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Reinforced Management of Controlled Drugs and Prevention of Drug Abuse

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the Schedule 1 and 2 Controlled Drugs**
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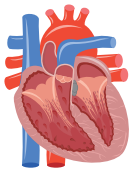
There are many drugs, all of them cannot be touched.



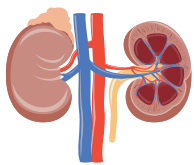
Nervous system
Hallucinations, mental illness, memory impairment, and delusion



Respiratory system
Lung infections, cough with sputum, and respiratory diseases



Blood circulation system
Palpitations, arrhythmias, and tachycardia



Urinary system
Bladder damage, oliguria, lower abdomen pain, and renal insufficiency

Harm of drugs to various parts of the body

Schedule 1

Heroin,
Morphine,
Opium,
Cocaine

Schedule 2

Amphetamine,
MDMA,
Marijuana,
LSD,
Psilocybine

Schedule 3

FM2,
Ketamine,
Nimetazepam,
Mephedrone,
PCA

Schedule 4

Alprazolam,
Diazepam,
Lorazepam,
5-Meo-DIPT,
Tramadol

Say No To Drugs 5 self-defense skills

1

Reject directly,
say no to drugs



2

Stay away and
leave immediately



3

Shift the subject
and attention



4

Self-deprecating



5

Persuade with friendship



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 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 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

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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 2018 Revisions to related regulations on controlled drugs

| Date of amendment | Name of the regulation | Descriptions |
|-------------------|---|---|
| February 13 | An amendment to the Article 2 of the attached table of " <i>Regulations Governing the Allocation and Purchase Limitation of Schedule 1 and 2 Controlled Drugs</i> " | 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 " <i>Enforcement Rules for the Controlled Drugs Act</i> " | 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. |

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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

History of the pharmaceutical plant

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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.

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Section 3 Improve Warning and Monitoring Mechanism of Drug Abuse

Origin of Policy

The endless drug abuse problems endanger the health of the citizens. To prevent against 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 Cases 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 healthcare 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 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 58 times combined for the approved institutions in 2018.

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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 regularly report the illegal drugs testing results to TFDA UDARS, then TFDA collects 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 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 methamphetamine, ketamine, heroin all decreased 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.

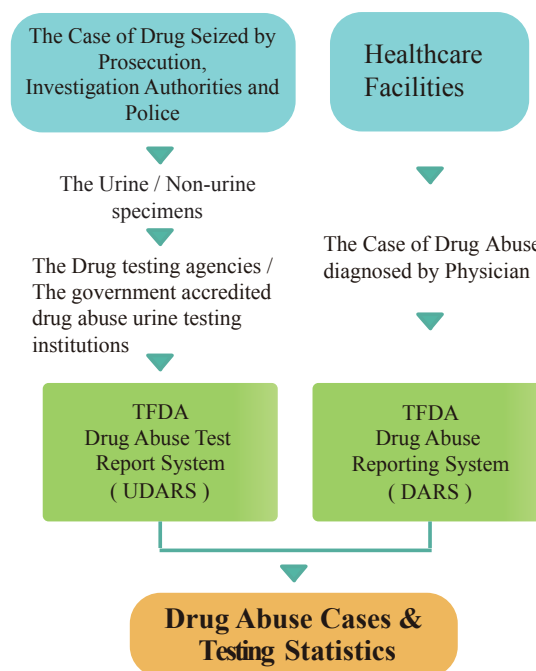


Figure4-3 Drug abuse and cases and testing statistics

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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 site; at the same time, active pharmaceutical ingredients warehoused in the field at a pharmaceutical company were inspected, in order to prevent any illegal circumstances.

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



Figure4-4

Demonstration of Raman inspection for the active pharmaceutical ingredients

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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" and 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.

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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.

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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

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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 NPS discovered year after year. According to UNODC, There were at least 888 NPS found until the end of 2018 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 in food" was held on June 27, 2018. TFDA invited experts and scholars from the United States, Japan, South Korea, Malaysia, Thailand, Indonesia and Taiwan (Figure 4-8) 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 of new psychoactive substances in food"

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2. Improvement of testing techniques

TFDA has 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 4-9, the specimen labeled "zinc polycarboxylate cement") submitted by the District Court.

In addition, *Mitragyna speciosa*, native in Southeast Asia, caused dozens of death in the United States. It may cause tachycardia and confusion. TFDA has successfully detected Mitragynine in two bags of unknown brownish green powder (Figure 4-10) 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

