PSB Notification No. 1009-1
October 9, 2024

To: Prefectural Governors

Director of Pharmaceutical Safety Bureau,
Ministry of Health, Labour and Welfare
(Official seal omitted)

Partial Revision of "Approval Applications for Drugs"

Marketing approval applications for drugs have been handled according to "Approval Applications for Drugs" (PFSB Notification No. 1121-2 of the Pharmaceutical and Food Safety Bureau, dated November 21, 2014, hereinafter referred to as "Director-General Notification"). Please be aware that Attached Table 2-(2) of Director-General Notification has recently been revised as follows based on the report in switch OTCWG, and thoroughly notify related businesses and organizations under your jurisdiction of the revision.

This notification applies to approval applications for drugs filed on October 9, 2024 or later.

Note

"5 for E (bioequivalence)" and "G (data on clinical study results)" in the right column of "(4) Drugs with new active ingredients requiring guidance (over-the-counter)" in Attached Table 2-(2) are changed to △.

(Reference: Whole text after revision)

Section 1 General Rules

1 In accordance with the provisions in Article 14 of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Act No. 145 of 1960, hereinafter referred to as "Act") after the revision by the Act Partially Amending the Pharmaceutical Affairs Act, etc. (Act No. 84 of 2013), marketing approval of drugs require the following process: When a party intends to market a drug files the application, necessary review of active ingredients and content, dosage and administration, indications, adverse reactions, etc. of the drug related to the application shall be conducted, and the Minister of Health, Labour and Welfare shall grant approval for each product based on the review. At the time of approval application, presentation of sufficient evidence to verify the quality, efficacy, and safety of the drug related to the application using the data confirmed to be ethical, scientific, and reliable based on the academic standards of medicine, pharmaceutical sciences, etc. at that time is also required.

2 The following terms are used in this notification.

(1) New drugs refer to new drugs specified in Article 14-4, Paragraph 1, Item 1 of the Act.

(2) Prescription drugs refer to drugs that are used by physicians or dentists or supplied for the purpose of use based on the prescription or instruction given by physicians or dentists.
Drugs that fall in any of the following categories shall be treated with prescription drugs, in principle.

A Prescription medications, poisonous drugs, and powerful drugs. Poisonous drugs and powerful drugs that are not used directly on the human body (e.g., insecticides) are excluded.

B Drugs that are used by physicians or dentists themselves or indicated for diseases that possibly lead to serious illness, disability, or death unless they are used under the guidance and supervision of physicians or dentists

C Other drug use of which by physicians or dentists themselves or under the guidance and supervision of physicians or dentists is considered, based on their dosage forms, pharmacological actions, etc., to be appropriate

(3) Drugs requiring guidance refer to drugs requiring guidance specified in Article 4, Paragraph 5, Item 3 of the Act.

(4) Over-the-counter drugs refer to over-the-counter drugs specified in Article 4, Paragraph 5, Item 4 of the Act.

(5) Drugs with new active ingredients refer to drugs containing ingredients that are not contained in any of the drugs already approved for marketing or drugs listed in Japanese Pharmacopoeia (hereinafter referred to as "approved drugs, etc.") as active ingredients.

(6) Drugs with new routes of administration refer to drugs with the same active ingredients as those of approved drugs, etc., but different administration routes (i.e., oral, subcutaneous/intramuscular, intravenous, percutaneous, transrectal, transvaginal, ocular, otic, nasal, inhaled, etc.).

(7) Drugs with new indications refer to drugs with the same active ingredients and routes of administration as those of approved drugs, etc., but different indications.

(8) Follow-on biologics refer to drugs that show comparability with biotechnology-derived pharmaceuticals already approved for marketing.

(9) Drugs in new dosage forms refer to drugs with the same active ingredients, routes of administration, and indications as those of approved drugs, etc., but new dosage forms that require different regimen, etc. developed by pharmaceutical alterations such as those for control of release. Drugs in an additional dosage form specified in (11) are excluded.

(10) Drugs with a new dosage refer to drugs with the same active ingredients and routes of administration as those of approved drugs, etc., but different dosage.

(11) Drugs in an additional dosage form refer to drugs with the same active ingredients, routes of administration, indications, and dosage and administration as those of approved drugs, etc., but different dosage forms or strength.

(12) Combination drugs refer to drugs containing 2 or more active ingredients.

(13) New combination drugs refer to prescription combination drugs that differ from combination drugs listed in Japanese Pharmacopoeia or combination drugs approved for marketing as prescription drugs in active ingredients or combination ratio. Combination prescription drugs with similar formulations specified in (14), digestive enzyme preparations,

and cataplasm, etc. with mild actions that are considered not to be novel when comprehensively evaluated are excluded.

(14) Combination prescription drugs with similar formulations refer to prescription combination drugs judged to have similar active ingredients and combination ratio to those of combination drugs listed in Japanese Pharmacopoeia or combination drugs approved for marketing as prescription drugs.

(15) Biological products, etc. refer to biological products such as vaccines and blood products, recombinant DNA technology-derived drugs, cell culture-derived products, and other biotechnology-derived pharmaceuticals/drugs of biological origin listed in Minimum Requirements for Biological Products.

(16) Drugs with new active ingredients requiring guidance (over-the-counter) refer to drugs requiring guidance and over-the-counter drugs (hereinafter referred to as "guidance/OTC drugs") other than drugs with new active ingredients, containing ingredients that are not contained in already approved guidance/OTC drugs as active ingredients.

(17) Drugs with new routes of administration requiring guidance (over-the-counter) refer to guidance/OTC drugs other than drugs with new routes of administration, that have the same active ingredients as those of already approved guidance/OTC drugs, but have different routes of administration.

(18) Drugs with new indications requiring guidance (over-the-counter) refer to guidance/OTC drugs other than drugs with new indications, that have the same active ingredients and administration routes as those of already approved guidance/OTC drugs, but have different indications.

(19) Over-the-counter (requiring guidance) drugs in new dosage forms refer to drugs in new dosage forms that have the same active ingredients, routes of administration, and indications as those of already approved guidance/OTC drugs, but have new dosage forms that require different regimen, etc. developed by pharmaceutical alterations such as those for control of release, and are classified into either drugs requiring guidance or over-the-counter drugs.

(20) Over-the-counter (requiring guidance) drugs with a new dosage refer to drugs with a new dosage that have the same active ingredients and routes of administration as those of already approved guidance/OTC drugs, but have different dosage, and are classified into either drugs requiring guidance or over-the-counter drugs.

(21) Over-the-counter (requiring guidance) new combination drugs refer to drugs consisting of ingredients contained in already approved guidance/OTC drugs as active ingredients, that have combinations of active ingredients different from and not considered similar to those of already approved guidance/OTC drugs, and are classified into either drugs requiring guidance or over-the-counter drugs. Specifically, drugs from A to F in 1 (1)[1] in Section 2 of the summary in PFSB Notification No. 0331053 of the Pharmaceutical and Food Safety Bureau, dated March 31, 2008 are over-the-counter (requiring guidance) new combination drugs.

(22) OTC combination drugs with similar prescription refer to drugs consisting of ingredients contained in already approved over-the-counter drugs as active ingredients that have combinations of active ingredients similar to the formulation of already approved over-the-counter drugs.

(23) OTC drugs with similar dosage forms refer to over-the-counter drugs other than drugs in new dosage forms, that have the same active ingredients, administration routes, and indications as those of already approved over-the-counter drugs, but have different dosage forms, and do not fall into the category of (19).

(24) Other over-the-counter drugs refer to over-the-counter drugs that do not fall into the categories from (1) to (23).

Section 2 Data that should be attached to marketing application form

1 The studies for preparation of the data to be attached to marketing application forms must be those conducted properly in compliance with Good Laboratory Practice (GLP) for Drugs, Good Clinical Practice (GCP) for Drugs, and the data integrity standards for product applications at facilities with sufficient equipment by experienced investigators based on the academic standards of medicine, pharmaceutical sciences, etc. at that time.

2 Data that should be attached to marketing application forms must be prepared in Japanese, in principle. However, if original data are in English, it is acceptable to submit the original and its summary in Japanese.

3 The methods for editing the data to be attached to marketing application forms and the guidance for preparation of these data shall be separately specified as necessary.

4 The content of the data listed in Article 40, Paragraph 1, Item 1 of "Ministerial Ordinance for Enforcement of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices after revision" (Ministry of Health and Welfare Ordinance No. 1 of 1961) associated with "Ministerial Ordinance on the Development of Related Ministerial Ordinances in Accordance with Enforcement of Cabinet Order on the Development of Related Cabinet Orders and Transitional Measures in Accordance with the Act Partially Amending the Pharmaceutical Affairs Act and Enforcement of the Act Partially Amending the Pharmaceutical Affairs Act (Ordinance No. 87 of Ministry of Health, Labour and Welfare in 2014) are largely the data listed on the right column in Attached Table 1.

5 The scope of data to be attached to marketing application forms shall be the data shown in the right column in accordance with the categories in the left column in Attached Table 2, in principle.

In this case, if it is difficult to determine the classification category, the category with a larger number of required data shall be adopted, and if two or more categories are applicable, data required for each category shall be required. However, if it is technically impossible to conduct the studies for preparation of the data or implementation of studies is considered meaningless from the viewpoint of the type, usage, etc. of the drug concerned, it is unnecessary to attach the data concerned.

6 For drugs falling under the categories from (1) to (9-2) of Attached Table 2-(1) and drugs falling under the categories from (1) to (7)-[2] of Attached Table 2-(2), an outline of the data that accurately and concisely summarizes the content of the attached data and includes information on indications, dosage and administration, draft precautions, and reasons for setting them should be submitted. In principle, the outline of data must be written in Japanese.

7 When an application for a drug that is considered to have the same ingredients and content, dosage and administration, and indications as those of a new drug is made during the re-examination period of the new drug, data equivalent to or more than those for the new drug concerned need to be attached.

8 When an application for a drug considered to have the same ingredients and content, dosage and administration, and indications as those of a guidance/OTC drug for which a survey on the safety in its use is required pursuant to the provisions in Article 79 of the Act is made during the survey concerned, data equivalent to or more than those for the drug requiring the survey need to be attached.

9 Even if the above 7 or 8 are applicable, in the case of an application for partial change in approved product information based on Article 14, Paragraph 9 of the Act, some of the data to be attached do not need to be attached for that reason.

10 When an excipient that has not been used as an excipient in already approved drugs, etc. is added or a previously used excipient is used for a different route of administration or in an amount exceeding the amount for previous use, data on the quality, safety, etc. of the excipient concerned should also be submitted.

11 Data to be attached to marketing application forms for in vitro diagnostics shall be in accordance with PAB Notification No. 662 of the Pharmaceutical Affairs Bureau, dated June 29, 1985, "Handling of in vitro diagnostics."

12 Notwithstanding the foregoing, data to be attached to marketing application forms for the drugs that are intended solely for use for diagnosis of diseases and are applied to the human skin and insecticides or disinfectants that are not used directly on the human body shall be separately specified.

Section 3 Revision of Notification

1 Unless separate notifications, etc. are issued, existing notifications, etc. shall continue to be applied by reading the "Pharmaceutical Affairs Law" as the "Pharmaceuticals and Medical Devices Act" and "over-the-counter drugs" as "guidance/OTC drugs."

2 Notifications, etc. shall be revised in accordance with the revised Act, as necessary.

Attached Table 1

Left column	Right column
A Origin or history of discovery and usage conditions in foreign countries etc.	1 Origin or history of discovery 2 Usage conditions in foreign countries " 3 Characteristics and comparison with other drugs, etc. "
B Manufacturing process, specifications, etc.	1 Structural determination and physicochemical properties, etc. " 2 Manufacturing process " 3 Specifications "
C Stability	1 Long-term storage test " 2 Stress test " 3 Accelerated test "
D Pharmacological actions	1 Primary pharmacodynamics " 2 Secondary pharmacology/safety pharmacology " 3 Other pharmacology "
E Absorption, distribution, metabolism, and excretion	1 Absorption " 2 Distribution " 3 Metabolism " 4 Excretion " 5 Bioequivalence " 6 Other pharmacokinetics "
F Acute toxicity, subacute toxicity, chronic toxicity, teratogenicity, and other toxicities	1 Single-dose toxicity " 2 Repeat-dose toxicity " 3 Genotoxicity " 4 Carcinogenicity " 5 Reproductive and developmental toxicity " 6 Local tolerance " 7 Other toxicities "
G Clinical data	Clinical data "
H Descriptions in package inserts, etc. specified in Article 52, Paragraph 1 of the Act	Descriptions in package inserts, etc. "

Attached Table 2-(1) Prescription drugs

Left column	Right column							
	A	B	C	D	E	F	G	H
	1 2 3	1 2 3	1 2 3	1 2 3	1 2 3 4 5 6	1 2 3 4 5 6 7		
(1) Drugs with new active ingredients	○ ○ ○	○ ○ ○	○ ○ ○	○ ○ △	○ ○ ○ ○ × △	○ ○ ○ △ ○ △ △	○	○
(2) New combination drugs	○ ○ ○	× ○ ○	○ ○ ○	○ △ △	○ ○ ○ ○ × △	○ ○ × × × △ ×	○	○
(3) Drugs with new routes of administration	○ ○ ○	× ○ ○	○ ○ ○	○ △ △	○ ○ ○ ○ × △	○ ○ × △ ○ △ △	○	○
(4) Drugs with new indications	○ ○ ○	× × ×	× × ×	○ × ×	△ △ △ △ × △	× × × × × × ×	○	○
(5) Drug with new dosage forms	○ ○ ○	× ○ ○	○ ○ ○	× × ×	○ ○ ○ ○ × △	× × × × × × ×	○	○
(6) Drugs with a new dosage	○ ○ ○	× × ×	× × ×	○ × ×	○ ○ ○ ○ × △	× × × × × × ×	○	○
(7) Follow-on biologics	○ ○ ○	○ ○ ○	○ △ △	○ × ×	△ △ △ △ × △	△ ○ × × × △ △	○	○
(8) Drugs in an additional dosage form (during re-examination period) (8-2) Drugs in an additional dosage form (not during re-examination period)	○ ○ ○	× ○ ○	△ △ ○	× × ×	× × × × ○ ×	× × × × × × ×	×	○
(9) Combination prescription drugs with similar formulations (during re-examination period) (9-2) Combination prescription drugs with similar formulations (not during re-examination period)	○ ○ ○	× ○ ○	○ ○ ○	△ △ ×	× × × × × ×	○ △ × × × △ ×	○	○
(10) Other drugs (during re-examination period) (10-2) Other drugs ((10) related to changes in the manufacturing process of biological products, etc.) (10-3) Other drugs (not during re-examination period) (10-4) Other drugs ((10-3) related to changes in the manufacturing process of biological products, etc.)	× × ×	× △ ○	× × ○	× × ×	× × × × ○ ×	× × × × × × ×	×	○ 1)

Note 1) The symbols and numbers in the right column indicate the symbols and numbers of the data specified in Attached Table 1. In principle, ○ means that the data should be attached, × means that it is unnecessary to attach the data, and △ means that the necessity shall be judged for each drug.

Note 2) Note 1) in the right column shall be as follows.

1) In principle, it is not necessary to attach the data in H only for the application for the content that does not cause changes in the descriptions in the package insert such as changes in the manufacturing process or test method.

Attached Table 2-(2) Guidance/OTC drugs

Left column	Right column							
	A	B	C	D	E	F	G	H
	1 2 3	1 2 3	1 2 3	1 2 3	1 2 3 4 5 6	1 2 3 4 5 6 7		
(1) Drugs with new active ingredients	○ ○ ○	○ ○ ○	○ ○ ○	○ ○ △	○ ○ ○ ○ × △	○ ○ ○ △ ○ △ △	○	○
(2) Drugs with new routes of administration	○ ○ ○	× ○ ○	○ ○ ○	○ △ △	○ ○ ○ ○ × △	○ ○ × △ ○ △ △	○	○
(3)-[1] Drugs with new indications	○ ○ ○	× × ×	× × ×	○ × ×	△ △ △ △ × △	× × × × × × ×	○	○
(3)-[2] Drug with new dosage forms	○ ○ ○	× ○ ○	○ ○ ○	× × ×	○ ○ ○ ○ × △	× × × × × × ×	○	○
(3)-[3] Drugs with a new dosage	○ ○ ○	× × ×	× × ×	× × ×	○ ○ ○ ○ × △	× × × × × × ×	○	○
(4) Drugs with new active ingredients requiring guidance (over-the-counter)	○ ○ ○	× × ○	△ × △ 2)	× × ×	△ × × × △ ×	△ △ × × × △ △	△	○
(5)-[1] Drugs with new routes of administration requiring guidance (over-the-counter)	○ ○ ○	× × ○	△ × △ 2)	× × ×	△ × × × × ×	△ △ × × × △ △	○	○
(5)-[2] Drugs with new indications requiring guidance (over-the-counter)	○ ○ ○	× × ×	× × ×	× × ×	△ × × × × ×	× × × × × × ×	○	○
(5)-[3] Over-the-counter (requiring guidance) drugs in new dosage forms	○ ○ ○	× × ○	△ × △ 2)	× × ×	△ × × × × ×	× × × × × × × ×	○	○
(5)-[4] Over-the-counter (requiring guidance) drugs with a new dosage	○ ○ ○	× × ×	× × ×	× × ×	△ × × × × ×	× × × × × × × ×	○	○
(6) Over-the-counter (requiring guidance) new combination drugs	○ ○ ○	× × ○	△ × △ 2)	× × ×	△ × × × × ×	△ △ × × × × △ ×	○	○
(7)-[1] OTC combination drugs with similar prescription	× × ○	× × ○	△ × △ 2)	× × ×	△ × × × × ×	△ △ × × × × × ×	×	○
(7)-[2] OTC drugs with similar dosage forms	× × ○	× × ○	△ × △ 2)	× × ×	△ × × × × ×	× × × × × × × ×	×	○
(8) Other over-the-counter drugs (products meeting approval standards, etc.)	× × ○ 1)	× × ○	△ × △ 2)	× × × ×	× × × × × × ×	× × × × × × × ×	×	×

Note 1) The symbols and numbers in the right column indicate the symbols and numbers of the data specified in Attached Table 1. In principle, ○ means that the data should be attached, × means that it is unnecessary to attach the data, and △ means that the necessity shall be judged for each drug.

Note 2) Notes 1) and 2) in the right column shall be as follows.

1) For drugs that meet the approval standards, it is acceptable to attach a comparison table of the active ingredients and their content in the approval standards and the product submitted for registration. For drugs other than those meeting the approval standards, the rationale for the formulation design, efficacy, safety, etc. shall be sufficiently explained.

2) Long-term storage test results are required for the products for which the stability for at least 3 years cannot be estimated from the accelerated test.

However, if the shelf life can be tentatively set at 1 year or longer by a long-term storage test at the time of application, the approval application may be made even in the middle of the long-term storage test. In such a case, the applicant shall submit by the time of approval the results of the long-term storage test that was continued thereafter.