information files before entering the market, and the manufacturing site must comply with the Good Manufacturing Practice (GMP) as a replacement of the current registration system of medicated cosmetics (it is called the specific purpose cosmetics in the new act). It will speed up the process for the product entering the market, provide online product information to consumers, ensure the production quality of cosmetics, and ensure the health and safety of cosmetics. In addition, the new regulations stipulate that product sources and flows information are required, spontaneous reporting obligations of businesses, and inspection on the imported cosmetics at borders, to ensure consumer's rights via the comprehensive regulations. TFDA has conducted about 120 educational trainings and explanation sessions for the draft of sub- regulations since 2013 and will continue to conduct more related sessions in the future, to assist the businesses to understand the new laws.
2. TFDA has stipulated the drafts of 18 sub-regulations and regulations which were authorized by the parent law in 2018. All of regulations have been consulted and discussed with experts of laws and regulations based on the draft version in TFDA, and the drafts were pre-announced according to legal procedures to seek opinions and feedbacks, to make the legal process more comprehensive.

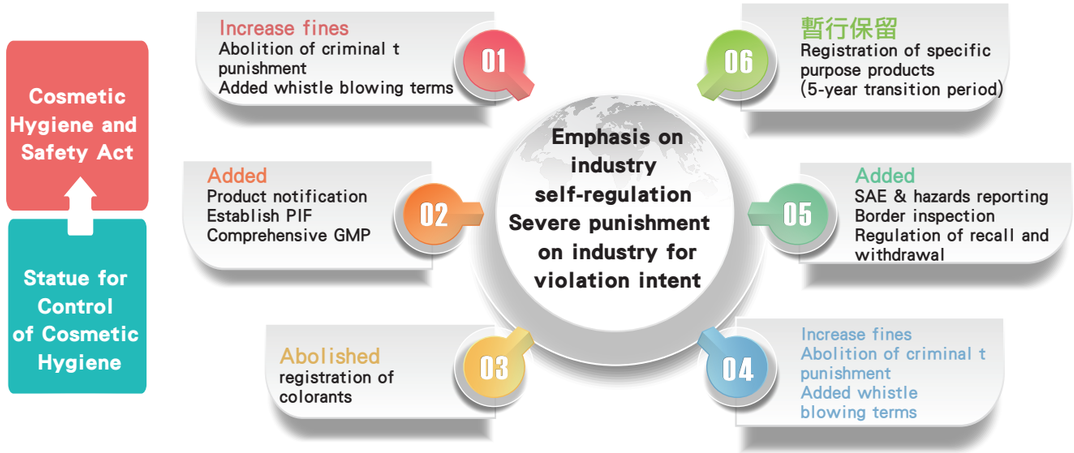


Figure5-3 The key points of the Cosmetic Hygiene and Safety Act

Outcomes and Benefits

The cosmetics businesses will be given reasonable preparation periods to lessen the impact on the cosmetics industry, including various sub-regulations and regulatory orders such as the Regulations Governing Notification of Cosmetic Products, Regulations for Cosmetic Product Information File Management, and the manufacturing site must comply with the Good Manufacturing Practices, etc. In the future, the domestic cosmetics management system will meet the international standards. Through the regulatory harmonization, it is expected to lessen the regulatory impacts on cosmetics industry in the international market, enhance the international competitive advantages of cosmetics industry in Taiwan, ensure the safety of consumers, and facilitate the development in the industry.

Section 4 Cosmetic ingredients and limits

Origin of Policy

Taiwan had established management regulations for the control of heavy metals in cosmetics, as the heavy metal is harmful to the health of human body. However, the international management regulations of cosmetics had been amended and there had reports regarding Barium poison, and thus we amended the domestic “Regulations on the Residue Limit for Impurity Heavy Metal Cadmium Contained in Cosmetics” and stipulated the "Regulations on the Management of Barium in Cosmetics" for the nation. TFDA also amended the hair dye ingredients and the precautions for the use of hair dye stipulated in the "Standard for Cosmetics Containing Medical or Poisonous Drugs," to ensure the safety of consumers in the rapidly developing cosmetics industry.

Implementation Measures

TFDA referred to the management regulations in Korea, China and ASEAN, and enacted the “Regulations on the Residue Limit for Impurity Heavy Metal Cadmium Contained in Cosmetics” on March 28, 2018. TFDA referred to the management regulations in European Union, ASEAN and China, and enacted the “Regulations on the Management of Barium in Cosmetics” on March 28, 2018. In addition, we referred to the management regulations of hair dyes in the EU, China and Japan, and announced the revise of the hair dye ingredients and the precautions for the use of hair dye stipulated in the "Standard for Cosmetics Containing Medical or Poisonous Drugs" on April 3, 2018.

Outcomes and Benefits

In the “Regulations on the Residue Limit for Impurity Heavy Metal Cadmium Contained in Cosmetics” announced and amended by TFDA, the residue amount of heavy metal cadmium contained in the final product was amended from 20 ppm to 5 ppm for the reason that the cosmetics may contain natural residue in trace amount of heavy metal cadmium due to the use of raw materials or technical difficulty in the manufactured process. Furthermore, TFDA announced the “Regulations on the Management of Barium in Cosmetics” to regulate the ingredient Barium salts (except for barium sulfate, barium sulfide and pigment insoluble barium salts, lakes and pigments), which are harmful to human health and must not be added to cosmetics. In addition, we announced the revise of the hair dye ingredients and the precautions for the use of hair dye stipulated in the "Standard for Cosmetics Containing Medical or Poisonous Drugs", to ensure the health and safety of consumers.

Section 5 Establish a laboratory management system for precision medicine molecular testing

Origin of policy

Precision medicine is one of the investments focuses of the global biomedical community. In this area, a patient’s personal data obtained through diagnosis and biological testing (such as genetic, proteomic and/or metabolic tests) and demographic profile (such as gender, ethnicity and medical history of the family, etc.) are used to customize treatments for the patient by comparing and analyzing the information with other entries within an established genomic database. Precision medicine promises a future with maximized treatment effects, minimized adverse events and efficient use of medical resources. TFDA therefore determines to release a guidance document, “Guidance on Laboratory Developed Tests and Services (LDTS) for precision medicine molecular testing”, to support the development of related industries in the nation. The objectives of this guidance document include improving the quality of laboratories performing such testing and promoting the development of molecular testing technology in Taiwan.

Implementation Measures

TFDA initiated several research projects on the regulatory frameworks and trends of laboratories conducting precision medicine molecular testing in the United States, China, the European Union, Australia and Japan. Except for understanding the international practices, TFDA also established an expert-based special task force to conduct six expert meetings and three seminar sessions to explore the domestic needs in Taiwan. With a great honor, the TFDA hosted the “international seminar on Laboratory Developed Tests and Services (LDTS) for precision medicine molecular testing industry” and invited experts in molecular testing from the US and China to share their regulatory and technical experience. The former Premier Lai Ching-Te, as the Premier at that time, gave an opening speech at the international seminar, which gave a strong signal that the government values the importance of precision medicine (Figure 5-4).◦

Figure5-4 group photo of “International seminar on Laboratory Developed Tests and Services (LDTS) for precision medicine molecular testing industry”

Figure5-5 Principle of the Guidance on Laboratory Developed Tests and Services (LDTS) for precision medicine molecular testing

In order to understand the current operation of laboratories performing molecular testing and evaluate the feasibility of the drafted guidance, TFDA worked with ten laboratories in Taiwan to simulate the inspection and guide the laboratory development. The experience and output obtained through the mock inspections are used as important references to finalize the guidance and optimize the inspection operations.

After several expert conferences, public information sessions, and inter-department discussions, TFDA released the "Guidance on Laboratory Developed Tests and Services (LDTS) for precision medicine molecular testing" on December 17, 2018. This guidance document is intended to serve as a reference for domestic laboratories performing molecular testing to improve their quality in testing and service. It is believed that this guidance document has set a milestone for the precision medicine industry in Taiwan. The foundation of this guidance is a well-balanced relationship between patient safety and development of the industry. It is also harmonized with the ISO 15189 standard and can be used as a reference for laboratories to establish their quality management system. The framework of the guidance is as shown in Figure 5-5

Outcomes and Benefits

On the basis of the "Guidance on Laboratory Developed Tests and Services (LDTS) for precision medicine molecular testing," TFDA subsequently released several documents including "Application notes on the registration of laboratory for precision medicine molecular testing," "Management regulations of laboratory for precision medicine molecular testing" and "Review of application for registration of laboratory for precision medicine molecular testing and operational principles of non-regular inspections" to inform the industry about the details of LDTS registration. These guidance documents, released step by step, now form a comprehensive regulatory framework for LDTS for precision medicine molecular testing in Taiwan.

06 Special Project

- **Establishment of a special area for stopping rumors and myths of food and drugs**

- **Improve the capability of the National Laboratory**
  - Participate in the events held by the European Network of Official Cosmetics Control Laboratories (OCCLs)
  - Become a member of the General European Official Medicines Control Laboratory Network (GEON), the second official laboratory in Asia

06 Special Project

Section 1 建置食藥膨風廣告專區

Origin of Policy

The growing popularity of the Internet has rapidly changed the way of the information communication and consumption pattern. The online shopping through the communication software and social network websites has also replaced the traditional method for the general public, and the convenience of online shopping facilitates the propaganda of illegal advertisements. TFDA has been supervising and managing advertisements; however, the Internet has no borders and TFDA does not have the jurisdictional rights to request the overseas website platform (with server set up abroad) to provide user's registration information given the website is suspected of publishing exaggerated, misleading advertisements or declaring the medical efficacy.

Implementation Measures

1. Inter-department discussion on management of illegal advertisements posted on overseas websites

In order to protect people's health, safety and consumer's rights, TFDA invited the Ministry of Economic Affairs, the Ministry of Foreign Affairs, the Ministry of Justice, the National Police Agency of the Ministry of the Interior, the National Communications Commission to convene the meeting of "management of online social community and non-domestic websites that violate the domestic health related regulations" in May 2018 for the discussion of feasible ways of managing overseas websites. Although it is not easy to obtain information regarding foreign website, yet all departments stated that they would try their best to uncover relevant clues and provide assistance in order to solve such cases.

2. To establish "Section of Misleading Advertisement of Food and Drugs"

To ensure people's right to know and in case of purchase of falsely advertised products, TFDA had set up a "Section of Misleading Advertisement of Food and Drugs" on the official website and started operation since May 30, 2018, to announce suspected illegal advertisements on overseas websites, including website name, URL, illegal phrase, for general public to look up for the reference of future purchase (Figure 6-1).

In the meantime, TFDA will be releasing such info in multiple channels including media coverage, TFDA Facebook page, Food and Safety Weekly (Figure 6-2) and QR code links to raise public awareness.

Figure6-1 "Section of Misleading Advertisement of Food and Drugs"

Outcomes and Benefits

The Section of Misleading Advertisement of Food and Drugs has disclosed 59 announcements by the end of 2018; the majority is food advertisements from foreign websites, which takes up to nearly 80%, and the webpage has accumulated 565,000 views so far. TFDA will continue to monitor and supervise illegal advertisements and provide illegal ad information of foreign websites so that more people are not tricked by exaggerated and false advertisements and health of general public can be secured as well.

Figure6-2 Food and Safety Weekly: New trick for weight-loss ad. Traps of exaggeration you must know!

Section 2 Establishment of a special area for stopping rumors and myths of food and drugs

Origin of Policy

The rise of social media and mobile communication applications have created and spread rumors in food, drugs, cosmetics, and medical devices. In view of online rumors and myth prescriptions that may affect the general public, TFDA established a "special area for stopping rumors and myths of food and drugs" in April, 2015. We expect the reliable scientific materials and articles of experts will help the public to receive the right information on food and drugs, so to stop the rumors and myths.

Implementation Measures

1. Proactively collecting rumors and accept the public's publication articles

In addition to proactively collecting rumors on the Internet and media by TFDA staffs, the public can also use the "service Email" on TFDA's official website or refer to the "publication to stop rumors" on the good online publication articles of food and drugs, and submit their publication articles to TFDA for review and help others by answering their questions and stopping the rumors and myths.

2. Consulting experts for the right solutions

We understand the importance of empirical researches and thus invite experts from various fields such as medicine, pharmacy, toxicology, risk assessment, nutrition and food science to provide professional consultations and right solutions.

3. Stop rumors immediately and provide reminders

We will immediately stop rumors regarding matters that are closely related to the public's livelihood, and thus many people constantly visiting the special area for stopping rumors and myths of food and drugs. For example: Is the "list of top ten foods that cause cancer" true?", "Does shampoo contained dimethicone ingredient hurt people's hair or cause baldness?", "Can the residue drugs be flushed down the toilet?" and the rumors of "MSG is poisonous" come around from time to time, and thus TFDA has clarified these rumors in the special area for stopping rumors and myths of food and drugs. If the public see similar rumors, they can go to the "special area for stopping rumors and myths of food and drugs" on TFDA's official website, or go to the "rumor stopper" on the good online publication articles of food and drugs to check the relevant articles, or go to the official website to subscribe the e-newsletter for rumors to stay informed.

Outcomes and Benefits

We had categorized the rumors myths and more than 350 of them have been busted and released to the public. The number of rumors in food category accounts for nearly 60%, followed by medicines, cosmetics and medical devices, the official website has accumulated a total of 8.92 million clicks and the citations by domestic and foreign media have more than 2,200 of its reports. In addition, TFDA delivers knowledge of food and medicine through diver approaches such as on its official website, the "food lover" Facebook fan group, "good online publication articles of food and drugs" (Figure 6-3), to enhance the promotional effect and stop rumors.

In response to various instant communication media, web forums and the growing popularity of the Internet, TFDA will continue to collect various topics regarding food and drugs, to provide the right information for the public; we welcome people who are interested to post and share with their friends and family, to become a smart consumer.

Figure6-3 Good online publication articles of food and drugs

Section 3 Improve the capability of the National Laboratory

Origin of Policy

TFDA is responsible for research and inspection of foods, medicines and cosmetics. including development and amendment of testing methods, investigation and research, supply of standards, and provide technical support and assistance. TFDA actively promote international collaboration, to obtain latest technologies and information, as well as to improve the capabilities of the National Laboratory to keep up with the world.

Implementation Measures

1. Participated in the events held by the European Network of Official Cosmetics Control Laboratories (OCCLs)

The European Network of Official Cosmetics Control Laboratories (OCCLs) is a platform established by the European Union. Besides, EU also established the "Committee for Cosmetics and Consumer Health (CD-P-COS)" in 2018 to further strengthen the collaboration of cosmetics management in EU. TFDA participated in testing methods peer review about nitrosamines and proficiency testing about heavy metals in cosmetics held by OCCLs in 2018. TFDA also participated in the first and second joint session of OCCLs and CD-P-COS in March and October respectively which held in Strasbourg, France. TFDA published the testing methods development results about analyzing Δ9-Tetrahydrocannabinol (Δ9-THC) and Cannabidiol (CBD) in the cosmetics (Figure 6-O), and exchanged comments with EU experts.

2. Become a member of the General European Official Medicines Control Laboratory Network (GEON), the second official laboratory in Asia

The European Commission and the Council of Europe cofounded a collaborative network which includes official Medicines Control laboratories of EU members and non-EU countries in 1994. It is expected to improve the drug quality control ability of member states and countries by sharing information about testing method development, proficiency testing and post-market monitoring results. At present, EU countries, Canada and Australia successively joined the GEON.

TFDA's "Biopharmaceutical Laboratory" officially became a member of the GEON in 2018, which is the second official laboratory in Asia. This indicates that the laboratories' capabilities in human vaccines and other biopharmaceutical drugs receive international recognition.(Figure 6-4).

TFDA actively participates in the technical activities in the network about method peer review and collaborative study about biological standard.

TFDA also joined the working group of gene treatment product inspection to enhance the ability about drug quality. In the future, we look forward to continuously enhance the quality and technology of national laboratories by gaining the international recognition in the drug and cosmetics to ensure consumer's safety.

COUNCIL OF EUROPE

European Directorate for the Quality of Medicines & HealthCare

OMCL NETWORK QUALITY MANAGEMENT SYSTEM

ATTESTATION

The EDQM, European Directorate for the Quality of Medicines & HealthCare, hereby declares that

Taiwan Food and Drug Administration
161-2 Kunyang St, Nangang District, Taipei 11561, Taiwan
Section audited: Division of Research and Analysis – Section of Biologics

has been audited in accordance with the EDQM instruction 2107/07 on the OMCL Network Mutual Joint Audit Scheme.

The above-mentioned OMCL is entitled to declare that it has satisfactorily implemented a Quality Management System in accordance with *ISO/IEC 17025*, with the relevant texts of the *European Pharmacopoeia*, with the *Quality Management Guidelines* and the *Terms of Reference* of the General European OMCL Network.

Detailed information can be found in the Audit Report, which is consigned in document ***PA/PH/OMCL-(17) 23 DEF*** and the Follow-up Report ***PA/PH/OMCL-(18) 05 DEF*** corresponding to the **MOA 18/17**, as well as in the enclosed Scope of Assessment. The original documents are archived at the Department of Biological Standardisation, OMCL Network & HealthCare (DBO) of the EDQM and the Director of the OMCL has received a certified copy.

Attestation number: **EDQM/MUA-130**

Strasbourg, 3 March 2018
Valid until: August 2021

Dr. Karl-Heinz Buchheit
Head of DBO, EDQM

Figure6-4 OMCL Quality Management System Certification in the Network

3. Profieiency testing and collaborative study results

TFDA's National Laboratory participated in 17 Profieiency testing and 5 Collaborative studies (Table 6-1) in 2018, with all outcomes being satisfactory as the Laboratories' capabilities for inspection received international recognition..

Table6-1 TFDA participated in profieiency testing and the collaborative studies in 2018

Organizer	Capacity test/international collaborative study Research name	Research result
Food Analysis Performance Assessment Scheme (FAPAS)	Pesticide Residues in Lemon Pur e	Satisfactory
Food Analysis Performance Assessment Scheme (FAPAS)	β-agonists in Bovine Liver	Satisfactory
Food Analysis Performance Assessment Scheme (FAPAS)	Metals in Offal (Liver)	Satisfactory
Food Analysis Performance Assessment Scheme (FAPAS)	Processing Contaminants in Vegetable oil	Satisfactory
Food Analysis Performance Assessment Scheme (FAPAS)	Experiment on the accuracy of capability test in mixing beef, sheep, pork or turkey into chicken	Satisfactory
Food Analysis Performance Assessment Scheme (FAPAS)	Identification of fish species	Satisfactory
Food Analysis Performance Assessment Scheme (FAPAS)	Proficiency test for allergens such as milk, egg and gluten in cake	Satisfactory
Food Analysis Performance Assessment Scheme (FAPAS)	Detection of Salmonella spp. in salad	Satisfactory
Food Analysis Performance Assessment Scheme (FAPAS)	Enumeration of Bacillus cereus in cooked rice	Satisfactory

Organizer	Capacity test/international collaborative study Research name	Research result
Food Analysis Performance Assessment Scheme (FAPAS)	Detection of Listeria monocytogenes/Listeria spp. in RTE Meal	Satisfactory
Food Analysis Performance Assessment Scheme (FAPAS)	Sulfur dioxide in prawns	Satisfactory
United States Department of Agriculture /Grain Inspection, Packers and Stockyards Administration (USDA/GIPSA)	Proficiency test for genetically modified soybean and corn	Satisfactory
Australia IFM Quality Services Pty Ltd	Detection of Vibrio parahaemolyticus, Vibrio cholerae and E.coli count in seafood	Satisfactory
(US Collaborative Testing Services. Inc., CTS)	Court inspection Proficiency testing	Satisfactory
EU's European Network of Official Cosmetics Control Laboratories (OCCLs)	Aromatic allergen substances in cosmetics	Satisfactory
Singapore Health and Science Administration (HSA)	Heavy metals (arsenic, lead, mercury) in lipsticks	Satisfactory
European Directorate for the Quality of Medicines (EDQM)	Proficiency testing study for MMR (measles, mumps and rubella virus vaccine) vaccine potency assay	Satisfactory
European Directorate for the Quality of Medicines (EDQM)	4th tetracosactide Chemical Reference Substance (CRS) Collaborative study	-
European Directorate for the Quality of Medicines (EDQM)	WHO 3rd generation Erythromycin international standard Collaborative study	-
European Directorate for the Quality of Medicines (EDQM)	human insulin chemical reference substance (CRS) Collaborative study	-
European Directorate for the Quality of Medicines (EDQM)	insulin porcine chemical reference substance (CRS) Collaborative study	-
UK National Institute for Biological Standards and Control (NIBSC)	WHO's 1st generation enterovirus EV-A71 vaccine antigen international standard collaborative study	-

* International standard collaborative study, indicated by "-".

Outcomes and Benefits

By participating in regular meetings and technical activities held by international organizations, TFDA not only enhance the inspection quality and capabilities but also establish collaborative relationship with other laboratories and experts worldwide to obtain valuable experiences, technologies and management information and keep up with the world.

07 Annex