THE PHARMA LEGAL HANDBOOK

JAPAN

PHARMA BOARDROOM

THE PHARMA LEGAL HANDBOOK ANSWERS ESSENTIAL QUESTIONS ABOUT THE LEGAL AND REGULATORY ENVIRONMENT FOR PHARMACEUTICALS IN JAPAN.
IT IS A MUST-HAVE FOR ANY COMPANY OPERATING IN THE COUNTRY OR LOOKING TO ENTER THE MARKET.

PREPARED IN ASSOCIATION WITH NISHIMURA & ASAHI, THE LARGEST INTERNATIONAL LAW FIRM IN JAPAN, IT SHOULD ANSWER ANY QUESTIONS LINKED TO REGULATION, PRICING, CLINICAL AND PRECLINICAL TRIALS, MARKETING, MANUFACTURING, TRADEMARKS AND PATENTS.

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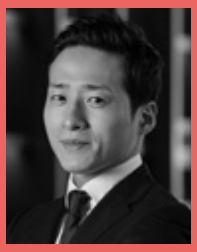
She held tenure as a Corporate Officer and General Counsel at GE Healthcare Japan Corporation (manufacture and sale of medical devices and Bio products) from 2005 to 2009, taking on responsibility for legal affairs, IP and compliance across the board. She has also assumed the position of General Counsel of Asia Pacific to oversee legal affairs and compliance in the APAC region. Furthermore, Mariko was appointed as an outside statutory auditor at Nihon Medi-Physics Co., Ltd. (manufacture and sale of pharmaceutical products), an affiliate of GE Healthcare Japan, continuing to hold the position until she left GE Group in 2009.

Following registration with the Japanese Bar Association in 1992, Mariko joined Nishimura & Partners (currently Nishimura & Asahi) in 1995, with expertise in intellectual property, entertainment, general corporate, bankruptcy, and civil rehabilitation. During her tenure at Nishimura & Partners, she was seconded to Gibson, Dunn & Crutcher LLP, a US law firm, as well as working at a US medical device company as Vice President & General Counsel. After returning to Nishimura & Partners, she became a partner in 2003 and served until she became an in-house counsel of GE Healthcare Japan Corporation until 2005.

Thus, she is an in-house counsel pioneer in the Japanese healthcare industry. She was selected as one of the top 100 Corporate Counsel in Asia Pacific in the GC Powerlist of the Legal 500 in 2014.

In 2019, she received an award as a Corporate and M&A lawyer by Best Lawyers® 10th Edition of The Best Lawyers in Japan (2020).



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He is currently working on a book detailing a Japanese law designed to secure quality, efficacy, and safety of pharmaceutical, quasi-pharmaceutical, cosmetic products and others. In that book, which will be published in due course by N&A, he takes charge of the chapters of quasi-pharmaceutical and cosmetic products.

He obtained his Juris Doctor degree from the University of Tokyo School of Law in 2013 after receiving his Bachelor of Laws from Kyoto University in 2011.

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01

REGULATORY, PRICING, AND REIMBURSEMENT OVERVIEW

1. What are the regulatory authorities with jurisdiction over drugs, biologicals, and medical devices in your country?

2. What is the regulatory framework for the authorization, pricing, and reimbursement of drugs, biologicals, and medical devices?

3. What are the steps to obtaining authorization to develop, test, and market a product?

4. What are the approximate fees for each authorization?

5. For how long are marketing authorizations/registrations valid? How are marketing authorizations/registrations renewed?

6. How does the authorization process differ between brand-name products and generic products? Are there differences for local manufacturers versus foreign-owned manufacturers?

7. How are combination products (drug + drug, drug + biologic, drug + device, biologic + device, drug + biologic + device) regulated?

8. How is compliance with regulation monitored and evaluated? Is the regulatory regime comparable with the U.S. Food and Drug Administration or the European Medicines Agency expectations and requirements?

9. What is the potential range of penalties for noncompliance?

10. Is there a national healthcare system? If so, how is it administered and funded?

11. How does the government (or public) healthcare system function with private sector healthcare?

12. Are prices of drugs and devices regulated and, if so, how?

13. How are drugs and devices used by patients paid for? What roles do public and private payers play?

14. Who dispenses drugs and devices to patients and how are those dispensers compensated?

15. What are the professional and legal responsibilities of those who dispense drugs and devices? What role do they play in providing patient care, information, and safety?

01 REGULATORY, PRICING, AND REIMBURSEMENT OVERVIEW

1. What are the regulatory authorities with jurisdiction over drugs, biologicals, and medical devices in your country?

The Ministry of Health, Labour and Welfare (MHLW) and the Pharmaceuticals and Medical Devices Agency (PMDA)

2. What is the regulatory framework for the authorization, pricing, and reimbursement of drugs, biologicals, and medical devices?

Authorization is governed by the Pharmaceuticals and Medical Devices Law.

Pricing of drugs and biologicals is governed by the NHI (National Health Insurance) Drug Pricing Standard which is established by MHLW under the Health Insurance Act. The calculation method of drug pricing and the price of each drug is announced by MHLW after consultation with the Central Social Insurance Medical Council.

Pricing of medical devices is included in the Medical Fee, which is also established by MHLW under the Health Insurance Act, and the calculation method and the price thereof is announced by MHLW after consultation with the Central Social Insurance Medical Council.

Reimbursement is governed by the Health Insurance Act.

3. What are the steps to obtaining authorization to develop, test, and market a product?

To develop and test a product, it is necessary to obtain a manufacturing/marketing business license, depending on the type of business.

To market a product, in addition to the above, the license holder must obtain marketing authorization for each such product.

4. What are the approximate fees for each authorization?

Fee for a manufacturing/marketing license varies depending on the type of license, but the fee is approximately 100,000 to 150,000 yen. Fee for marketing authorization for each product varies depending on the product.

5. For how long are marketing authorizations/registrations valid? How are marketing authorizations/registrations renewed?

Manufacturing/marketing license is valid for five years, so the license holder must renew it every five years. Marketing authorizations are valid until and unless withdrawn by the government for appropriate reasons or abandoned by the authorization holder, both of which rarely happen.

6. How does the authorization process differ between brand-name products and generic products? Are there differences for local manufacturers versus foreign-owned manufacturers?

Clinical trial data is required to obtain authorization for brand-name products. Normally, product creators spend more than 10 years from basic research to obtaining authorization. For generic products, only stability tests and bioequivalence tests are required, as opposed to clinical trials. Thus, generic products can obtain authorization in a short time, normally 2 years from the start of testing. Currently, applications for authorization of generic products are only accepted twice a year, in February and August.

7. How are combination products (drug + drug, drug + biologic, drug + device, biologic + device, drug + biologic + device) regulated?

Basically, the same rules apply to combination products. To ensure the safety of combination products, the single drugs used in combination products must be in the market for one year or more, with exceptions for some special combination products (such as HIV drugs).

8. How is compliance with regulations monitored and evaluated? Is the regulatory regime comparable with the U.S. Food and Drug Administration or the European Medicines Agency expectations and requirements?

Compliance with regulations is monitored and evaluated by PMDA and the local government of each prefecture. Basically, compliance with regulation is harmonized with FDA and EMA.

9. What is the potential range of penalties for noncompliance?

Potential penalties include suspension of part or all of a business, cancellation of authorizations, or up to 3 years imprisonment or a fine of up to 3 million yen or both, depending on the type of noncompliance/misconduct.

10. Is there a national healthcare system? If so, how is it administered and funded?

There is a national healthcare system. Japan's universal insurance system began with introduction of the Health Insurance Act in 1961. This system ensures that all people's healthcare costs are covered by public insurance and people have free access to any healthcare provider. People have to pay insurance fees to the health insurance program they join, and then when the individual goes to a healthcare provider, the cost is covered by National Health Insurance (other than a portion the individual patient must pay). The individual's payment portion varies from 10% to 30% depending on the individual's age, and if an individual's payments exceed a certain amount, which is decided based on his or her income, the residual amount is covered by the National Health Insurance.

People have an obligation to join a health insurance program. Company employees join the health insurance program which his/her employer has joined. Most other people join the national health insurance program, and there are several special insurance programs such as the public employee union program.

The national healthcare system is primarily funded by insurance fees paid by the program members. For example, a company employee has an obligation to pay half of his/her insurance fee to the insurance program, and the other half is paid by the employer. However, current healthcare costs are far beyond the

total of insurance fees. Thus, there is an added public expense. Most recently, approximately one half of the total healthcare costs was covered by insurance fees, approximately 40% was covered as a public expense, and approximately 10% was covered by individual payment by the patients.

11. How does the government (or public) healthcare system function with private sector healthcare?

Most of the hospitals in Japan belong to the private sector (approximately 80%).

The basic function is the same between private sector and public sector care, but the public sector has special missions such as providing healthcare in remote places where no other hospitals exist, assisting patients as a safety net, and providing advanced healthcare based on advanced research and study.

12. Are prices of drugs and devices regulated and, if so, how?

Prices of drugs and devices are regulated under the Health Insurance Act.

Pricing of drugs and biologicals are governed by the NHI (National Health Insurance) Drug Pricing Standard which is regulated by MHLW under the Health Insurance Act. Calculation methods for drug pricing and the price of each drug is announced by MHLW after consultation with the Central Social Insurance Medical Council.

Pricing of medical devices is included in the Medical Fee, which is also regulated by MHLW under the Health Insurance Act, and the calculation method and price is announced by MHLW after consultation with the Central Social Insurance Medical Council.

13. How are the drugs and devices used by patients paid for? What roles do public and private payers play?

Drugs and devices prescribed by doctors and used by patients are covered by National Health Insurance, other than the portion individual patients must pay, under the Health Insurance Act.

14. Who dispenses drugs and devices to patients and how are those dispensers compensated?

Doctors prescribe the drugs and pharmacies dispense the drugs to patients. When a pharmacy dispenses a prescribed drug, the patient has to pay a portion of the total cost, and the other portion is reimbursed to the pharmacy by the National Health Insurance payer.

The cost of devices used by doctors for patients is reimbursed to the doctor by the National Health Insurance payer. Patients only pay the hospital a portion of the doctor fees, including service fees.

15. What are the professional and legal responsibilities of those who dispense drugs and devices? What role do they play in providing patient care, information, and safety?

Under the Health Insurance Act, a doctor must register as an insurance doctor. Only registered insurance doctors can prescribe drugs and dispense devices covered under the national insurance system.

Also, only a pharmacy which is designated as an insurance pharmacy under the Health Insurance Act can dispense drugs.

Insurance doctors and insurance pharmacies have obligations under the Health Insurance Act, and non-compliance may result in cancellation of their licenses.

02

PRECLINICAL & CLINICAL TRIAL REQUIREMENTS

16. Are clinical trials required to be conducted locally as a condition (stated or implicit) for marketing approval?

17. How are clinical trials funded?

18. What are the requirements for preclinical and clinical trial protocols?
Who must approve the protocols?

19. What are the requirements for consent by participants in clinical trials?

20. May participants in clinical trials be compensated?

21. How are participants in clinical trials protected and indemnified against any harm that arises as a result of participation in the trial?

02 PRECLINICAL & CLINICAL TRIAL REQUIREMENTS

16. Are clinical trials required to be conducted locally as a condition (stated or implicit) for marketing approval?

Under the Pharmaceutical and Medical Device Act (PMD Act), in general, clinical trials relating to applications for marketing authorization approval must be conducted locally. However, data from foreign clinical trials can be used as a reference, depending on the conditions of such foreign clinical trials.

In case of additional indications, public knowledge-based applications are allowed, if foreign countries which have harmonized approval system approved a product and have substantial usage experience. In this exceptional case, local clinical trials are not required.

17. How are clinical trials funded?

Clinical trials are funded by the company which plans to obtain the marketing authorization.

In addition to clinical trials funded by pharmaceutical companies, investigator-initiated clinical trials are allowed, for which research grants are often provided by national centers.

18. What are the requirements for preclinical and clinical trial protocols? Who must approve the protocols?

There is no official requirement for preclinical trial protocols, but they have to comply with Japan GLP.

Clinical trial protocols must be submitted to PMDA. Official approval is not required, but PMDA will review and check the documents at the time of submission.

19. What are the requirements for consent by participants in clinical trials

The investigator must obtain written consent from participants. Before obtaining the written consent, the investigator has to provide written information to the participants that must include information specified in the GCP rules, including the purpose of the clinical trial, the name and access information of the investigator, methods used in the clinical trial, possible adverse events, and trial compensation.

20. May participants in clinical trials be compensated?

Yes. The participants are paid a reasonable amount to compensate them for the burden of participation. Also, for patient participants, other medical expenses related to the clinical trial are paid by the sponsor.

21. How are participants in clinical trials protected and indemnified against any harm that arises as a result of participation in the trial?

The sponsor of the clinical trial is obligated to compensate participants for medical expenses, a medical allowance, and compensation, and also has to prepare for such payments, including obtaining insurance.