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Regulatory Approval process for marketing drug in Japan

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Abstract

For the development of new drug, it requires a greater amount of research work in chemistry, Manufacturing, control, Preclinical and clinical trials. The drug approval process in all regulatory market carrying responsibilities on multiple factors such as data, safety, efficacy to public health in a country. Current constrain of affairs reveals diverse countries need to follow different regulatory requirements for Regulatory approval process for marketing drug in the different regulatory market of the country to ensure safety and efficacy of the product. In order to conduct a regulatory process for approval of a drug, every country has their unique regulation, guidelines, legislation and respective regulatory authority. Japan has its own regulatory authority for drug and medical device called the Ministry of Health, Labour, and Welfare (MHLW), Pharmaceuticals and Medical Devices Agency (PMDA), respectively. In the Japan Ministry of Health, Labour, and Welfare are overseeing the approval procedure of New drug, Generic Drug and Orphan Drug also. In that regard, the Drug Approval process followed in Japan ensures that every company has adhered to specific guideline available in their respective website. The drug comes to market with safety, efficacy to enhance the health of people in Japan by scrutinised process. It results into the longevity of human, which is so apparent in their demographic chart of Japan's Population.

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INTRODUCTION

The pharmaceutical field is being very important and essential in the contemporary world. Ministry of Health, Labour, and Welfare (MHLW), Pharmaceuticals and Medical Devices Agency (PMDA) is responsible for regulating pharmaceutical product and medical device in Japan.

But the Ministry of Health, Labour, and Welfare (MHLW) has many responsible roles other than regulating regulatory processes such as childcare, labour care and public assistance to people in Japan. MHLW also oversees pharmaceutical regulatory affairs in Japan other than veterinary drugs, whose regulation are done by under Ministry of Agriculture, Forestry and Fisheries of the Japanese Government.

Classification of pharmaceutical products

New drug

New drugs, which is considered as drugs, consists of ingredients, desirable dosage, appropriate administration route, or indications, which may or may not clearly different from those of already listed drugs in the Japan Pharmacopeia (JPMA, 2019).

Generic drug

By considering the Guideline for bioequivalence

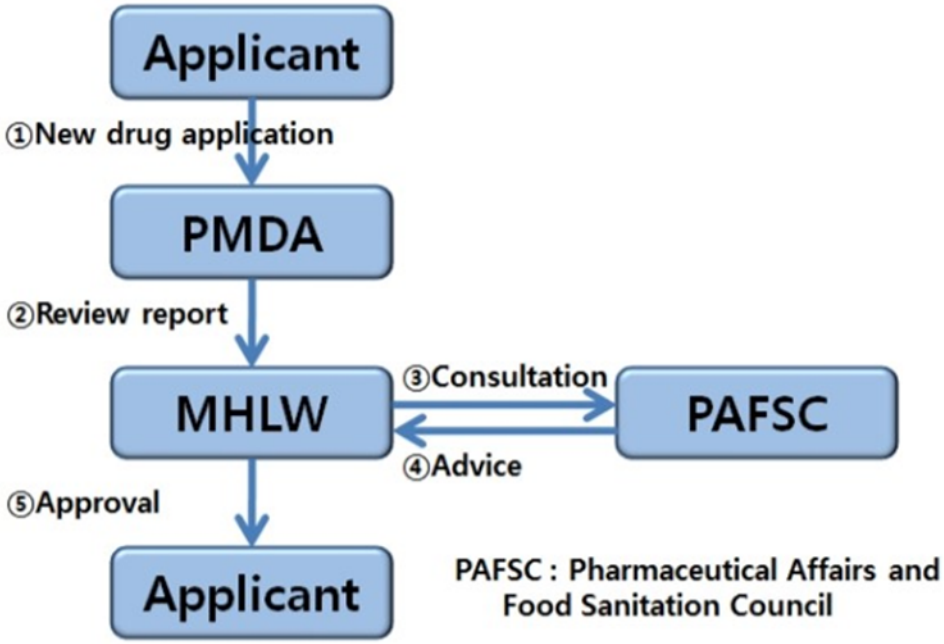

Figure 1: New Drug Marketing Approval Process

studies of generic products, "Generic product" means the products, which composition, strengths, dosage forms, and regimens are similar to innovator's product (JPMA, 2019).

Orphan drug

Article 77 classifies or designated drug as an orphan drug in Japan, depending on the Act on Securing Safety, Efficacy and Quality of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics.

After receiving applications from the applicants for orphan designation, MHLW may classify medical devices and drugs only if satisfies the specified criteria, such as the number of patients suffered from the disease should be less than 50,000 in Japan.

DRUG APPROVAL SYSTEM

Clinical trial notification for new drug development-Overview

For new drug manufacturing and marketing, collected data should be submitted with approval applications in order to conduct clinical studies. Good Clinical Practice, along with its study protocol required by MHLW beforehand. It also has a set of standards needs to be met by a sponsor of clinical trials and also set numerous requirements to be fulfilled by the sponsor.

Type of clinical trial notification

1. Industry-Sponsored Clinical Trial
2. Investigator Initiated Clinical Trial

Products requirement of clinical trial notification

New drug, their administration routes, their combination drugs, indications or dosage and administration, drugs manufactured using gene recombinant technology, drugs considered to be biological products, drugs containing the same active pharmaceutical ingredients, for which the re-examination duration has not been over yet (Riku, 2005).

Interview advice meeting

Quality of clinical should be enhanced and improved at par with standards. So, there is a consultation for clinical study protocols established by PMDA.

Review period

Clinical trials contract can be ended only after thirty days of the initial intimation of the study protocol received by the PMDA. Protocols can be submitted after the start of the study, but within 30 days for drugs, shall be used in the emergence period, where it has a serious effect on the health of human.

New drug application (NDA)

Procedure

Applicant must submit an application to PMDA for Marketing Authorisation. The work of PMDA in approval of the New Drug Application (NDA)

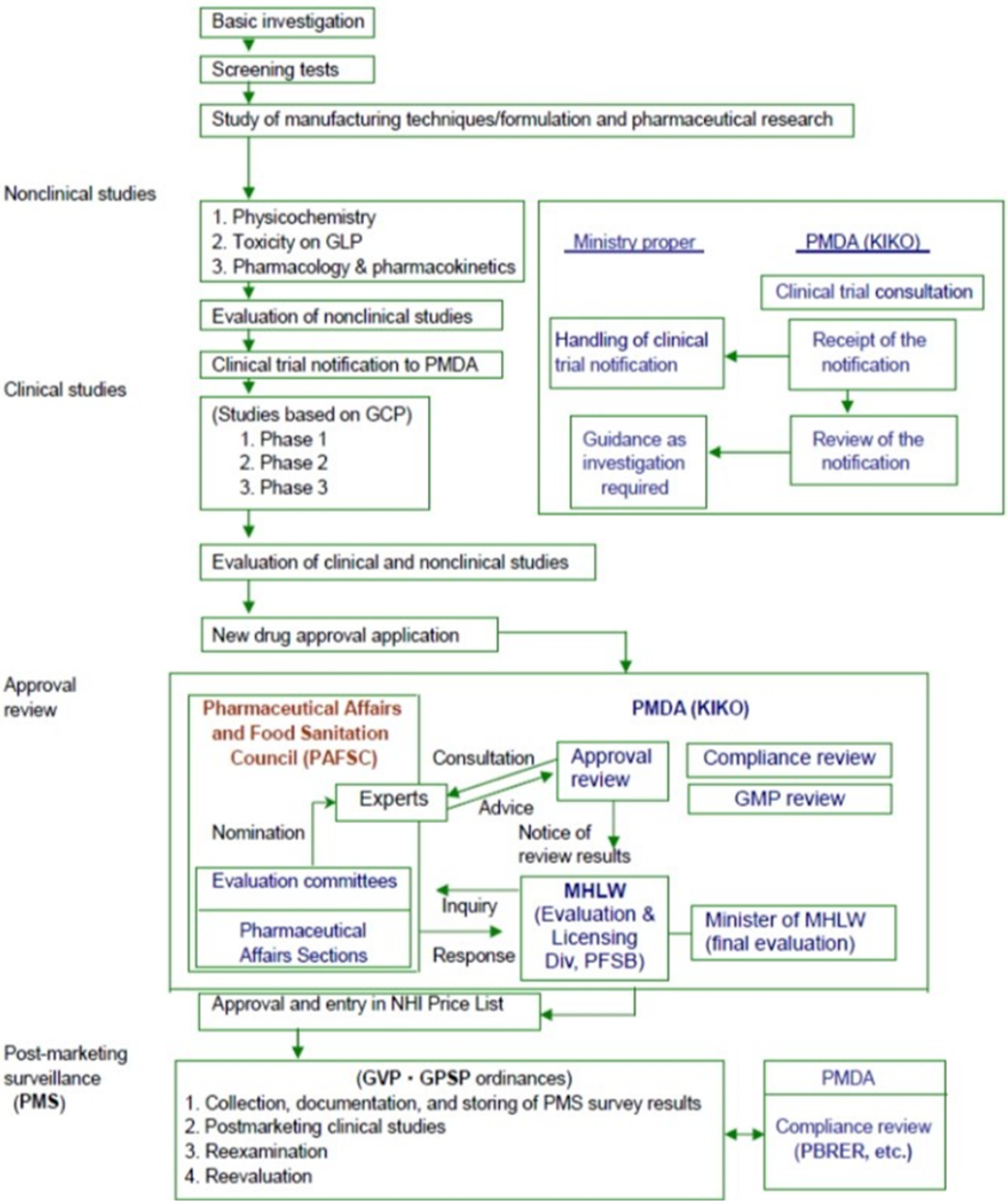

Figure 2: Flowchart of New Drug Development and Approval

involved is Approval review and clinical trial consultation. After PMDA receives an application, PMDA will undertake a review of the application data, Good Clinical Practice, on-site inspection by review teams of the PMDA.

Then finally, they prepare a review report once marketing authorization are received by the PMDA. The Review process is done by expert meetings to discuss very important problems, which consists of review team members and also experts.

A general review conference will be conducted and participated by experts, team members and representatives of the applicant. "list of persons involved in the compilation of attached data" and "list of competitive products and companies" in relation to clinical trials involved person shall submit an application after submission of the application but prior to review meeting and meeting of the committee on drugs is necessary to submit. Figure 1 has expressed an overview of the New Drug Marketing Approval Process.

PAFSC consultation

After the PMDA review, Related committees and the Pharmaceutical Affairs Committee shall be consulted with PAFSC on the basis of the review report. It will be ensured that whether standards are met with compliance review of GMP, Once PAFSC report is obtained. The Applicant will get a grant from the minister for manufacturing of new drug or grant of market approval.

Review period

In general, the standard review period for approval of a new drug by MHLW is 1 year. Then, the allotted time for an applicant is also 1 year. So, Approval for marketing extends up to a maximum period of 2 years. If the longer time required by the applicant to respond to inquires, MHLW asked the applicant to withdraw the application. Time period to review is changed to 9 months for priority reviews and 12 months for ordinary. It is shown by the Minister in 2012 that the median, standard timeline for review of new drug approval is 12 months (Kuribayashi *et al.*, 2015).

Required documents

Origin or background of discovery, Manufacturing methods, conditions of use in foreign countries, standards and test methods, Pharmacological action data, Stability data, Absorption, distribution, metabolism, and excretion data, Acute, subacute, and chronic toxicity, teratogenicity, and other types of toxicity data and Clinical studies data. Complete procedure of Approval of New Drug can be easily understandable by analysing the Figure 2.

Use of foreign clinical data

There were two issued notifications for relation to an acceptance of foreign clinical data,

1. “Handling of Data on Clinical trials on Drugs Performed in Foreign Countries”.
2. “Ethnic Factors to be Considered in the Acceptance of Foreign Clinical Trial Data” and its Q & A.

Drug capability to affect the ethnic factors have to be evaluated. The foreign data can be accepted if it is extrapolated to the Japanese population. Acceptance is left to the discretion of authorities based on its safety and efficacy.

If accepted, it is necessary to perform studies after consultation with PMDA. It is mandatory to conduct pharmacokinetic studies in Japanese people as the bridging study. In order to achieve efficient development and to eliminate time lag in approval, basic concepts of global clinical trials have been compiled to function it smoothly to achieve safety concerns (PMDA, 2018).

FEE STRUCTURE

For approval of new product manufacturing/marketing approval, fees are ¥533,800 to MHLW and ¥30,535,100 to PMDA. For approval of generic product marketing, Licence for marketing generic prescription drugs, fees are ¥28,100 to MHLW and ¥632,200 to PMDA. Licence for marketing business fees are ¥28,100 to MHLW, ¥110,300 to PMDA.

CONCLUSION

Japan remains a demanding market in the current scenario for drug approval because of its demographic values. Primary responsibility is to safeguard public health. Public regulatory authorities should ensure the Pharmaceutical company complies with the required regulation. By keeping watch on regulatory changes, a company should consult for appropriate filling without hurdles.

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Conflict of Interest

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