THE LIFE SCIENCES LAW REVIEW

SEVENTH EDITION

Editor
Richard Kingham

THE LAWREVIEWS

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PREFACE

The seventh edition of *The Life Sciences Law Review* covers a total of 34 jurisdictions, providing an overview of legal requirements of interest to pharmaceutical, biotechnology and medical device companies. The chapters are arranged so as 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.

The past year has seen a number of significant developments. After many years of negotiations and false starts, the United States and EU have finally begun to implement a programme of mutual recognition of inspections of drug manufacturing establishments, thus simplifying the shipment of drug products between the jurisdictions and freeing resources to carry out more inspections in third countries. In the meantime, the United States continues to debate whether to repeal the comprehensive medical care legislation enacted during the Obama administration, and is now considering measures to improve the transparency of pricing for prescription drugs. The United Kingdom is addressing changes to drug regulatory systems that must accompany the country's planned withdrawal from the EU, and drug and device manufacturers are actively planning for the effects of Brexit on their supply chains. The governments in India and China continue to consider changes in their regulatory systems for drugs and medical devices.

It is vitally important that lawyers who advise companies in the life sciences sector and the business executives whom they serve have a working knowledge of the regulations and policies that govern drugs, biologics and medical devices. It is equally important to keep up to date with developments in the regulatory systems, which govern access to the market, pricing and reimbursement, advertising and promotion, and numerous other matters that are essential to success. It is our hope that this annual publication will be helpful in this respect.

All of the chapters have 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 publication.

Richard Kingham
Covington & Burling LLP
Washington, DC
March 2019

Chapter 30

TAIWAN

Katherine 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 different aspects of this sector, 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) is the competent central authority that governs all health-related matters, such as healthcare professionals and institutions, foods, cosmetics, medicines, medical devices and national health insurance (NHI). The Taiwan Food and Drug Administration (TFDA), one of the sub-agencies of the MoHW, is the entity responsible for the enforcement of laws and regulations related to foods, cosmetics, medicines and medical devices, and the issuance of all licences, permits and authorisations.

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.

i Classification

Both medicines and medical devices are 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.

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In general, the term 'medical devices' covers 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.[2] Several meetings were held by the TFDA in 2016 and 2017 to gather comments from the public; a revised draft was approved in late 2017 by the MoHW and the Executive Yuan (the highest administrative body in Taiwan (EY)) and was submitted to the Legislative Yuan (LY) in December 2017. A bill becomes effective after it has passed three readings and has been announced by the president. The draft passed its first reading on 29 December 2017; however, there has been no further progress on the bill to date.

There are no 'borderline' cases as regards medicines and medical devices in relation to cosmetics and cosmeceutical products, foods and food additives. Since the MoHW is the sole central authority with competence to enforce the relevant laws, such as the PAA, the Statute for Control of Cosmetic Hygiene, the Food Safety and Sanitation Control Act and the Health Food Control Act, the MoHW reviews all cases and determines the necessary classifications.

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 the chemicals are manufactured for medical or industrial products. There are no borderline cases at the moment.

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 Safety Studies for Medicinal Products (the Guidelines) amended by the MoHW in March 2006 and June 2014, 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 Food and Drug Administration 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 the provisions stipulated in, international practice, excluding toxicokinetics studies.

iii Clinical trials

For clinical trials conducted to obtain marketing approval for medicaments, the PAA and its subordinate Guidelines for Good Clinical Practice (GCP), promulgated by the MoHW, must 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) must be considered. While there have been no specific regulations governing other types of trials, the Human Subjects Research Act (HSRA) was enacted in December 2011 to provide

2 See more classification details in Section II.v.

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 conducting clinical trials for medicaments registration purposes, in which case the GCP prevails, or when conducting human trials, in which case the MCA prevails, 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 the 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 must 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 this responsibility. Allocation of liability between institutions or investigators and sponsors is mostly determined in 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 that have not been registered with or approved by the MoHW if the medicaments are part of a project-related importation programme. An application must first pass the internal review of the institutional review board or ethics committee of the teaching hospital that is applying. In its application to the MoHW, the teaching hospital should submit an approval from the ethics committee, any medical literature regarding treatment, the patient's consent and documents providing evidence that the medicaments have obtained marketing approval from the competent sanitation authority of the country where they are manufactured. While the legal basis of a project-related importation programme is provided in certain administrative rules, Article 48–2 was added to the amendments to the PAA, effective as of 2 December 2015, to provide a higher-ranking legal basis for project-related importation programmes.

In addition, pursuant to the Rare Disease Prevention and Medicaments Act, government agencies, healthcare institutions, patients with rare diseases or their relatives, and relevant foundations or associations may also apply for project-related importation programmes for rare-disease medicaments that have not been registered with or approved by the MoHW. 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 providing evidence that the medicaments have obtained marketing approval from the competent sanitation authority of the country where they are manufactured, and safety and efficacy data.

After the project-related importation programme application has been approved by the MoHW, the imported medicaments should be labelled as samples and should not be available 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), the Regulations for Registration of Biosimilar Products (RRB), the Regulations for Registration of Biosimilar Monoclonal Antibody Products (RRMA), and the Regulations for Registration of Human Cell Therapy Products (RHCT) provide application procedures for the registration of, and obtaining marketing approval for, medicines, medical devices, botanical medicines, biosimilar products in general, and biosimilar monoclonal antibody products, respectively. In general, applicants registering new chemical entity (NCE) medicines have 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 has constantly been amended to simplify the procedures or to relax the application requirements for registering drugs, and was most recently amended in January 2018. One of the most important changes is that a post-marketing risk management plan (RMP) becomes a requirement when filing the application, to ensure the applicant manages risk after marketing approval is granted.

As for medical devices, they are subdivided into the three classes under the RMD: Classes 1, 2 and 3. Registration of Class 1 medical devices merely involves simple paper review, but 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 United States or EU Member States, and to reflect and clarify the TFDA's current practice, and was partly amended in March 2017 to simplify or clarify certain documentation requirements.

With respect to the RBM, RRB, RRMA and RHCT, the TFDA indicated in the foreword of the Regulation that it does not have much experience in reviewing applications for registering botanical medicines, biosimilar, biosimilar monoclonal antibody and human cell therapy products so the RBM, RRB, RRMA and RHCT will be subject to further amendments after the TFDA gathers more information from the relevant industries and becomes more experienced in this regard; the TFDA welcomes discussion and comments from the public. Additionally, the TFDA has proposed a draft Cell and Genetic Therapy Product Control Act in early 2017, and the EY has proposed a draft Regenerative Medicinal Products Control Act in October 2018; both drafts are still under discussion.

The application fee for registration of NCE, biological medicines or biosimilar products is in the region of NT$600,000. The application fee for 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 approval, 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 (the prospective marketing approval holder) must be a company duly registered under the laws of Taiwan

and must hold a pharmaceutical company licence. Therefore, international pharmaceutical firms usually set up subsidiaries or branches in Taiwan or appoint agents to comply with these requirements.

As regards special circumstances, there is no alternative mechanism to accelerate approval of products for urgent medical needs, although the MoHW did accelerate its review of H1N1 vaccines during the H1N1 pandemic in 2009. Article 48–2 of the PAA, mentioned in Section II.iv, also gives a legal basis for obtaining an accelerated approval for a project-related importation programme; however, this form of approval is given on a case-by-case basis and has a shorter duration than ordinary marketing approvals. However, there are special regulations for biological medicines and herbal medicines under the RRM, and 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

Where previously brand-name pharmaceutical firms provided information about their NCE patents and, when granting marketing approval for NCEs, the MoHW would publish the relevant patent numbers or patent file numbers, this submission of patent information was only for the MoHW's records and files, and was not linked to patent enforcement. However, a bill to amend the PAA passed three readings by the LY on 29 December 2017 (PAA 2017) to include a patent linkage mechanism similar to that used in the US system. The date on which these patent linkage-related provisions in the PAA 2017 will become effective is subject to the determination of the EY, since the administrative body will require time to prepare for the implementation of the patent linkage mechanism. The TFDA published draft Enforcement Rules of Patent Linkage in September 2018, but further changes will be made to these draft Enforcement Rules to reflect comments gathered from the public consultation, and thus the implementation date of the patent linkage mechanism is still unknown. In short, according to the PAA 2017, the holder of a new drug authorisation (the NDA holder) should report its related patents within 45 days, and the applicant for the generic drug is obliged to declare to the TFDA and inform the NDA holder that the generic drug does not infringe any patents of the reference new drug. After being informed, the NDA holder, relevant patentees or exclusive licensees should initiate patent infringement litigation within 45 days if it disagrees with the declaration. The TFDA, after being notified of the aforementioned litigation, shall stay the issuance of the generic drug authorisation for 12 months. The applicant for the generic drug that first overcame the patent infringement issue will be granted with the drug authorisation by the TFDA and enjoy a 12-month market exclusivity. In addition, any agreement between the NDA holder, patentees, exclusive licensees and the applicant of the generic drug regarding the 12-month market exclusivity should be submitted to the TFDA and the Taiwan Fair Trade Commission (TFTC) for review.

The PAA provides data exclusivity and study exemption clauses to balance the benefit of brand-name and generic firms. The relevant provisions were amended in the PAA 2017 and the amended provisions have become effective; these provide a three-year data exclusivity with the effect that the TFDA will not issue any marketing approval for a generic within five years of the issuance of marketing approval to the innovator. The PAA 2017 introduces a two-year

data exclusivity for a medicine with a new indication or a newly changed indication with the effect that the TFDA will not approve the new indication or a newly changed indication to a generic within three years of the issue of approval of that indication to the innovator.

An article similar to the *Bolar* provision was added to the Patent Act of December 2011, which provides that the research and studies conducted for the registration of medicaments in this or other jurisdictions, regardless of whether they were conducted prior to or after an application for registration, will be covered by the study exemption. On the other hand, it is provided in the Orphan Drug Act that the pharmaceutical firm that holds the first marketing approval for an orphan drug may enjoy 10 years' exclusivity for that marketing approval, 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 in respect of a medicine or a medicine manufacturing process, if exploitation of that patent would require regulatory approval pursuant to other laws and if regulatory approval could only be obtained after publication of the 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 in the Patent Act to help developing countries prevent pandemics and other serious diseases.

vii Post-approval controls

The marketing approval holder must be a company duly registered under the laws of Taiwan and 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, which is that a full-time resident engineer with a relevant medical device background must be employed. This proposed legislation is the subject of intensive debate within the industry. In addition, starting from January 2019, it is mandatory for a pharmaceutical dealer to meet the Good Distribution Practice (GDP) requirements to sell and distribute medicinal products in Taiwan.

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 continuing safety of marketed medicaments and to compel the marketing approval 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 marketing approval has been granted, any variations or amendments to the approved contents of the packages, leaflets or labels have to undergo review and further approval by the MoHW. Marketing approval is generally valid for five years (those for rare-disease medicaments are for 10 years); an application for marketing-approval renewal

must be filed at least six months before expiry of the existing marketing approval. If any post-approval trials or studies are conducted, they have to comply with the HSRA guidelines. If the marketing approval holder is aware that it is unable to supply the product or there might be a shortage of the product, it should notify the TFDA at least six months before that 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-related importation programme to address the needs of 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, transfer of premises ownership and expansion of product lines all 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 inspections pursuant to the PAA and the Regulations of Medicament Manufacturer Inspection. The TFDA launched an overall inspection of local manufacturers of active pharmaceutical ingredients (APIs) during the period from March to June 2013, to ensure that the ingredients in API products manufactured locally were in compliance with the products' application and registration data. Thirty-three pharmaceutical products contained ingredients that deviated from their application and registration data so they were 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 approvals 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. 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 medicines, and should docket the information in the corresponding system established by the TFDA. Details of this practice will be further regulated and promulgated by the TFDA.

ix Advertising and promotion

According to the PAA, medicaments can only be advertised with prior approval by the MoHW and an application for this approval must be filed by the pharmaceutical firm holding marketing approval for the medicaments. Following approval, the advertisement should be published or broadcast 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. Advertisements for prescription medicaments can only be published in medical academic journals. Direct-to-patient promotions and advertisements for prescription medicaments are prohibited.

The term 'pharmaceutical advertisements' is broadly defined under the PAA to cover any act effectively deemed as communicating the medical efficacy of medicaments with the aim of soliciting and promoting 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 have been cases in which pharmaceutical firms provided information leaflets to healthcare professionals for their reference, but those leaflets were disseminated by healthcare professionals to their patients; the MoHW viewed this as disguised promotion so the pharmaceutical firms were fined. The courts usually uphold such views.

In May 2014, a health awareness advertisement that aimed to bring the public's attention to a disease caused by a certain virus and the possibility of preventing the disease by use of a vaccine (without mentioning the name of any vaccine) has been investigated jointly by the TFDA and the Department of Health of the Taipei City Government, the competent local authority. The advertisement was ultimately deemed to be a disguised pharmaceutical advertisement to promote the vaccine since there is only one vaccine product registered in Taiwan that is used for preventing the disease. The advertisement was later suspended by the TFDA and the Taipei Department of Health and the vaccine marketing approval holder 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 employers and can only sell those 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 approval holders can only license sales of their products to distributors or wholesalers who have a pharmaceutical dealer licence and are qualified to conduct the business of selling medicaments, and who have GDP certification. Salespersons hired by such distributors and wholesalers must also comply with the aforementioned 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 an application for marketing approval, and the MoHW will rule on the classification and state it on the marketing approval. 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, above.

xii Imports and exports

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

For medicaments manufactured and sold under marketing approvals, and intended for sale abroad through export, if an import certificate from the importing country is required, the manufacturer must 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 four classes depending on addictive intensity, with Class 1 being the most addictive. Import, export, sales and manufacture of Class 1 and Class 2 controlled medicines can only be carried out by TFDA-established factories, while for Class 3 and Class 4 controlled medicines the same processes can be carried out by pharmaceutical firms after obtaining marketing approval pursuant to the RRM.

All controlled medicines can only be dispensed and supplied with a prescription from a physician. When supplying controlled medicines, the identification certificate, name, address and uniform serial number of the receiver and the quantity of the controlled medicines received must be listed in detail and be kept with the prescription for future inspection. This 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 refuse any 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 of between NT$20,000 and NT$50 million for violations of 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 to halt the manufacture and import of counterfeit and inferior medicines. For serious violations or refusal to cooperate, authorities may publish the name of the violating pharmaceutical firms, reject renewal applications for medicaments, revoke marketing approvals and shut down business operations. If a 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), 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 have to pay for medical expenses other than a co-payment and registration fee. Healthcare providers will apply for reimbursement from the NHIA. The National Health Insurance Act (the NHI Act) was extensively amended in January 2010 (and slightly amended in June 2011 and November 2017). As a result, the calculation of premiums, based on different classifications of insured persons, was entirely restructured from 1 January 2013; this is also known as second-generation NHI. Although 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 on 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; it was subject to minor amendments during the period from August 2013 to March 2017 to clarify certain provisions. In general, the reimbursement price of brand-name medicaments is determined by referring to the reimbursement prices of these products in 10 developed countries. The reimbursement price of generics is set to be approximately 80 per cent of the price of a 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 these gaps. Since 1999, the NHIA has launched a biannual market survey of actual sale prices and the volume of reimbursed medicaments (the PV Survey) and used the results as a benchmark to lower reimbursement prices to reflect actual market prices. As a result, pharmaceutical firms have to further lower their sales prices to sell medicaments to healthcare providers, which is more disadvantageous for brand-name pharmaceutical firms. A price-volume agreement between the NHIA and marketing approval holder is available under the PB Scheme for newly added medicines and indications. In this respect, the NHIA has published a draft amendment in July 2018 to the PB Scheme to include the managed-entry agreement (MEA) mechanism, which will allow the NHIA and the marketing approval holder more room to negotiate the drug price and budget, and to allocate the risk more reasonably.

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 expiry of patent protection based on prevailing market conditions. Accordingly, the NHIA published the Adjustment Guidelines of NHI Reimbursement Prices (the Price Adjustment Guidelines) on 2 October 2013, which were slightly amended between February 2015 and February 2017. According to these guidelines, the following three categories of drugs will each have their 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 a patent in Taiwan, but that 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 that patent expired more than five years ago) or a new drug that was protected by a patent in Taiwan but that patent expired on or before 1 January 2013.

The price of Category 1 and Category 3 drugs should be adjusted biannually based on the PV Survey, while Category 2 drugs should be adjusted annually for five consecutive years after expiry of the patent concerned, based on a less favourable formula than that of Category 1 and Category 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. The implementation of the DET has been extended until the end of 2019. 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 to be protected by compound or pharmaceutical composition patents, the price cut decisions have been widely disputed by marketing approval 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 medicament supply agreements with healthcare providers. 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 TFTC, the authority competent to enforce the Fair Trade Act (which deals with antitrust and fair competition issues in Taiwan), jointly produced 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, and they also produced 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 provides an opportunity 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 EY, within 30 days of receipt of a decision pursuant to the Administrative Petition Act.

If the petitioner is not satisfied with the EY'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 avenues for pursuing an administrative suit: the high administrative courts and the Supreme Administrative Court. The high administrative courts review both factual and legal issues, whereas 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 (the 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' decisions relating to their prescriptions; and (3) any honorarium, hospitality, entertainment and gifts at such events and meetings should not be excessive. The IRPMA Code was amended in 2012 to ensure the honorarium standards therein comply with the Integrity and Ethics Directives for Civil Servants (see below), and the Code has been constantly updated since then; the most recent amendment was published in 2018. As for local pharmaceutical associations, neither the Taiwanese Generic Pharmaceutical Association nor the Chinese Pharmaceutical Manufacture and Development Association has published similar guidelines. However, the Taiwan Advanced Medical Technology Association (TAMTA), an entity composed of medical-device innovators, has published similar guidelines in its Code of Ethics.

Healthcare professionals employed by public hospitals in Taiwan are deemed to be civil servants and so are subject to the Civil Service Employment Act and the Integrity and Ethics Directives for Civil Servants. As provided in the Integrity and Ethics Directives, civil servants may not receive any unjustifiable gifts, cash or cash equivalents from private entities, and honorariums for attending a meeting or event are capped at NT$5,000 per hour; if a civil servant also receives an author's remuneration for any such activity, the 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 Civil Service Act for violating the Integrity and Ethics Directives. The MoHW also promulgated in 2006 the Physician's Code of Conduct: Guidelines Governing the Relationships between Physicians and Corporations to provide ethical standards for physicians employed by public hospitals or private entities. It is stipulated that physicians should maintain 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 Physician Act for violations of the Physician's Code of Conduct. Pharmaceutical firms should refrain from abetting or aiding healthcare professionals in violating the Integrity and Ethics Directives or the Physician's Code. A draft amendment to the Physician's Code was published by the TFDA in March 2015, which incorporates the contents of the IRPMA Code. This draft has provoked wide discussion and controversy within the industry and may still take some time to be finalised and promulgated.

Civil servants are narrowly defined in the Criminal Code. Only healthcare professionals employed by public hospitals responsible for procurement or listing of medicaments are deemed to be 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.

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 the approved medicaments, the user or his or her relatives may request relief pursuant to the Medicaments Injury Relief Act. Pharmaceutical firms have to allocate between 0.2 and 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 an injury caused by the use of medicaments not deemed to be a medicaments injury, the user who suffered the injury would have to claim damages against the relevant pharmaceutical firms on the basis of tort law; it is possible that any dispute that arises would have to be resolved through civil litigation. The user would have to prove that he or she did suffer injury, that the injury was caused by the use of medicaments and that the damages claimed were well grounded. There have been cases in which patients have sued 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, as pharmaceutical firms are obliged to ensure their products meet these standards, the firms should compensate users of these products. The courts, however, generally hold the view that because the MoHW has set in place a complex system of review of medicaments, unless substantial evidence is provided, pharmaceutical firms cannot be deemed to have violated their 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. To distinguish between the proper exercise and abuse of intellectual property rights, the Taiwan Fair Trade Commission (TFTC) has promulgated the Guidelines on Reviewing Cases Involving Enterprises Issuing Warning Letters for Infringement on Copyright, Trademark and Patent Rights (the TFTC 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 TFTC Guidelines, brand-name pharmaceutical firms have to notify relevant generic firms requesting cessation of the infringement prior to or simultaneously with the issuance of the warning letter, and have 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 the report, given its professional background; however, it still filed the 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 and unduly affected fair trade by preventing Genovate's product from entering the market.

As set out in Section II.vi, the patent linkage mechanism has been included in the PAA 2017, and the TFTC and TFDA are authorised to jointly promulgate the guidelines to deal with the potential pay-for-delay issue; developments in this area should be closely monitored.

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 approval. Under the PAA, an application to transfer marketing approval must be jointly filed by the original marketing approval holder and the new holder, but the agent (the original holder) will usually not cooperate with the licensor (the prospective holder).

Under these circumstances, international pharmaceutical firms would usually consider filing parallel marketing approvals. However, because the TFDA holds a conservative view on issuing parallel marketing approvals, the review process may be prolonged indefinitely. Therefore, if possible, it would be advantageous for an international pharmaceutical firm to set up a subsidiary in Taiwan for the purpose of holding marketing approvals. When mergers and acquisitions involve a transfer of marketing approval, it is essential to draft clauses to protect the acquirer's right to obtain marketing approval as planned.

VIII CURRENT DEVELOPMENTS

The most drastic change in the life sciences sector is the recent inclusion of patent linkage in the PAA 2017. As the TFDA will have to establish in more detail the implementing regulations for patent linkage, further developments regarding the promulgation of these regulations by the relevant administrative agencies, and their impact on the industries concerned, 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 of the draft would not fundamentally or suddenly change current practices in the 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.

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