The Life Sciences Law Review

Fifth Edition

Editor
Richard Kingham

Law Business Research

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EDITOR'S PREFACE

The fifth edition of *The Life Sciences Law Review* covers a total of 37 jurisdictions, providing an overview of legal requirements of interest to pharmaceutical, biotechnology and medical device companies. The chapters are arranged to describe requirements throughout the life cycle of a regulated product, from discovery to clinical trials, the marketing authorisation process and post-approval controls. Certain other legal matters of special interest to manufacturers of medical products – including administrative remedies, pricing and reimbursement, competition law, special liability regimes and commercial transactions – are also covered. Finally, there is a special chapter on international harmonisation, which is of increasing importance in many of the regulatory systems that are described in the national chapters.

Now, more than ever, it is important for leaders in the pharmaceutical and medical device industries and their advisers to be knowledgeable about the laws and regulations in major jurisdictions around the world. In the past year, there have been significant developments in the regulation of drugs and medical devices, especially in the United States, where a new law – the 21st Century Cures Act – was passed at the end of 2016. There are prospects for further developments in the coming year. The new president and the Republican-controlled Congress will consider legislative measures affecting the pharmaceutical and medical device sectors, including proposed repeal of the Affordable Care Act, continuing inquiries into pricing of medical products and reauthorisation of user fee laws that fund a substantial part of the drug and device approval processes. The United Kingdom will initiate formal proceedings to begin the process of withdrawing from the European Union, with potential consequences for the medical products sectors. Other jurisdictions, including China and India, are considering reforms to their regulatory systems for medicinal products.

Each of the chapters has been written by leading experts within the relevant jurisdiction. They are an impressive group, and it is a pleasure to be associated with them in the preparation of this annual publication.

Richard Kingham
Covington & Burling LLP
Washington, DC
March 2017

Chapter 33

TAIWAN

Katherine YC Juang, Jill Niu and Daisy Wang[1]

I INTRODUCTION

The Taiwanese government places great importance on the life sciences sector with the aim of developing it. Although there is an abundance of laws and regulations governing this sector, such as the Rare Disease Prevention and Medicaments Act, which deals with orphan drugs, the most important law is the Pharmaceutical Affairs Act (PAA). The government strictly scrutinises relevant industries and business operations and often takes a conservative stand on borderline cases to ensure the protection of the public. The Ministry of Health and Welfare (MoHW) (which, before the government reform of 23 July 2013, was known as the Department of Health (DoH)) is the competent central authority that governs all health-related matters, such as foods, cosmetics, medicines, medical devices and national health insurance (NHI). In 2010, the Bureau of Medical Affairs (the Bureau), which used to be the agency handling matters related to medicines and medical devices under the DoH, and the Bureau of Sanitation merged to form the Taiwan Food and Drug Administration (TFDA) to centralise and strengthen regulatory enforcement; after the government reform of July 2013, the TFDA remains a sub-agency of the MoHW. Although the MoHW is the competent central authority, the enforcement of all health-related laws and regulations and the issuance of all licences, permits and authorisations in the name of the MoHW are handled by the TFDA.

II THE REGULATORY REGIME

The PAA provides the basic structure for the regulation of medicines and medical devices, and the MoHW has promulgated more than 100 subordinate regulations, guidelines and standards to clarify the implementation of the PAA.

1 Katherine YC Juang is an associate partner, Jill Niu is a partner and Daisy Wang is a senior counsellor at Lee and Li, Attorneys-at-Law.

i Classification

Medicines and medical devices are both regulated by the PAA. The PAA provides definitions for medicines and medical devices (jointly, 'medicaments'), to define the scope of its application. Under the PAA, 'medicines' are restricted to raw materials and preparations of any of the following:

a medicines used in diagnosing, curing, alleviating and preventing the diseases of human beings regardless of whether they are listed in the pharmacopoeia, listed by the PAA or recognised by the MoHW;

b other medicines capable of sufficiently affecting the body and physiological functions of human beings; and

c medicines used in preparing the above-mentioned medicines.

In general, 'medical devices' cover instruments, machines, and apparatuses and their accessories, fittings and parts, used in diagnosing, curing, alleviating and directly preventing diseases of human beings or that may affect the body or functions of human beings. Owing to the different characteristics of medicines and medical devices, the TFDA intends to establish a separate set of statutes for medical devices and proposed a draft Medical Devices Act in early 2015, wherein different levels of administrative and advertisement requirements are provided in more detail depending on the risk classification of the medical devices.[2] Several meetings have been held by the TFDA in 2016 to gather comments from the public. It is still too early to tell when the bill will be finalised within the TFDA and be submitted to the legislative body for legislation process.

Cosmetics and cosmeceutical products, such as cosmetics containing medical or poisonous ingredients, are regulated by the Statute for Control of Cosmetic Hygiene. For cosmeceutical products, the MoHW has promulgated the Standards for Cosmeceuticals, which lists ingredients permitted to be used in cosmetics. The Supreme Court has ruled that if a cosmetics product contains a medical ingredient listed in the aforementioned Standards, the Statute for Control of Cosmetic Hygiene should be considered; however, if the ingredient is not listed, the PAA should be considered. Similarly, although foods and food additives are regulated by the Food Safety and Sanitation Control Act and health food is regulated by the Health Food Control Act, if a medical ingredient contained within foods, food additives or health food products is not listed as a permitted ingredient for food products as published by the MoHW, the PAA needs to be considered. Since the MoHW is the sole competent central authority of the PAA, the Statute for Control of Cosmetic Hygiene, the Food Safety and Sanitation Control Act and the Health Food Control Act, regardless of which is the applicable law, all cases will be reviewed by the MoHW, which will determine the necessary classification.

With respect to chemicals, toxic chemicals are regulated by the Toxic Chemical Substances Control Act, with the Environmental Protection Administration as the competent central authority, while precursor chemicals are regulated by the Narcotics Prevention and Control Act and the Categories and Regulations Governing Inspection and Declaration of Industrial Precursor Chemicals, with the MoHW and the Industrial Development Bureau as the competent central authorities, depending on whether such chemicals are manufactured for medical or industrial products. There are no borderline cases at the moment.

2 See more classification details in Section II. v, *infra*.

ii Non-clinical studies

Currently, there are only two Taiwanese regulations related to non-clinical studies: the Good Laboratory Practice for Non-clinical Laboratory Studies (GLP) and the Guideline for the Non-clinical Pharmacology/Toxicology Studies for Medicinal Products Applications (the Guidelines) amended by the MoHW in March 2006 and June 2000, respectively. As indicated in their respective prefaces, the GLP and the Guidelines were drafted by the MoHW by referring to the Good Laboratory Practice for Non-clinical Laboratory Studies promulgated by the United States FDA and other relevant regulations or guidelines of the International Conference on Harmonisation, the OECD and other developed countries. Hence, the GLP and the Guidelines are generally in line with, and cover all of the provisions stipulated in, international practice, excluding toxicokinetics studies.

iii Clinical trials

For clinical trials conducted to obtain marketing authorisation of medicaments, the PAA and its subordinate Guidelines for Good Clinical Practice (GCP), promulgated by the MoHW, need to be considered. For human trials initiated and conducted by teaching hospitals or healthcare institutions, for the purpose of improving medical care or preventing diseases, the Medical Care Act (MCA) and its subordinate Regulations on Human Trials (RHT) need to be considered. While there have been no clear regulations governing other types of trials, the Human Subjects Research Act (HSRA) was enacted in December 2011 to provide general regulations on research (including trials) involving human subjects. In light of this development, all clinical trials and human research should comply with the HSRA, unless the GCP prevails when conducting clinical trials for medicaments registration purposes or the MCA prevails when conducting human trials as the GCP and the MCA are special laws of the HSRA.

In general, approval from an institutional review board or ethics committee and informed consent of the subjects are required prior to conducting any research involving human subjects, unless exempted by the MoHW. As for clinical trials under the PAA and human trials under the MCA, approval from the MoHW or TFDA and research institutional review board or ethics committee and informed consent from subjects are mandatory requirements. Where a pharmaceutical firm acting as a sponsor engages an institution and an investigator to conduct clinical trials under the GCP, a clinical trial agreement (CTA) must be executed and any financial support from the sponsor needs to be specified therein. It is also required under the GCP that the sponsor should be responsible for compensation and insurance for injuries inflicted on the human subjects; however, the institutions and investigators do not have such responsibility and local insurance companies do not provide such insurance services to the institutions and investigators. Therefore, allocation of liability between institutions or investigators and sponsors will be determined solely on the terms of the CTAs. Although the GCP does not stipulate that the sponsor must be established in Taiwan, in practice, local hospitals prefer to enter into CTAs with sponsors or their clinical research organisations (CRO) established in Taiwan to ensure that, in the case of legal dispute, they can claim against local entities. Safety reporting requirements and mechanisms have also been established to ensure the protection of human subjects' safety and to ensure that a trial could be terminated as soon as the study is no longer deemed safe. Since there are no special laws or regulations governing investigator-initiated studies, the GCP should be applicable; for example, an investigator should assume the sponsor's responsibility as set out in the GCP and a CTA must be executed to specify financial support from a pharmaceutical firm, if any.

iv Named-patient and compassionate use procedures

A teaching hospital may treat seriously ill patients with medicaments not yet registered with or approved by the MoHW if they are a project of import medicaments. An application must first pass the internal review of the institutional review board or ethics committee of the applying teaching hospital. In such application to the MoHW, the teaching hospital should submit the ethics committee's approval, medical literature regarding treatment, patient's consent and documents evidencing that such medicaments have obtained marketing authorisation from the competent sanitation authority of the country where the medicaments are manufactured. While the legal basis of the above project of import is provided in certain administrative rules, Article 48–2 was added to the amendments to the PAA, effective on 2 December 2015 (PAA 2015) to provide a higher-ranking legal basis for such project of import.

In addition, pursuant to the Rare Disease Prevention and Medicaments Act, projects to import rare-disease medicaments that have not been registered with or approved by the MoHW may also be applied for by government agencies, healthcare institutions, patients with rare diseases or their relatives, and relevant foundations or associations. The documents required for submission to the MoHW are similar to those mentioned above: the patients' consent, a treatment plan issued by a healthcare institution, documents evidencing that such medicaments have obtained marketing authorisation from the competent sanitation authority of the country where the medicaments are manufactured and safety and effect data.

After the project of import application is approved by the MoHW, the imported medicaments should be labelled 'sample' and are not for sale. Therefore, teaching hospitals may not charge their patients for the costs of the medicaments. If the applicant is an individual, entity, agency, or institution, he or she may apply for reimbursement from the MoHW for 80 to 100 per cent of the costs.

v Pre-market clearance

The Regulations for Registration of Medicines (RRM), the Regulations for Registration of Medical Devices (RMD), the Regulations for Registration of Botanical Medicines (RBM, promulgated in April 2013), the Regulations for Registration of Biosimilars Products (RRB, promulgated in June 2015), and the Regulations for Registration of Biosimilar Monoclonal Antibody Products (RRMA, promulgated in September 2013 and amended in December 2015) provide application procedures for the registration and marketing authorisation of medicines, medical devices, botanical medicines, biosimilar products in general, and biosimilar monoclonal antibody, respectively. In general, applicants of new chemical entity (NCE) medicines would need to submit relevant information and data relating to, *inter alia*: clinical trials; formulation basis; testing specifications; methods and certificates of analysis of raw materials and finished products; and manufacturing records. The RRM was constantly amended to simplify the procedures or to relax the application requirements for registering drugs, and was last amended in April 2016. One of the most important changes is that a post-marketing risk management plan (RMP) becomes a requirement when filing the application so as to ensure the applicant manages risk after marketing authorisation is granted. As for medical devices, they are subdivided into the three classes of the RMD: Classes 1, 2 and 3. While registration of Class 1 medical devices merely involves simple paper review, registration of Classes 2 and 3 medical devices requires submission of detailed documents, particularly the free-sale certificate and clinical trials data. The RMD was comprehensively amended in September 2014 to restructure the provisions, to simplify the application procedure for medical devices that have already been approved in the

US or EU Member States, and to reflect and clarify the TFDA's current practice. With respect to the RBM, RRB and RRMA, the TFDA indicated in the foreword of the Regulation that it does not have much experience in reviewing applications for registering botanical medicines, biosimilar, and biosimilar monoclonal antibody products so the RBM, RRB and RRMA will be subject to further amendments after the TFDA gathers more information from the relevant industries and becomes more experienced in this regard, and the TFDA welcomes discussion and comments from the public.

The application fee of registration for NCE, biological medicines or biosimilar products is in the region of NT$600,000. The application fee for the registration of other types of medicines and medical devices ranges from NT$15,000 to NT$50,000. According to the suggested timeline published by the MoHW, it takes approximately one year to obtain NCE marketing authorisation, 200 days for other kinds of new medicines, 220 days for new medical devices and only 80 days for Class 1 medical devices. The applicant (prospective marketing authorisation holder) must be a company duly registered under the laws of Taiwan holding a pharmaceutical company licence. Therefore, international pharmaceutical firms usually set up subsidiaries or branches in Taiwan or appoint agents to comply with the above qualifications.

For special circumstances, there is no alternative mechanism to accelerate approval of products for urgent medical needs, however, during the H1N1 pandemic in 2009, the MoHW did accelerate its review of H1N1 vaccines. Alternatively, Article 48–2 of the PAA, mentioned in Section II. iv, *supra*, also gives legal basis for obtaining an accelerated approval for project of import; nonetheless, such approval is given on a case-by-case basis and has shorter duration than an ordinary marketing authorisation. There are, however, special regulations of biological medicines and herbal medicines regulated by the RRM, while the RMD specifies that customised medical devices must also meet the requirements set out in the Regulations on Pharmaceutical Toll-Manufacturing and Contract Analysis. For generic products, relevant information and data of bioavailability and bioequivalence (BA/BE) must be submitted. The Guidelines for BA/BE Studies promulgated by the MoHW provide guidance on how such studies should be conducted.

vi Regulatory incentives

Although it is provided in the PAA that brand-name pharmaceutical firms should provide information on their NCE patents and when granting marketing authorisation of NCEs, the MoHW would publish the relevant patent numbers or patent file numbers, such submission of patent information is only for the MoHW's records and files and will not be linked to the enforcement of the patents. As Taiwan strives to join the Trans-Pacific Partnership (TPP) agreement, it needs to further demonstrate, among other things, its commitment to strengthening the patent protection of medicines products. In this regard, the TFDA and the Taiwan Intellectual Property Office (TIPO), the central competent authority in charge of matters related to intellectual property, has conducted relevant research in recent years. After the research, the TFDA proposed a bill to amend the PAA (the Bill) to include a patent linkage mechanism similar to the US system and deal with the potential pay-for-delay issue. The TIPO has consistently provided its assistance in clarifying patent-related issues. Several hearings to gather the market players' and the general public's opinion on such amendments were held in 2015 and 2016. The Bill was finalised and submitted to the legislative body for review in August 2016 and passed the first reading in mid-September 2016. It is currently

being reviewed by the health committee within the legislative body, but the legislation is becoming more uncertain as the TPP seems likely to grind to a halt. Further developments regarding relevant legislation should be closely monitored.

The PAA does provide data exclusivity, market exclusivity, and study exemption clauses to balance the benefit of brand-name and generic firms. The currently effective PAA provides a five-year data exclusivity and five-year market exclusivity for NCEs. Nonetheless, a medicine with new indication or with newly changed indication is not provided with any data or market exclusivity. In the Bill mentioned above, amendments related to the data exclusivity and market exclusivity are also included. The data exclusivity for NCEs is shortened to a three-year protection, while the five-year market exclusivity remains unchanged. On the other hand, the Bill newly introduces two-year data exclusivity and three-year market exclusivity for the medicine new indication or with newly changed indication. It is possible that the exclusivity related amendments would pass the legislation review separate from the patent linkage-related provisions if the latter require further discussion.

The PAA, which contains provisions similar to the *Bolar* provision, stipulates that research, teaching and testing prior to application for registration by generic pharmaceutical firms are exempted from the scope of patent right protection of new medicines. However, because of the unclear wording employed in such provisions, their application has caused much confusion within the industry. A new provision was thus added to the recently amended Patent Act (which was passed in December 2011 and came into effect on 1 January 2013) for clarification: research and studies conducted for the registration of medicaments in this or other jurisdictions, regardless of whether they are prior to or after application for registration, would be covered by the study exemption. On the other hand, it is provided that the pharmaceutical firm that holds the first marketing authorisation of an orphan drug may enjoy 10 years' exclusivity for that marketing authorisation so as to encourage the development or introduction of orphan drugs in Taiwan.

In addition, it is provided under the Patent Act that where there is an invention patent directed to a medicine or a manufacturing process thereof, if exploitation of such patent would require regulatory approval pursuant to other laws and if regulatory approval could only be obtained after publication of said invention patent, the patentee may apply for one and only one extension of the term of the invention patent, for up to five years, based on the regulatory approval. A compulsory licensing mechanism has been included into the Patent Act to help developing countries prevent pandemics and other serious diseases.

vii Post-approval controls

The marketing authorisation holder must be a company duly registered under the laws of Taiwan holding a pharmaceutical dealer licence. In addition, the pharmaceutical firm must employ a full-time resident pharmacist as part of its management. For a manufacturer engaged in the manufacturing of biological medicines, a resident technician with a degree in medical science, pharmacy or biology from a domestic or foreign university or college and possessing professional knowledge backed with more than five years of experience in the manufacturing of microbiological and immunological medicines must be employed to supervise the manufacturing. A similar mechanism for medical devices is included in the draft Medical Devices Act mentioned in Section II.i, *supra*, which is that a full-time resident engineer with a relevant medical device background must be employed. Such proposed legislation is under intensive debate within the industry.

The MoHW, as required under the PAA, has promulgated the Regulation of Medicaments under Monitoring to implement five-year post-approval surveillance to ensure the ongoing safety of marketed medicaments and to compel the marketing authorisation holder to report an adverse event caused by medicaments. After the surveillance period, the PAA still requires healthcare institutions, pharmacies and pharmaceutical firms to report serious adverse events caused by medicaments to the MoHW. The Regulation Governing the Reporting of Severe Adverse Reactions to Medicines was promulgated to provide the relevant reporting procedures. This Regulation was amended on 21 November 2013 to include pharmaceutical products being subject to the RMP or participating in post-marketing surveillance studies as part of the mandatory reporting category and to provide more detailed procedures for such reporting.

After a marketing authorisation has been granted, any variations or amendments to the approved contents of the packages, leaflets or labels would need to undergo review and further approval by the MoHW. A marketing authorisation is generally valid for five years (those for rare-disease medicaments are for 10 years); application for marketing authorisation renewal must be filed at least six months before the expiration of such marketing authorisation. If any post-approval trials or studies are conducted, they need to comply with the HSRA guidelines. It is also added in the PAA 2015 that if the holder of a marketing authorisation is aware that it is unable to supply the product or there might be a shortage of such product, it should notify the TFDA at least six months before such situation occurs. If the shortage of supply is caused by force majeure, the holder should notify the TFDA within 30 days of the event. The TFDA may proceed with a project of import to solve the need of the patients.

viii Manufacturing controls

Medicaments must be manufactured by medicament manufacturing factories. Medicament manufacturing factories must obtain a factory registration licence pursuant to the Factory Management Act and a medicament manufacture licence pursuant to the Standards for Medicament Factory Establishment. As specified in the Standards, if a factory passes the MoHW's inspection pursuant to the Good Manufacturing Practices for Medicaments (GMP), it may further obtain a certificate of GMP. A manufacturer may only commence manufacturing upon receipt of the medicament manufacture licence and if its factory passes the GMP inspection, unless exempted by the MoHW through public notice. In addition, the manufacturing of medicaments must comply with GMP standards. PIC/S GMP has been adopted by the TFDA since December 2007. For imported products, the foreign manufacturer must pass the Quality System Documentation examination.

Relocation, expansion and ownership transfer of premise, and expansion of product lines require approval from the competent local sanitation authority and renewal of a GMP licence upon passing the GMP inspection by the MoHW.

The competent authorities are entitled to conduct inspection pursuant to the PAA and the Regulations of Medicament Manufacturer Inspection. The TFDA launched an overall inspection of local API manufacturers, during the period from March to June 2013, to ensure that the ingredients of API products manufactured locally are in compliance with such products' application and registration data. Thirty-three pharmaceutical products contained ingredients that deviated from their application and registration data so they have been suspended from the market for further BA/BE tests. The TFDA intends to conduct such inspections regularly to ensure the safety and efficacy of the pharmaceutical products manufactured locally. In addition, the MoHW issued a ruling on 25 September 2013 requiring that all API factories

being established or relocated after 1 July 2014 and all API factories applying for marketing authorisations for new APIs after 1 July 2014 must meet the requirements of the GMP; all other API factories had to meet GMP standards by 31 December 2015, the aim being to improve manufacturing quality in Taiwan. It is also added in the PAA 2015 that the sellers or manufacturers of certain categories of medicine to be announced by the TFDA should set up a system to track the source and sales flow of such medicine, and should docket such information in the corresponding system established by the TFDA. Details of such practice will be further regulated and promulgated by the TFDA.

ix Advertising and promotion

According to the PAA, medicaments can only be advertised upon prior approval of the MoHW and application for such approval must be filed by the pharmaceutical firm holding the marketing authorisation of such medicaments. Upon approval, the advertisement should be published or broadcasted with the name of the holder and the approval number or numbers. During the approved term of publication or broadcast, the approved particulars of medicaments cannot be modified. Advertisement of prescription medicaments can only be published in medical academic journals. Direct-to-patient promotion and advertisement for prescription medicaments is prohibited.

The term 'pharmaceutical advertisements' is broadly defined under the PAA to cover any act that would effectively be deemed as communicating the medical efficacy of medicaments with the aim to solicit and promote sales. It is also specified in the PAA that interviews, news reports or propaganda containing information implying or suggesting medical efficacy will be regarded as pharmaceutical advertisements. In this regard, the TFDA and the local competent sanitation authorities are usually strict. There are cases where pharmaceutical firms provided information leaflets to healthcare professionals for their reference but such leaflets were disseminated by healthcare professionals to their patients; the MoHW held that this was disguised promotion so the pharmaceutical firms were fined. The courts usually uphold such a view.

In May 2014, a health awareness advertisement that aimed at bringing the public's attention to a disease caused by a certain virus and the possibility of preventing such disease by use of a vaccine (without mentioning the name of any vaccine) has been investigated into jointly by the TFDA and the Department of Health of the Taipei City Government, the competent local authority. The advertisement was ultimately deemed a disguised pharmaceutical advertisement to promote the vaccine since there is only one vaccine product registered in Taiwan that is used for preventing such disease. The advertisement was later suspended by the TFDA and the Taipei Department of Health and the marketing authorisation holder of such vaccine was fined. This shows the stringent implementation of relevant provisions by local authorities.

x Distributors and wholesalers

Salespersons employed by pharmaceutical firms are only permitted to promote sales after their employment has been registered with the competent local sanitation authority. They can only sell medicaments manufactured or sold by their respective employers and can only sell such products to pharmacies, pharmaceutical firms, healthcare institutions and medical research institutions. Salespersons should not commit the acts of peddling, street vending, tampering with medicaments without authorisation and illegal advertising.

There are no specific regulations governing the licensing of distributors and wholesalers. However, in keeping with the PAA, marketing authorisation holders can only license sales of their products to distributors or wholesalers with a pharmaceutical dealer licence, qualified for conducting the business of selling medicaments. Salespersons hired by such distributors and wholesalers must also comply with the above regulations concerning salespersons.

xi Classification of products

Medicaments are subdivided into prescription-only and over-the-counter. There are no specific procedures on classification. Pharmaceutical firms are required to provide their deemed classification when filing the application for marketing authorisation and the MoHW will rule on such classification and name such on the marketing authorisation. Sales of prescribed medicaments can only be made by pharmaceutical firms and pharmacies, while sales of over-the-counter medicaments can be made by general retailers. The different limitations on promotions are outlined in Section II.ix, *supra*.

xii Imports and exports

Only pharmaceutical firms holding marketing authorisation for a medicament are eligible to import the product. Marketing authorisation holders are, however, permitted to license a third-party pharmaceutical firm to import such product as long as such licence is notified to the MoHW and the MoHW has acknowledged receipt.

For medicaments manufactured and sold under marketing authorisations, intended to be sold abroad through export, if an import certificate from the importing country is required, the manufacturer needs to obtain an export certificate from the MoHW prior to exportation. In this regard, the MoHW may, upon consideration of insufficiency to meet domestic demands, restrict or limit exportation of medicaments.

xiii Controlled substances

Addictive narcotic medicines and psychotropic medicines are defined as controlled medicines and are regulated by the Controlled Medicines Act. Controlled medicines are subdivided into Classes 1 to 4 depending on addictive intensity, with Class 1 being most addictive. Import, export, sales and manufacture of Classes 1 and 2 controlled medicines can only be performed by the TFDA-established factories, while such handling of Classes 3 and 4 controlled medicines can be performed by the pharmaceutical firms upon obtaining marketing authorisation pursuant to the RRM.

All controlled medicines can only be dispensed and supplied upon prescription of a physician. When supplying controlled medicines, the identification certificate, name, address, and uniform serial number of the receiver and the quantity of controlled medicines received need to be listed in detail and be kept with such prescription for future inspection. Such information, data and records should be kept for five years.

xiv Enforcement

The MoHW may, from time to time, send officials to inspect the premises of pharmaceutical firms, healthcare institutions and pharmacies, and to sample-test medicaments. Pharmaceutical firms, healthcare institutions and pharmacies cannot reject such inspection and sample test without just cause. Competent local sanitation authorities should also conduct annual inspections of pharmaceutical firms and pharmacies.

The MoHW or competent local sanitation authorities may impose administrative fines from NT$20,000 to NT$50 million for violating statutory requirements and may even impose consecutive fines for continuous violations. The cap of the administrative fines has increased from NT$25 million to NT$50 million in the PAA 2015 to halt the manufacture and import of counterfeit and inferior medicines. For serious violations or refusal to cooperate, authorities may publish the name of such violating pharmaceutical firms, reject renewal application of medicaments, revoke marketing authorisation and shut down business operations. If such violation involves a criminal offence, such as the manufacture, import or sale of counterfeit, prohibited or defective medicaments, authorities can forward the case to the judiciary.

III PRICING AND REIMBURSEMENT

The NHI was launched in March 1995 and is a compulsory social insurance programme. All Taiwanese citizens and foreign nationals living in Taiwan with an alien resident certificate are obliged by statute to enrol in the programme. The NHI has extensive coverage of medicaments, taking up approximately 90 per cent of the market. The insurer of the NHI is the National Health Insurance Administration (NHIA, which, before the government reform of 23 July 2013, was known as the Bureau of National Health Insurance), a subordinate agency of the MoHW. The NHIA is responsible for collecting premiums from the insured. When the insured use medical services, they do not need to pay for medical expenses other than a co-payment and registration fee. Healthcare providers will apply for reimbursement with the NHIA. The National Health Insurance Act (the NHI Act) was extensively amended in January 2010 (and slightly amended in June 2011), so the calculation of premiums, based on different classification of the insured, was entirely restructured from 1 January 2013; this is also known as second-generation NHI. While pharmaceutical firms had no role in first-generation NHI, an article was added to the amended NHI Act enabling pharmaceutical firms to voice their opinions with regard to rules on the inclusion of medicaments onto the NHI reimbursement list and determination of reimbursement price standards.

Medicaments included on the NHI reimbursement list and their reimbursement prices are determined by the NHIA pursuant to the Pharmaceutical Benefit Scheme for NHI (the PB Scheme), which was also extensively amended by the NHIA, promulgated by the MoHW in December 2012 and effective on 1 January 2013 to cope with the changes made to the NHI Act, and was subject to minor amendments in the period from August 2013 to July 2016 to clarify certain provisions. In general, the reimbursement price of brand-name medicaments is determined by referring to the reimbursement prices of such products in 10 developed countries. The reimbursement price of generics is set to be approximately 80 per cent of the price of brand-name product. As there are usually gaps between the higher reimbursement prices and the lower market prices (known as drug-price black holes), healthcare providers have been making profits from such gaps. Since 1999, the NHIA has launched a biannual market survey of actual sales prices and volume of reimbursed medicaments (the PV Survey) and used the survey results as a benchmark to lower reimbursement prices so as to reflect actual market prices. As a result, pharmaceutical firms have to further lower their sales prices in order to sell medicaments to healthcare providers, which is more disadvantageous towards brand-name pharmaceutical firms. A price-volume agreement between the NHIA and marketing authorisation holder is available under the PB Scheme for newly added medicines and indications.

Additionally, the amended NHI Act includes a provision that the NHIA should adjust reimbursement prices based on prevailing market conditions; prices for patented medicines should be gradually lowered to reasonable prices within five years of the expiration of patent protection based on prevailing market conditions. Accordingly, the NHIA published the Adjustment Guidelines of NHI Reimbursement Prices (Price Adjustment Guidelines) on 2 October 2013, which were slightly amended on 4 February 2015. According to these guidelines, the following three categories of drugs will each have its own price adjustment formula:

a Category 1: a new drug that is protected by patent (either compound or pharmaceutical composition) in Taiwan;

b Category 2: a new drug that was protected by patent in Taiwan, but such patent expired less than five years ago; and

c Category 3: a drug that does not fall into Category 1 or 2 (a drug that has never been protected by patent in Taiwan, a new drug that was protected by a patent in Taiwan but such patent expired more than five years ago) or a new drug that was protected by patent in Taiwan but such patent expired on or before 1 January 2013.

The price of Categories 1 and 3 drugs should be adjusted biannually based on the PV Survey, while Category 2 drugs should be adjusted annually for five consecutive years after the expiration of the patent concerned, based on a less favourable formula than that of Category 1 and 3 drugs. The NHIA will also implement the Drug Expenditure Target (DET) for the period from 1 January 2013 to 31 December 2015 to improve the transparency and predictability of pricing and reimbursement in the market; under the DET, the price of all categories of drugs will be adjusted annually. The price cuts were periodically made pursuant to the Price Adjustment Guidelines. Owing to the stringent view of the NHIA regarding whether a drug can be deemed protected by compound or pharmaceutical composition patents, the price cut decisions have been widely disputed by marketing authorisation holders. On 18 December 2015, the NHIA published a draft to relax the criteria of drugs under patent protection; the draft was passed in February 2016 and more drugs now have patent protection under the Price Adjustment Guidelines.

Owing to the comprehensive coverage of NHI medicaments in the market, pharmaceutical firms have a disadvantageous position when negotiating medicaments supply agreements with healthcare providers. In order to ensure a fair business relationship between healthcare providers and pharmaceutical firms, according to the amended NHI Act, in March 2013 the MoHW and the Fair Trade Commission (FTC), the competent authority of the Fair Trade Act (which deals with antitrust and fair competition issues in Taiwan), jointly produced the guidelines for definitive contract clauses to be used in agreements between healthcare providers and pharmaceutical firms, covering matters that must and must not be recorded in such agreements, as well as a template agreement.

IV ADMINISTRATIVE AND JUDICIAL REMEDIES

If a pharmaceutical firm receives an administrative penalty imposed by the MoHW or local authority, it may file an opposition against the authority's decision within 15 days of receipt of the decision pursuant to the PAA. The authority is required to re-examine the matter and issue a new decision. The opposition is not a compulsory procedure, but most pharmaceutical firms will file an opposition before pursuing further administrative or judicial

remedies, which offers a chance to have a discussion with the authority. Regardless of whether an opposition is filed, the pharmaceutical firm may file an administrative petition with the supervising agency of the MoHW, the Executive Yuan, within 30 days of receipt of a decision pursuant to the Administrative Petition Act.

If the petitioner is not satisfied with the Executive Yuan's decision, it may further initiate an administrative suit against both the penalty decision and the petition decision before the administrative courts within two months of receipt of the petition decision. There are two instances for administrative suit: the high administrative courts and the Supreme Administrative Court. While the high administrative courts would review both factual and legal issues, the Supreme Administrative Court only reviews legal issues.

V FINANCIAL RELATIONSHIPS WITH PRESCRIBERS AND PAYERS

There are no laws or regulations that directly regulate the relationships between pharmaceutical firms and physicians or healthcare professionals who make decisions relating to the utilisation or reimbursement of medicaments. The International Research-Based Pharmaceutical Manufacturers Association (IRPMA), an entity composed of international pharmaceutical firms operating in Taiwan, has issued the IRPMA Code of Practice (IRPMA Code) to provide guidance to its members when interacting with healthcare professionals. The IRPMA Code suggests that: (1) all events and meetings held or sponsored by pharmaceutical firms should be purely for scientific or educational purposes; (2) interactions at such events and meetings should not in any way be conducted with the intention of affecting the independence and integrity of the healthcare professionals' decision relating to their prescriptions; and (3) any honorarium, hospitality, entertainment and gifts in such events and meetings should not be excessive. The IRPMA Code was amended in 2012 to ensure the honorarium standards therein comply with the Ethics Directives for Civil Servants (see below). As for local pharmaceutical associations, neither the Taiwanese Generic Pharmaceutical Association nor the Chinese Pharmaceutical Manufacture and Development Association have published similar guidelines. A draft Code for Relationship between Physicians and Companies was published by the TFDA in March 2015, which incorporates the contents in the IRPMA Code. Nonetheless, the draft has provoked wide discussion and controversy in the industry and may still take some time to be finalised and promulgated.

It is worth noting that in Taiwan, healthcare professionals employed by public hospitals are deemed civil servants and so are subject to the Civil Service Employment Act and the Ethics Directives. As provided in the Ethics Directives, civil servants may not receive any unjustifiable gifts or cash or cash equivalents from private entities and honorarium for attending a meeting or event that is capped at NT$5,000 per hour; if a civil servant also receives an author's remuneration for such activity, such remuneration should not exceed NT$2,000 per 1,000 words. Healthcare professionals employed by public hospitals will be subject to a penalty pursuant to the Service Act of the Civil Servant for violated the Ethics Directives. The MoHW has also promulgated the Code of Conduct for the Relationship between Physicians and Corporations (the Physicians Code) in 2006 to provide ethical standards for physicians employed by public hospitals or private entities. It is stipulated that physicians should keep their independence and integrity relating to prescription decisions, should not be unduly affected by pharmaceutical firms and should not receive cash or cash equivalents or other improper gifts from pharmaceutical firms. Physicians will be subject to

a penalty pursuant to the Physicians Act for violating the Physicians Code. Pharmaceutical firms should refrain from abetting or aiding healthcare professionals in violating the Ethics Directives and the Physicians Code.

However, civil servants are narrowly defined in the Criminal Code. In other words, only healthcare professionals employed by public hospitals responsible for procurement or listing of medicaments will be deemed civil servants under the Criminal Code and will be subject to criminal liability for receiving bribes. Thus, the anti-bribery clause in the Criminal Code does not apply to most physicians.

The TFDA drafted an amendment in March 2015 to the Physicians Code to more broadly regulate the interaction between physicians and pharmaceutical companies, which incorporates most provisions in the IRPMA Code. This draft is being discussed by the TFDA and the pharmaceutical industry. The timeline for promulgation is uncertain.

VI SPECIAL LIABILITY OR COMPENSATION SYSTEMS

If a user of market-approved medicaments dies or becomes disabled or seriously ill (medicaments injury) because of an adverse reaction to such approved medicaments, such user or his or her relatives may request relief pursuant to the Medicaments Injury Relief Act. Pharmaceutical firms need to allocate 0.2 to 10 per cent of their previous year's sales revenue from medicaments to injury-relief funds. The Medicaments Relief Foundation was established in 2001 to manage contributions from pharmaceutical firms and to handle medicaments relief claims.

As for injury caused by the use of medicaments not deemed a medicaments injury, the user who suffered such injury would need to claim damages against relevant pharmaceutical firms based on tort law; it is possible that any dispute that arises will need to be resolved through civil litigation. The user would need to prove that he or she did suffer injury, that such injury was caused by the use of medicaments and that the damages claimed are well grounded. There are cases where patients sue pharmaceutical firms based on the Consumer Protection Act (CPA) by arguing that the medicaments, although approved by the MoHW, did not meet the appropriate standards and that, while pharmaceutical firms have the obligation to ensure their products meet such standards, the firms should compensate users of such products. The courts, however, generally hold the view that since the MoHW has set in place a complex system of review of medicaments, unless substantial evidence is provided, pharmaceutical firms would not be deemed to have violated the obligations under the CPA.

VII TRANSACTIONAL AND COMPETITION ISSUES

i Competition law

Brand-name pharmaceutical firms will usually issue warning letters to healthcare providers informing them of patent disputes with generic firms. In order to distinguish between the proper exercise and abuse of intellectual property rights, the FTC has promulgated the Guidelines on Reviewing Cases Involving Enterprises Issuing Warning Letters for Infringement on Copyright, Trademark and Patent Rights (the FTC Guidelines) to provide necessary steps that a company must carry out before sending out warning letters to its competitors' (potential) trading counterparts. In accordance with the FTC Guidelines, brand-name pharmaceutical firms would need to notify relevant generic firms requesting

cessation of the infringement prior to or simultaneously with the issuance of the warning letter and would need to state the precise content and scope of the patent rights concerned and the concrete facts of infringement in the warning letter so that healthcare providers have sufficient knowledge of the rights that could possibly be or are being infringed.

Generally speaking, even if a brand-name pharmaceutical firm loses a patent infringement litigation, the court will not deem that there has been patent abuse since the patentee should have the right to defend its rights through litigation. An important judgment, however, rendered by the Intellectual Property Court (the IP Court) in 2011 provides a standard for determining patent abuse. Takeda Pharmaceutical Co Ltd (Takeda), a Japanese brand-name company, sued Genovate Biotechnology Co Ltd, a Taiwanese generic company, for patent infringement and sought a preliminary injunction. The preliminary injunction was granted and later became final; thus, Genovate was prevented from selling the drugs. It was subsequently found during litigation that the patent infringement assessment report submitted by Takeda to substantiate its application for a preliminary injunction was fundamentally erroneous, since the report found that a kind of preparation product could infringe a compound preparation patent. As a brand-name pharmaceutical firm, Takeda ought to have known of the inaccuracy contained in such report, based on its professional background. It still, however, filed such a report to obtain the preliminary injunction and to deceive the judge who did not have a technical background. The IP Court therefore held that Takeda's conduct amounted to patent abuse to unduly affect fair trade by preventing Genovate's product from entering the market.

As set out in Section II.vi, *supra*, there is no patent linkage mechanism in Taiwan. Therefore, the possibility of pay-for-delay cannot occur in Taiwan at the moment. There have, however, been discussions about whether brand-name pharmaceutical firms could acquire generic firms through hostile takeover in order to shelve generic products. Since there has been no actual case, no decision or opinion can be found. Nonetheless, as also mentioned in Section II.vi, *supra*, the TFDA has proposed the Bill to include patent linkage mechanism and also deal with the potential pay-for-delay issue.

ii Transactional issues

International pharmaceutical firms intending to terminate distribution licences with their local agents are often faced with the difficulty of regaining possession of the marketing authorisation. Under the PAA, an application for transferring marketing authorisation must be jointly filed by the original holder and the new holder, but the agent (the original holder) will usually not cooperate with the licensor (the prospective new holder).

Under such circumstance, international pharmaceutical firms would usually consider filing parallel marketing authorisations. Nonetheless, since the TFDA holds a conservative view on issuing parallel marketing authorisations, the review process may be prolonged indefinitely. Therefore, if possible, it would be favourable if international pharmaceutical firms set up subsidiaries in Taiwan for the purpose of holding marketing authorisation. When mergers and acquisitions involve transfer of market authorisation, it is essential to draft clauses to protect the acquirer's right in obtaining marketing authorisation as planned.

VIII CURRENT DEVELOPMENTS

The Computer-Processed Personal Data Protection Act was amended and renamed as the Personal Data Protection Act (PDPA) in May 2010; the PDPA came into effect in

October 2012. The PDPA provides a different set of regulations relating to informed consent when regulating the collection, processing and use of personal data. The conflict between the PAA (including the GCP) and the PDPA has been a focus of discussion in the industry, regarding whether provisions related to informed consent in the GCP should prevail, and whether the MoHW's clarification should be sought. Nonetheless, to date, the MoHW has not issued any interpretation in this regard. It is our understanding that the TFDA generally approves the clinical trial applications that only take into consideration the PAA and GCP requirements.

The most drastic change to the life sciences sector would be the future inclusion of patent linkage into the PAA. Owing to the halt of the TPP, the inclusion of patent linkage might require further consideration and discussion among the public. Currently the brand-name and generic pharmaceutical companies, respectively, are still intensively discussing the contents of the Bill with the TFDA and the legislators with a hope that the Bill will be revised in their favour. Both sides are supported with opinions of academic scholars and attorneys. Further developments regarding relevant legislation should be closely monitored.

As to the draft Medical Devices Act, the TFDA intends to separate the medical device-related regulations from the PAA so that there is room to gradually fine-tune the regulations in several stages in the future. It is also the view of some scholars that the contents thereof would not fundamentally and suddenly change the current practices in medical devices industry.

Appendix 1

ABOUT THE AUTHORS

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Katherine Juang is an associate partner at Lee and Li, Attorneys-at-Law and has been a member of the Taipei Bar Association since 2002. Ms Juang obtained a master's degree in law in Taiwan and her master's thesis dealt with the protection of medical information. She specialises in pharmaceutical regulatory compliance, data protection compliance, IP law and competition law. She advises various local and foreign clients on pharmaceutical regulatory matters, relevant patent litigation and compliance structure.

JILL NIU

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Jill Niu is a partner at Lee and Li, Attorneys-at-Law. Her practice focuses on medical and healthcare laws (including compliance of privacy and data protection in conducting clinical studies and marketing programmes), employment and labour laws, corporate governance and compliance, and tax litigation. Ms Niu also acts as a counsel to a local association of multinational pharmaceutical firms and has been advising the association on the code of marketing practices, including privacy and data protection issues, from the perspective of clinical trial laws and regulations. She has been a member of the Taipei Bar Association since 1992.

DAISY WANG

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Daisy Wang is a senior counsellor at Lee and Li, Attorneys-at-Law. After receiving an LLB from the National Taiwan University, Ms Wang pursued and received her LLM from the University of Illinois. She served with the National Bureau of Standards (the former IPO) for more than two years and joined Lee and Li in 1979 for handling patent and IP-related matters. Ms Wang is experienced in handling patent procurement and strategy consultation, patent dispute resolution, technology licensing etc., and, since the 1990s, has handled various leading patent and IP cases, including for Intel, Philips, ABB, Sony and Celanese. Since 2000, Ms

Wang has also helped clients with their Greater China patent and IP matters, including both prosecution and enforcement aspects. Since 1999, Ms Wang has been continually nominated as reputable IP professional via surveys done by various international organisations, such as *Asia IP*, MIP, *Who's Who Legal*, Chambers and Partners (*Chambers Asia*), IAM, the American Biographical Institute, Euromoney (*Expert Guides*) and *Intercontinental Finance Magazine*.

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