Chapter 5.

Management of Pharmaceuticals and Foods

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As Taiwan is now a member of the World Trade Organization (WTO) and the APEC, and the international trade of foods and drugs is increasing in volumes day by day, to face the impact of the opening of market, the rampage of illegal foods and drugs on market, and the overflow of controlled drugs, issues such as the safety management of foods and drugs, education of the public on the safe use of drugs, control of drug abuse, establishment of an international mutual recognition system, and the upgrading of the quality of domestic products have become more important. It is the responsibility of the Department of Health to protect the rights of knowing of the people, and to protect their health as well. At the same time, it is hoped that when choosing and buying drugs and foods, people should also know how to protect their own health. Major activities in 2005 are illustrated as follows.

Section 1. Safety Management of Pharmaceuticals and Foods

The quality of food and drug products, the flow of products and the services offered by the professionals are closely linked to the health of the public. For this, the Department has actively established a strict mechanism for the management of foods and drugs, and promoted GMP and international mutual recognition. Action has also been taken to intensify health education of the public, to disseminate accurate information, and thus to protect the health of the people.

1. Safety Management of Pharmaceuticals

Safe-use of drugs is a multi-facet issue. In addition, the misleading concepts of the general public on medical care and medication have brought about a volume of medicine use 6.5 times higher than that of the US. To protect the safe use of drugs of the people, the following measures have been promoted:

1) A management mechanism for the safe use of drugs has been established; and a program to avoid and prevent wrong use of drugs has been promoted. The separation of drug dispensing from prescribing is encouraged in communities; and in 74 communities in 20 counties and cities, pharmaceutical personnel, by consolidating local resources, go deep into communities to provide pluralistic pharmaceutical care services to the public.
2) To activate primary medical care and to build a humane community health care environment, a three-in-one community medical and pharmaceutical care service group plan has been promoted to develop regional collaborative models of medical and pharmaceutical care. There have been thus far ten successful cases; and eight counties and cities are developing small-scale pharmaceutical care service networks to provide the public with comprehensive medical care services in the three aspects of medical care, health care and pharmaceutical care.
3) A strict system on the review of clinical trial and pharmaceuticals has been set up to upgrade the quality and efficiency of review process, and to expedite the review process of new drugs. Labeling in Chinese of pharmaceuticals has also been actively promoted.
4) Lectures on the safe use of drugs have been organized in community colleges to disseminate correct information on the safe use of drugs, to provide the public with access to information on drug use. By the end of 2005, 444 pharmacists had been trained as lecturers; 7,217 people had taken the courses; and 55,802 pharmacies, dealers and manufacturers had participated in the lectures.
5) The safe use of Chinese medicines has been strengthened. The extraction, isolation and assessment of index ingredient standards from Chinese medicine materials have been completed for some 20 items.

(1) Quality control of Chinese medicine preparations (materials) has been improved to interrupt the supply of inferior-quality materials and to control the supply of high-quality materials.

(2) To promote the establishment of an Asia-Pacific center for the supply of Chinese medicine standards, the extraction, isolation and assessment of index ingredient standards from Chinese medicine materials have been completed for some 20 items.

(3) Laws and regulations on Chinese medicine and pharmacy have been reviewed and amended. To draft regulations on the GMP and concoction specifications, relevant international and local regulations on Chinese herbal medicines have been collected and compiled in volumes. Three workshops on Chinese medicine industries and their future directions, and on inspection and seizure of illegal medicines have been organized for 1,008 participants.

(4) Programs to develop the science and technology manpower of Chinese medicine and pharmacy industries have been implemented.

(5) An information network on the safe use of Chinese herbal medicine, (http://tcam.ccmp.gov.tw) was set up for public use on September 1, 2005, to provide the public with correct information, and to assure the safe use of Chinese herbal medicines.

(6) Plans for the development of a mechanism on the Chinese medicine manufacturing process and a Chinese medicine concoction base have been implemented.

6) To promote the development of new drugs and related manufacturing technologies, and to upgrade the industrial standards of the domestic manufacturing of drugs, the Department announced on November 20, 2000, in accordance with regulations of Article 41 of the Pharmaceutical Affairs Act, jointly with the Industrial Development Bureau of the Ministry of Economic Affairs, the Regulations Governing Incentive Measures for the Research and Development of Pharmaceutical Technologies. 15 applications have met the requirements after careful review; of them, five are for pharmaceuticals, three for medical devices, and six for manufacturing techniques. A total of NT$ 4.115 million was appropriated as incentives.

7) A single window for consultation on regulations concerning biotech products has been created to promote the development of biotechnology industries. 150 inquiries have been received.

8) A drug interaction databank system has been set up to store basic information of drugs and associated interactions together with the databank of the National Health Insurance on some commonly used drugs primarily by their codes, ingredients and scientific names to integrate it into a comprehensive drug interaction-related databank for hospitals, clinics and pharmacies to check to confirm at once if prescriptions contain any interactive drugs, and thus to assure the safety of drug use, the adequacy of prescriptions, and to avoid repeated use of drugs and reduce costs on the National Health Insurance, and thus to protect the safety of drug use. Currently, 17 medical centers, 18 regional and district hospitals, 24 DOH hospitals, 34 pharmacies, and the Bureau of National Health Insurance and its six branch bureaus have availed themselves to this service. By the end of 2005, 36,249 person-times had either visited the system or downloaded the information.

2. Safety Management of Foods

In the recent years, the so-called "black-heart foods", that is, the illegally marketed unsafe foods, have flooded the market to pose serious suspicions in the mind of the people when choosing and buying foods or when consuming them. To alleviate the worries of the public and to protect their health, the Department has set up a food consumption warning system and a food curriculum vitae system. They are illustrated as follows.

1) To strengthen the current system of food safety management, to comply with international practices, to reinforce the self-control system of food industries, to boost their responsibility for products, food safety related regulations have been reviewed for amendment. The draft amendment of the Food Sanitation Management Act was submitted to the Legislative Yuan on

Table 5-1 Food Safety Lights

Light	Denotation
Red	a. Hazardous to human health or not, should not be used for human consumption
	b. Immediate hazards to human
	c. Validity date exceeded
	d. Not safe and may be hazardous to human health
	e. In violation of the permissible amount standards for food safety and also hazardous to human health
	f. Food adulterated with drugs
	g. Assessment of health risks indicates high possibility of hazardous to human health.
Yellow	a. No immediate hazards to human health; hazards are suspected, and in-depth investigations or improvement are needed
	b. Food suspected of not safe
	c. In violation of the permissible amount standards for food safety, though not hazardous to human health, however the impact is large
	d. Assessment of health risk indicates suspicions of hazardous to human health
Green	a. Incomplete labeling
	b. Though may be hazardous, risk factors have been controlled
	c. All rumors; products are safe
	d. Assessment of health risk indicates very low possibility of hazardous to human health

December 5, 2005, for review and approval. Action has also been taken to complete the maxium residue limits for 93 pesticides, to decide on the criteria of the use scope, application and specifications standards for five food additives, and to supplement and revise sanitation standards for six food items. They are pubished on the website of the Department for public information to make food management more transparent.

2) Establishment of a food green-light mechanism: When food safety is in suspicion, professional scientific basis and risk assessment analysis are used as a communication platform, and through the professional assessment of the advisory group, the results are announced in the form of a consumption warning system. Red stands for foods unfit for human consumption; yellow is for foods without immediate risk but their safety is uncertain; and green is for foods with negligible risk. They help the public in correctly recognizing food safety (see Table 5-1 for details).

3) Establishment of a risk assessment and management system for food contaminants: Since August 2005, a mechanism has been set up to hold regular meetings with vice chairpersons the Council of Agriculture and the Environmental Protection Administration, both of the Executive Yuan, to integrate cross-ministerial resources, and to resolve issues concerned in time. Focusing on the management of environmental pollution and food safety at the sources of production, a set of management procedures for the reporting and response to environmental protection and food safety has been formulated. A task force coordination is also established.

4) Management of the "black-heart foods": To counterattack black-heart foods, in addition to classification, inspection and seizure, a special line, 0800-825748, has been set up for consumers to report. A special project for the inspection of food safety cross-county has been promoted. Publicity is intensified to educate the public on how to distinguish black-heart foods. The Food Sanitation Management Act is amended.

5) Fishery product industries are encouraged to practice the food safety control system. The second-stage inspections focusing on frozen fishery products have been conducted for 36 dealers.

6) Safety management of food industries: A Good Food Hygiene Practice is announced to generally promote the self-control by food industries, to improve the professional knowledge of the management personnel of health agencies, to supervise food industries to establish a self-control system, and thus to enhance their self-control capabilities and to attain the goal of controlling

food production at the sources of production. To encourage industries to establish the self-control system, the Department has also helped in the promotion of a non-mandatory GMP and CAS certification system so that the self-control capabilities of food industries can be enhanced indirectly through market mechanism.

7) Establishment of a food traceability system: Acting upon the concept of management at the source, supervision and management of the food distribution industries have been promoted to assure the sanitary quality control of foods in the process from production, manufacturing, transportation, sales to the hands of the consumers to protect the consumers of the sanitation of foods. The ROC CAS Agricultural Product Development Institute has been commissioned to conduct the sanitary assessment of the food distribution industries, focusing primarily on shopping malls. In total, 87 have participated in the assessment, and 85 have been qualified, giving a qualifying rate of 97%. Names of qualified malls and information concerning the procurement, consumption and storage of low-temperature foods are posted on the website of the Department, (http://food.doh.gov.tw)

8) Management of genetically modified food products: Mandatory labeling of the genetically modified food products has been practiced in three stages step by step and according to the extent of processing. Thus far, 12 applications for permit for genetically modified soybeans and corn have been reviewed and approved.

9) Monitoring mechanism for food poisoning incidents: In 2005, there had been 247 food poisoning incidents, affecting 3,530 victims, with one death. The number of incidents had decreased by 27 as compared to the 274 incidents of food poisoning in 2004; the number of victims affected had also declined by 462 (11.6%) as compared to the 3,992 cases of 2004. By pathogenic agents, 96 incidents are identified of their pathogenic agents, giving an identification rate of 38.9% (see Figure 5-1). By the site of food intake, most incidents, 102 incidents accounting for 41.3% of all, occurred at food supply business sites; 54 incidents (21.9%) occurred in schools; and 33 (13.4%) and 19 (7.7%) occurred at home or offices, respectively (see Figure 5-2).

3. Safety Monitoring Mechanism

To safeguard the safety of drug use and food consumption, to function as a gatekeeper for the public, the Department has made all efforts in the inspection and seizure of illegal foods and drugs, set up mail-boxes and toll-free telephone lines for reporting, and established a safety monitoring system to stop the rampage and hazards of illegal foods and drugs.

1) On September 9, 2004, a set of Regulations Governing Management of the Pharmacovigilance Monitoring was announced to risk management. Currently, 635 drugs are monitored under the

Figure 5-1 Food-borne Disease Outbreaks by Bacterial Origin

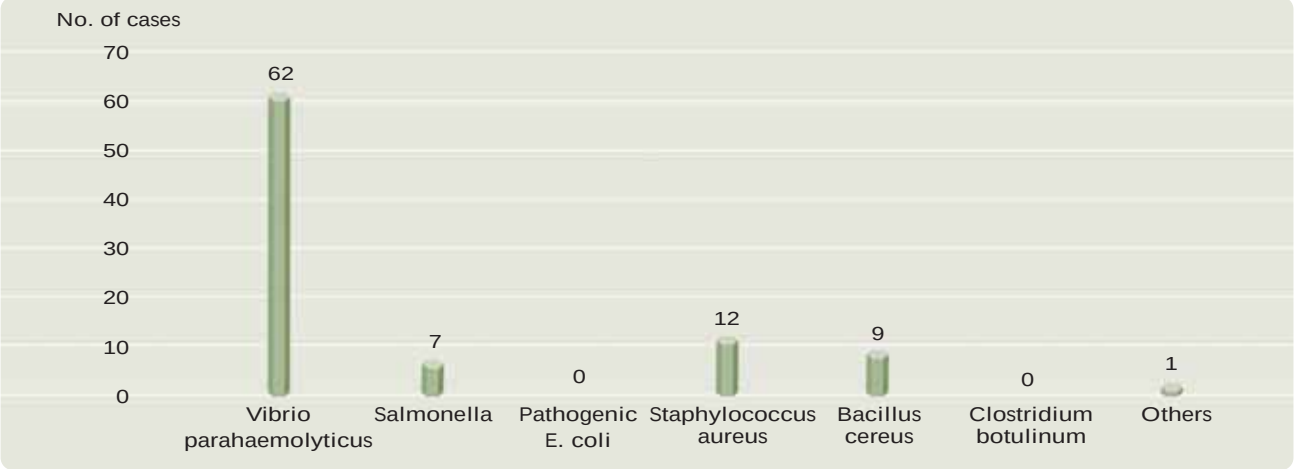
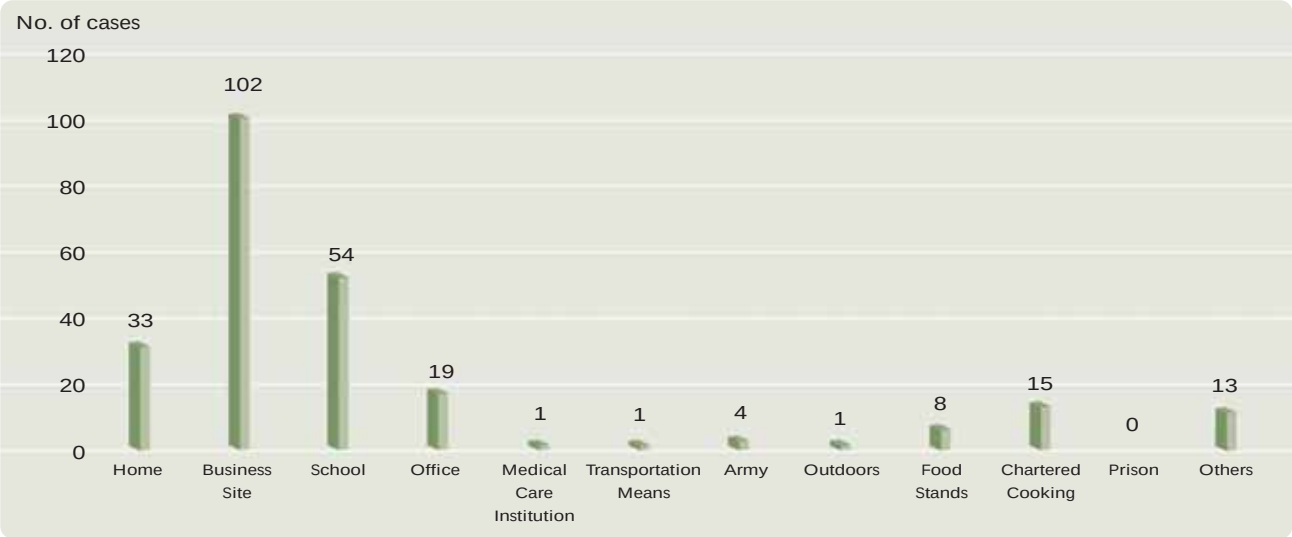


Figure 5-2 Food-borne Disease by Eating Places



regulations. Drug companies concerned are required to submit the periodic safety updated reports (PSUR) to the Department in accordance with regulations.

2) A national online reporting system for adverse drug reaction (ADRs) and a national center for the reporting of ADRs have been established. By the end of 2005, 12,615 reports on post-marketing drugs, 3,881 PSURs and 13,322 reports on serious adverse event (SAEs) on drugs in clinical trials had been received. On August 31, 2005, a set of Regulations Governing Reporting of Adverse Drug Reactions was announced; a drug safety monitoring website (Phamacovigilance in Taiwan;http://adr.doh. gov.tw) has been set up; and a quarterly newsletter on drug safety has been issued.

3) A National Drug Identification System has been set up to establish drug identification codes for domestic drug dealers and manufacturers, to construct a databank of instructions on drug use, to compile a manual for the identification of drugs from appearance, and to establish an online inquiry system. The professionals and the public are thus provided in pluralistic ways with information for the identification of drugs and for inquires about names of drugs.

4) Registration and market approval is conducted to assure the safe use of drugs:

(1) Registration and market approval of medical devices: With reference to the international regulatory trend, it was required on June 20, 2005, that all medical devices shall be included in the registration and market approval. They cannot be imported, manufactured or sold unless a permit license is issued. For items that no permit license was required previously, if applications for registration and market approval were made prior to June 20, 2005, they will be granted a six-month grace period. Thus far, 9,633 applications have been received and 6,965 permit licenses have been issued.

(2) Registration and market approval for foods:

a) The management of food safety is not done primarily by pre-marketing approval and licensing. However, a system of pre-marketing approval management is necessary for some foods of relatively high safety concerns. In accordance with regulations of Article 14 of the Food Sanitation Control Act, announcement has been made that food additives for single ingredient item, and imported foods in tablet and capsule forms may not be manufactured, processed, prepared, repacked, imported or exported without being inspected, registered and permit license issued. Thus far, 497 applications for

the registration and market approval of food additives and 3,047 for foods in tablet and capsule forms have been processed.

b) In accordance with regulations of the Health Food Management Act, health foods may not be manufactured, imported, or labeled or advertised as health foods, or emphasized as having health promotion functions, unless they are inspected, registered and approved. In 2005, 22 items had been approved as health foods.

(3) Research and development of new Chinese medicines is encouraged. The first permit license for a new domestically developed Chinese medicine qualified by IND and NDA was issued on March 30 2006. This fact indicates that Taiwan is capable of developing new drugs, and that the review of Chinese medicines in Taiwan is highly scientific. It is a new era in the development of Chinese herbal medicines.

5) A cross-ministerial special project meeting to fight against illegal drugs has been set up. County/city health bureaus are required to implement a special project on the inspection and seizure of illegal drugs, cosmetics and foods. Operational procedures for the inspection and management of mobile drug dealers, management of the illegal sales of drugs on websites, and operational procedures for the inspection and management of illegal drugs have been formulated to improve the efficiency and effects of inspections. A mail-box on website, (drug@doh.gov.tw) and a telephone line for reporting, 0800-058828, are set up.

6) Joint inspections:

(1) Cross-regional joint inspections are promoted. In the period July to December 2005, 431 cases of drugs and cosmetics violating regulations had been found; 189 cases had been penalized; and 63 cases suspected of counterfeit and prohibited drugs had been forwarded to the prosecutor's offices. In addition, 95 illegal Chinese medicine dealers, and 228 illegal Chinese medicines have been found and processed according to laws.

(2) An all-out monitoring of illegal advertisements by citizens has been promoted. In total, 193 illegal advertisements for drugs and cosmetics, 743 for foods, and 689 for Chinese medicines have been reported. They are forwarded to local health bureaus for processing.

4. Good Manufacturing and International Mutual Recognition

To improve the drug review system, to upgrade the quality of domestic pharmaceutical products and to strengthen their international competitiveness, good manufacturing practice and international mutual recognition have been actively promoted.

1) Effort has been made to continue to promote the pharmaceutical good manufacturing practice (GMP). Thus far, 168 domestic pharmaceutical plants have completed the first-stage cGMP validation; 162 the second-stage validation; and 156 the third-stage validation. In addition, 800 foreign pharmaceutical import plants have completed assessment for the second-stage cGMP validation; 1,012 have applied for the second-stage validation review, of them, 736 have passed the review.

2) The conventional Chinese medicine manufacturers are promoted and supervised to universally implement GMP. Since September 30, all of them are required to implement GMP. Thus far, 32 plants have successfully transformed; and 82 have commissioned out manufacturing. In total, 102 Chinese medicine manufacturers are practicing GMP.

3) Assessment of the GMP of medical devices is continued. 337 domestic medical device manufacturers have been registered; and the QSD registration for imported medical devices has been made for 2,516 factory-times. In coordination with the Ministry of Economic Affairs, an exchange of letter on medical devices has been signed with the EU to facilitate international harmonization and mutual recognition in the management of medical devices.

4) 13 hospitals have been subsidized to set up clinical trial centers for Chinese medicines; and 11 of them have been inspected. They are all qualified to conduct clinical trials of Chinese

medicines. Regulations concerning clinical trials and infrastructures have been formed to promote standards and to link with the international community.

Section 2. Management of Controlled Drugs

Statistics of the United Nations (UNODCCP , 2003) shows that the current population world-wide of drug abusers is as many as 200 million, accounting for about 3.4% of the world population. If the population under 15 years of age is excluded, the number of drug abusers will account for 4.7% of the world population. Marijuana is the most abused drug internationally by some 162.8 million people. Amphetamines are the next. Opium, cocaine and heroin are the third, fourth and fifth most abused drugs. Drug abuse has thus become a global problem. In the recent years, emerging drugs (or the so-called party-drugs) have run rampant, suggesting the importance of the management and control of controlled drugs.

1. Management Systems of Controlled Drugs

The aims of the control of controlled drugs are to understand the flow of controlled drugs in the country, to establish management systems for controlled drugs, to manage controlled drugs by level, and to license for management.

1) Classification management of controlled drugs by level: Controlled drugs are, by their potential for habitual use, dependency, abuse and danger to the society, classified into four schedules for management. Amineptine is announced a schedul ¢″controlled drug; and 2C-B, 4-bromo-2, 5-dimethoxyphenethylamine, a schedul ¢» controlled drug.

2) Establishment of a management system for the flow of controlled drugs: The licensing system is practiced. Businesses or institutions concerned must apply for registration licenses of controlled drugs before the drugs can be imported, exported, manufactured, sold and purchased. Thus far, 12,312 registration licenses, 1,936 permits for import/export, production, or research, and 34,673 prescription licenses for controlled drugs have been issued (see Table 5-2).

3) Auditing and inspection of controlled drugs:

(1) Routine auditing: Acting on the annual plan of the Department, local health bureaus make own arrangements for routine auditing.

(2) Priority auditing: Auditing is conducted jointly with local health bureaus according to the degree of abuse, unusual amount of consumption, or reporting of illegal use.

(3) Judicial auditing: Auditing is conducted in collaboration with prosecution, police and investigation authorities.

(4) Joint auditing: Auditing is conducted jointly with local health bureaus following the Special Project on the Joint Auditing of Illegal Drugs, Cosmetics and Foods of the Department.

(5) The Internet auditing: Advertisements on the Internet selling controlled drugs or toxic substances are audited. Violations are referred to the police authorities for investigation and action.

(6) Reporting and auditing of the flow of controlled drugs: The Internet media are used for the reporting of the balance of controlled drugs. Thus far, 38.88% of institutions and 89.61% of dealers are using the media for reporting. Data of reporting by documents are stored in computers to check the flow. Inspections are

Table 5-2 No. of Prescription Licence Issued for Controlled Drugs, 2005

Professional Category	No. Issued	No. of Practicing Professionals	% Issued
Physicians	34,498	30,845	89
Dentists	10,272	2,333	23
Veterinarians	2,974	7,304	44
Assistant Veterinarians	405	191	47
Total	48,149	34,673	72

strengthened against unusual flows. In total, 18,164 firm-times have been audited to find 186 violations, at a violation rate of 1.02%. They have been processed accordingly to prevent and stop the use for other purposes or abuse of controlled drugs.

4) An information system, (http://www.nbcd.gov.tw/company/SA21100.asp) is established to present information on the major ingredients of controlled drugs manufactured and sold, their indications, effective dates, prices, external appearances, and packing for the query of buyers. Procedures of procurement applications, time required for processing and amount authorized for each year are also presented for inquires to enable buyers of controlled drugs to access to information on procurement.

2. Prevention and Control of Drug Abuse

In the recent years, drugs have become more diversified. In addition to heroin and amphetamines, there have been many emerging abuse substances, medicines for medical use such as MDMA, LSD, Psilocybine, Erimin, Ketamine and FM2 that have become substitutes. To strengthen the prevention and control of emerging drugs, a reporting system has been established, and more diversified educational programs have been intensified to urge the public to value life, to refuse toxic substances, and thus to alleviate hazards of drug abuse.

1) To enforce prevention and control of the abuse of emerging drugs, a four-year plan to prevent and control the demands for emerging abuse substances has been formulated. The plan focuses on five areas: to construct a control mechanism against emerging drugs, to establish effective toxicity assessment criteria for emerging drugs, to build a national investigation mechanism for illegal use of drugs, to develop laboratory testing methods for emerging drugs and their metabolism, and to enhance international cooperation.

2) A system on the reporting of drug abuse has been established to present a more comprehensive and current situation of drug abuse. Thus far, 107 medical care institutions have joined in the reporting, an increase of 20 institutions over the previous year. In total, 12,872 cases have been reported. Reports on the abuse of controlled drugs and seizures of toxic substances are compiled for each month in one volume, Statistics on Cases of Drug Abuse and Laboratory Testing, for the reference of organizations concerned.

3) New anti-drug strategies have been formulated. The year 2005 was made National Anti-Drug Combat Year. The Ministry of Justice is made to chair the cross-ministerial anti-drug committee to urge ministries and departments concerned to boost control actions. The Department is primarily responsible for prevention to reduce hazards of toxic substances, and to prevent the transmission of communicable diseases through the shared use of needles and syringes.

4) Seed teachers for the prevention and control of drug abuse have been trained. 293 community-based drug abuse counseling stations have been set up to provide the public with counseling on drug abuse. An online learning program on hazards and control of some commonly abused drugs, http://elearning. hrd.gov.tw/TrainingASP3, has been developed jointly with the local training centers of the Central Personnel Administration, the Executive Yuan, to upgrade the effects of drug control.

5) Diversified programs on drug control have been conducted. An Anti-Drug Resource Online Museum is set up. Large-scale national surveys on the current status of drug abuse, and cross-country, cross-city epidemiological studies on emerging toxic substances have been conducted.

Section 3. Laboratory Testing for Drugs, Foods and Cosmetics

Laboratory testing covers testing of pharmaceutical products, active pharmaceutical ingredients, biological products, medical devices, foods, food additives, food utensils, containers, packing, food detergents and medicated cosmetics. Laboratory testing for drugs, foods, and cosmetics are conducted at both the national and the local levels. The Bureau of Food and Drug Analysis is responsible for the national laboratory services with more emphasis on the building of quality of laboratory

testing including the development of new testing methods, research, and promotion of good laboratory practices (GLP). The Bureau in addition to the routine administrative testing of all drugs and some foods, also provides supportive services in laboratory testing. Local laboratory testing is provided by laboratories of county/city health bureaus primarily for the testing of some food samples collected on inspections for food sanitation

1. Laboratory Testing

Laboratory testing for foods and drugs conducted by the Department includes, in addition to items necessary for the implementation of the programs of the Department, routine laboratory testing in support of county/city health bureaus and other organizations (institutions), and testing of surveys to monitor the quality and safety of products sold on market. Pharmaceutical products, medical devices, medicated cosmetics, Chinese medicines, raw materials and their preparations, pesticide and veterinary drug residues in foods, residues of drugs for animal use, chemical contaminants, microbes and their toxins, antibiotics, allergens, adulterated medicines and genetically modified food products are laboratory-tested by the Bureau of Food and Drug Analysis.

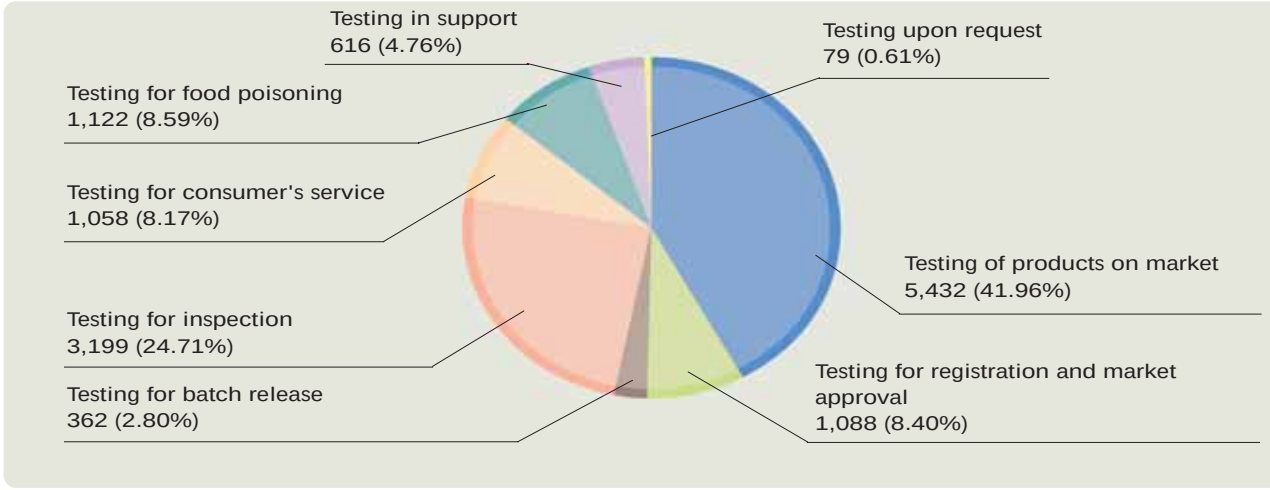
1) Administrative testings: testing is conducted for registration and market approval, and issuance of permit licenses for pharmaceuticals, medicated cosmetics, medical devices, health foods, genetically modified foods, and food additives, batch release of influenza vaccines, vaccines, blood products, botulism and others. There is also testing conducted for emergency incidents such as contamination of infant formulas, malachite green residue in fish, adulteration of animal ingredients in vegetarian-labeled food products.
2) Supervisory testing: testing is conducted for public health inspection samples, consumer protection service, and laboratory testing for food-borne outbreaks.
3) Supportive testings: testing is conducted upon request by other government authorities, such as the customs authorities to levy tax on imported goods, manufacturers for certificate of products for export; assistance to judicial courts, prosecution, police, customs authorities for the testing of drugs or foods confiscated as evidence.
4) In 2005, 1,088 cases for registration and market approval, 362 cases for batch release, 3,199 cases for inspection sample in support of health bureaus, 1,058 cases for consumers' service, 1,112 specimens of food poisoning incidents, 616 cases in support of other organizations, and 79 cases upon request had been completed (see Figure 5-3).

2. Quality of Laboratory Testing

To build a strict and efficient quality of laboratory testing, work has been done to conduct testing of products on market, develop new testing methods, and improve testing capacity of county/city health bureaus. The achievements are as follows.

1) Survey, assessment and testing of products on market: 28 survey programs on marketed products such as monitoring of pesticide residues in vegetables and fruits from packers have been conducted. 5,432 samlpes have been tested; and survey results of 11 of them have been released to the media and also posted on the website, http://www.nlfd.gov.tw, to make dealers and manufacturers become more responsible for their products, and also for the reference of consumers to protect their rights.
2) Promotion of the Good Laboratory Practice (GLP): The Bureau is vigorously promoting the GLP system to upgrade the quality of testing. The quality manual and system documents were announced in July 2001. In May 2002, the Taiwan Accreditation Foundation (TAF) laboratory accreditation was achieved. In coordination with the government policy of joining the World Trade Organization, local health bureaus have been supervised to set up the GLP system. 25 health bureaus have been accredited by the TAF. Nine contracted laboratories for food sanitation have been approved by the Department.
3) Development of new laboratory testing methods and scientific research: 31 papers on relevant testing methods have been published. In addition, review standards for 20 items of medical devices have been drafted; 13 official testing methods for foods, and seven items on minimum requirements

Figure 5-3 Types of Laboratory Testing and No. of Specimens



for biological products have been published. Research projects on the systematical study of drugs impurities, preparation of HBsAg testing sensitivity panel, determination of aristolochic acid in Asari Herba and its preparations by LC/MS/MS, monitoring of the background value of dioxin in food and human blood in Taiwan, and study on the detection method and monitoring of GMF have been conducted.

4) Supervision of county/city health bureaus: Local health bureaus have been supervised to improve their laboratory testing competency and capacities. Investigations of products on market are presented at workshops to improve the skills and capabilities of manufacturers and competency of local inspectors. Workshops to demonstrate testing of genetically modified food products for labeling control, and testing and management of adulterated food were organized for some 240 participants in 2005.

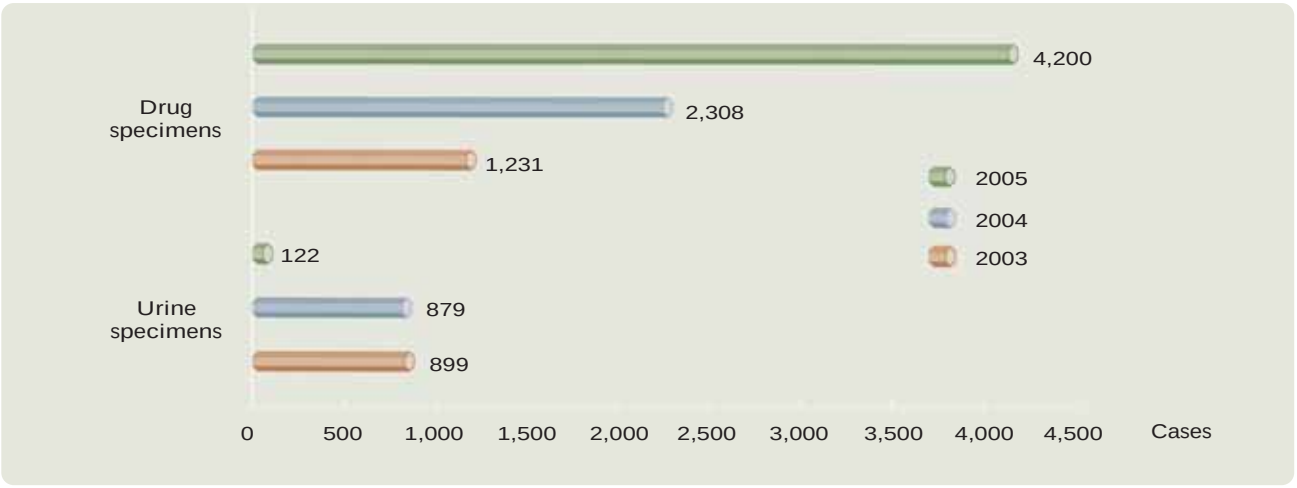
3. Laboratory Testing for Drug Abuse

To improve quality of laboratory testing for drug abuse, and to speed up testing, a laboratory testing system for drug abuse has been set up. Major activities are:

1) Laboratory testing for controlled drugs and re-testing of urine specimens have been conducted by the Department. Assistance is given to the prosecution, police and judicial authorities in the testing of specimens referred by them. In total, 4,322 specimens suspected of toxic substances or controlled drugs have been tested. Most of them are cases of toxic substances, increased by 35.6% over the 3,187 cases of 2004. Of them, 122 cases are urine specimens, and 4,200 non urine specimens. In urine specimens, morphine, and morphine and codeine together are detected in most cases; methamphetamine the next. In the non urine specimens, methamphetamines are detected the most; MDMA the next; and Ketamine the third (see Figure 5-4).

2) Analytical technology improvement in the testing of drugs in urines has been improved. Information on the trend of drug abuse in country, and certification specifications of international standards organizations for drug abuse have been collected for the timely amendment of the regulations governing the accreditation and management of drug abuse urine testing and medical institutions. Standards Governing Drug Abuse Urine Testing Laboratories Established by Government Agencies, and Regulations Governing Drug Abuse Urine Testing Operations, were announced. On October 12, 2005, Article 18 of the operational principles on the laboratory testing of urines for abused drugs was amended to allow laboratories without to use liquid chromatography-mass spectrometry method for testing when no gas chromatography-mass spectrometry method is available . Adequate cut-off values are set accordingly.

Figure 5-4 No. of Toxic Substances or Controlled Drugs Specimens Submitted for Laboratory Testing



3) Acting in accordance with regulations of Article 33-1 of the Narcotics Hazard Control Act, technical standards and accreditation regulations for the urine testing of abused drugs have been formulated. Laboratories are assessed onsite and performance tested regularly by the Department to assure their testing quality. Thus far, 13 laboratories have passed the accreditation of the Department to provide laboratory testing services for the urine testing of abused drugs such as methamphetamine, amphetamine, MDMA, MDA, morphine, codeine and marijuana. In 2005, some 153,100 urine specimens were tested, accounting for 91.2% of all urine specimens tested.

Section 4. Management of Special Medicines

Patients of rare diseases are medically and pharmaceutically of the less privileged groups; together with the hazards of the emerging communicable diseases, the Department has actively promoted the management of orphan drugs and the development and manufacturing of various biological preparations. In addition, to provide relief to victims who have suffered harms from the normal use of legal drugs, the Department is also promoting relief for drug hazards.

1. Management of Orphan Drugs

Since the implementation of the Rare Disease Control and Orphan Drug Act in August 2000, through the joint efforts of the government and the private sectors, the control of rare diseases has made some progress. Action has been taken to approve medicines required for the treatment of rare diseases, to strengthen medical care for patients of rare diseases, and to bring attention to all circles the issues of rare diseases. Since the implementation of the Act, the Department has announced 128 rare diseases and 148 orphan drugs for their treatment.

To strengthen the functions of the supply center for orphan drugs, the center, in addition to the supply of drugs on emergency basis, is also made responsible for training and education, and also for the integration of resources. In early 2005, the Rare Disease Control and Orphan Drug Act was amended to supplement regulations concerning the supply and manufacturing of special dietary foods for rare diseases to provide more comprehensive life care to patients of rare diseases. In the future, education on the prevention and control of rare diseases will be intensified; and social welfare policies for patients of rare diseases will be more vigorously promoted.

2. Development and Manufacturing of Serum Vaccines

For innovation, intellectual property rights and exclusive rights to market, action has been taken to develop domestic bio-technology industries, to promote the science and development, and

manufacturing of bio-technologies to upgrade international competitiveness.

1) Manufacturing, testing and development of bio-products
   (1) 1,190,700 doses of frozen dried BCG vaccines, 53,755 doses of cholera vaccine, 535,590 doses of absorbent tetanus-diphtheria combined toxoid (for adults), 39,690 doses of absorbent diphtheria-tetanus combined toxoid, 1,814,200 doses of alum-precipitated tetanus toxoid, 1,807 does of lyophized bivalent antivenin of *Tr.Mucrosquamatus*, and 3,558 doses of Bivalent Antivenin of *B.multicinctus* and *N.naja* art Lyophilized have been produced.
   (2) Factory inspections for the third stage cGMP have been completed.
   (3) Testing of bio-products has been done for 22 batches of products, 86 batches of raw fluids, 151 batches of raw materials and 43 batches of materials.
   (4) Eight patients have gone through clinical trials for antivenin *of daborla ruseilli siamensis*, and the cure rate is 100%. The bio-product in question is currently applying for permit license through registration and market approval.
2) Authorization, cooperation and transfer of bio-product manufacturing techniques
   (1) In collaboration with the Adimmune Corporation, technical transfer has been made for two products, absorbent diphtheria-tetanus combined toxoid and absorbent tetanus-diphtheria combined toxoid for adult use. In November 2005, a contract on cooperation in the development and research of Japanese encephalitis vaccines cellular culture manufacturing techniques was signed.
   (2) In collaboration with the Corporate National Health Research Institutes, training on the transfer of manufacturing techniques for bio-products has been conducted. Personnel of the Institutes have received training at the BCG vaccine, tetanus and diphtheria vaccine manufacturing zones, and also training in BCG, snake venom and microbiological testing.
3) Research and development of bio-products
   (1) Improvement of the manufacturing process of enterovirus 71 and analysis of their specific immunological features have been completed.
   (2) Duck eggs are used instead to manufacture Bivalent Antivenin of *B.multicinctus* and *N.naja art Lyophilized*. Some 15% and 75% savings in cost have been attained.
   (3) To meet outbreaks of the novel influenza, snow martens for experimental use have been brought in to help produce one strain of indigenous type A influenza antibody. Cooperation in the science and development of vaccines for the novel influenza is made.
   (4) The real-time PCR technique is used to analyze the potency of BCG vaccines, to establish standard curves for the testing of BCG 16SrRNA QPCR. The effective range is 4 x 105 cells. The growth differences of BCG are also tested.
4) Tamiflu is thus far the only internationally recognized effective medicine against novel influenza. The market, however, is running wild. For self-manufacturing, the Department placed on October 31, 2005, to the Intellectual Property Bureau of the Ministry of Economic Affairs, application for the patent rights of Tamiflu. The application was approved by the Bureau on November 25, and mass production of the medicine is underway.

3. Relief for Drug Hazards

To provide the public with a comprehensive and all-inclusive drug hazards relief system, the Department announced on October 12, 1998, a set of guidelines on drug hazards relief. The set of guidelines was implemented on January 12, 1999. People who have properly used medicines approved by the Department, and who, for personal physical differences or due to unforeseeable factors in the process of scientific development, have developed hazards of the medicines are entitled to prompt relief.

To make the drug hazards relief system more all-inclusive, and to provide victims of hazards as a result of the proper use of legal medicines with timely relief, the Drug Hazards Relief Act was announced for implementation on May 31, 2000. Thus far, 507 cases have been reviewed; of them, 214 are determined to be applicable to the drug hazards relief system, giving a payment rate of 42.21%, and a total amount of NT$ 82 million.