Publication registration number
11-1471057-000238-01

MINISTRY OF FOOD AND DRUG SAFETY
National Institute
of Food and Drug Safety Evaluation

Guide to Drug Approval System in Korea

April 2017

MINISTRY OF FOOD AND DRUG SAFETY
National Institute of Food and Drug Safety Evaluation

Abbreviation

MFDS : Ministry of Food and Drug Safety

NIFDS : National Institute of Food and Drug Safety Evaluation

CTD : Common Technical Document

DMF : Drug Master File

IND : Investigational New Drug Application

NDA : New Drug Application

GMP : Good Manufacturing Practice

Notice

1. Due to the purpose of this document, most of the information was quoted directly from the MFDS website and related regulations.
2. This document is limited only to pharmaceutical products, not applicable to biological and herbal products.
3. When referring to the contents of this document, check the up-to-date information including related laws and regulations, and revision of guidelines.

CONTENTS

Ⅰ. Drug Regulatory Agency[1)]

1. Ministry of Food and Drug Safety

1.1 Organization

The Ministry of Food and Drug Safety (MFDS) administers safety affairs related to food, functional food, drugs, narcotics, cosmetics, quasi-drugs, and medical devices, etc. The organization of the MFDS is as shown in the chart below (see Figure 1) and the Pharmaceutical Safety Bureau is responsible for pharmaceutical affairs.

1.2 Task

The Pharmaceutical Safety Bureau establishes comprehensive plans for safety management of drugs and narcotics, and manages affairs related to laws and regulations enactment/revision, quality control of drug, and clinical trials. Each Division under the Bureau is responsible for the following tasks:

(1) Pharmaceutical Policy Division:

- Develops policies related to drug safety management
- Enacts and revises drug related laws/regulations and notifications
- Controls drug approval system and develops related policies
- Designates orphan drugs and operates the Korea Orphan Drug Center
- Operates and manages the Central Pharmaceutical Affairs Council (CPAC)
- Supports expansion of export market for drugs

1) 「Enforcement Regulation on Organization of the Ministry of Food and Drug Safety and its Affiliates」

(2) Pharmaceutical Management Division:

- Establishes and coordinates pharmacovigilance plans
- Establishes and coordinates guidance and control plan for drug labeling, advertisement, and safety and distribution management
- Designates and controls drugs that may cause concerns of misuse/abuse
- Analyzes risk factors of each pharmaceutical product and reviews alternatives for safety management
- Manages the distribution reporting data of the Korea Pharmaceutical Information Service (KPIS)
- Establishes and manages comprehensive plan for collection and examination of drugs
- Establishes and manages comprehensive plan for recall and disposal of drugs
- Manages drug renewals

(3) Narcotics Policy Division:

- Develops policies and establishes/coordinates comprehensive plans for narcotics and their drug substances
- Enacts and revises narcotics and their drug substances related laws/regulations and notifications
- Approves importers/exporters, manufacturers, quasi-manufacturers, and products of narcotics
- Designates and controls narcotics and temporary narcotics
- Pursues international cooperation in narcotics and their drug substances

(4) Narcotics Management Division:

- Establishes and manages comprehensive plan for narcotics safety management
- Manages overall operation of the Narcotics Information Management System
- Establishes and coordinates general plan for distribution and vigilance of narcotics and their drug substances
- Establishes guidance and control plan for sale of narcotics, including prohibition of handling, advertisement, and labeling

(5) Pharmaceutical Quality Division:

- Controls Good Manufacturing Practice (GMP) of drug products and drug substances
- Establishes and manages comprehensive plan for on-site inspection on drug products and drug substances subject to registration
- Establishes GMP related training plan
- Designates and controls training center for personnel responsible for drug manufacturing/import
- Pursues international cooperation in GMP

(6) Clinical Trials Management Division:

- Enacts and revises notifications related to clinical trials, non-clinical trials, and bioequivalence tests
- Approves and manages overall drug clinical trial protocols and bioequivalence test protocols
- Approves the use of investigational drugs in case of emergency and for the purpose of treatment
- Enacts and revises test animal related laws/regulations and notifications

(7) Pharmaceutical Approval and Patent Management Division:

- Manages drug approval and patent related issues
- Registers and manages drug patent information and controls the patent list system
- Enacts and revises regulations related to registration and management of drug patent list
- Establishes and controls the patent list database for drug-approval patent linkage system
- Provides supports for drug patent lawsuits

(8) Pharmaceutical Safety Evaluation Division:

- Collects and manages ADR information of drug products and quasi-drugs
- Assesses ADR information
- Manages drug safety information and takes follow-up measures
- Supports and supervises the Korea Institute of Drug Safety & Risk Management (KIDS)
- Designates and operates training centers for personnel responsible for drug safety management

1.3 Regional Office of Food and Drug Safety

Regional Offices of Food and Drug Safety (hereinafter referred to as "Regional Office") are responsible for safety management including drug approval. The Regional Offices are responsible for the following tasks:

(1) Approval (only applicable to the case where drug equivalence test data are submitted) and notification of drug manufacturing/marketing and import;

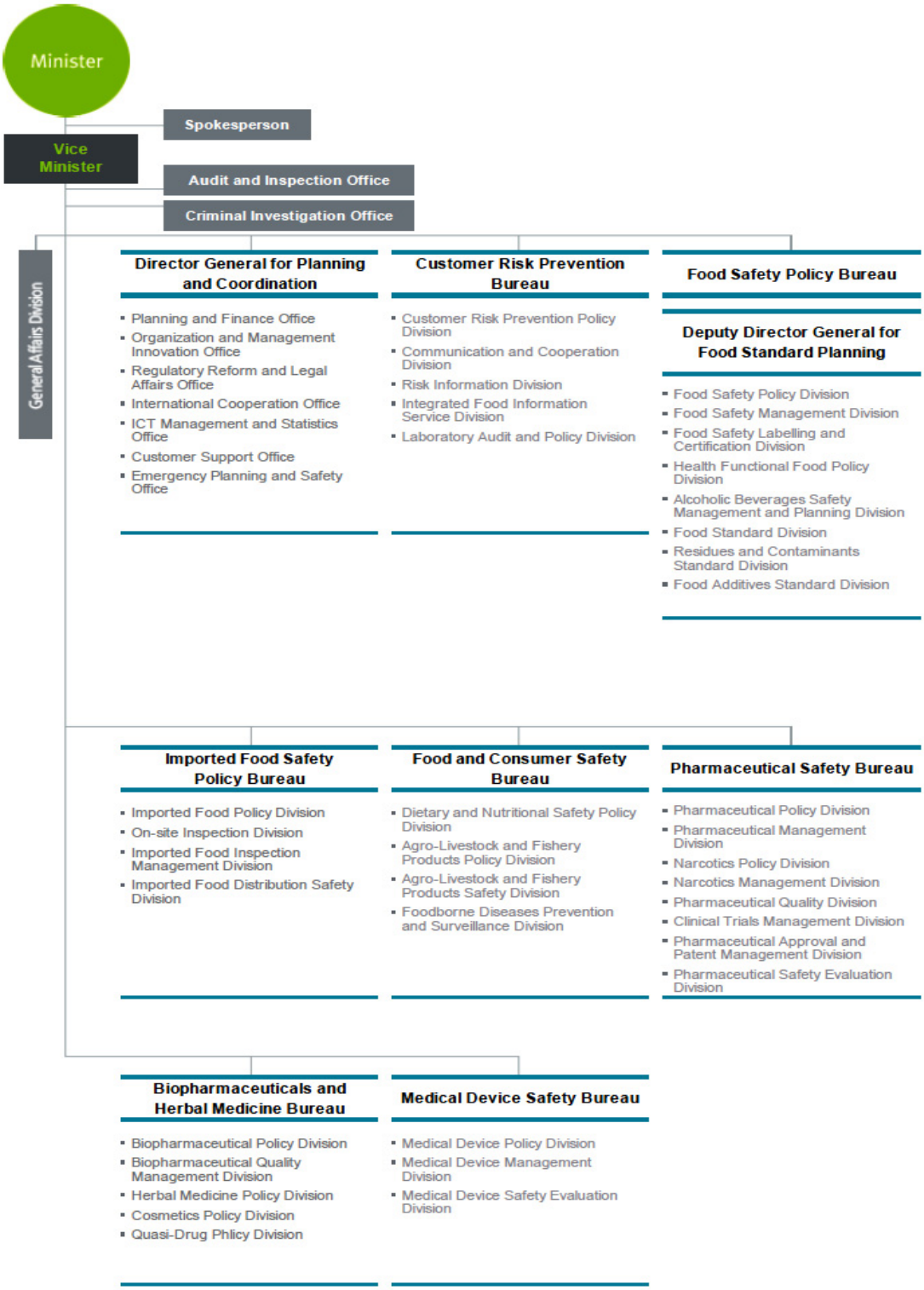
(2) Approval (only applicable to the case where safety and efficacy review data are not necessarily required for submission) and notification of quasi-drug manufacturing and import; and

(3) Other various tasks including inspection and supervision on drugs and GMP assessment, etc.

There are six (6) Regional Offices: Seoul Regional Office, Busan Regional Office, Gyeongin Regional Office, Daegu Regional Office, Gwangju Regional Office, and Daejeon Regional Office.

1.4 Website

- Ministry of Food and Drug Safety (MFDS): http://www.mfds.go.kr/eng
- MFDS e-Drug Service (ezdrug): http://ezdrug.mfds.go.kr (in Korean only)

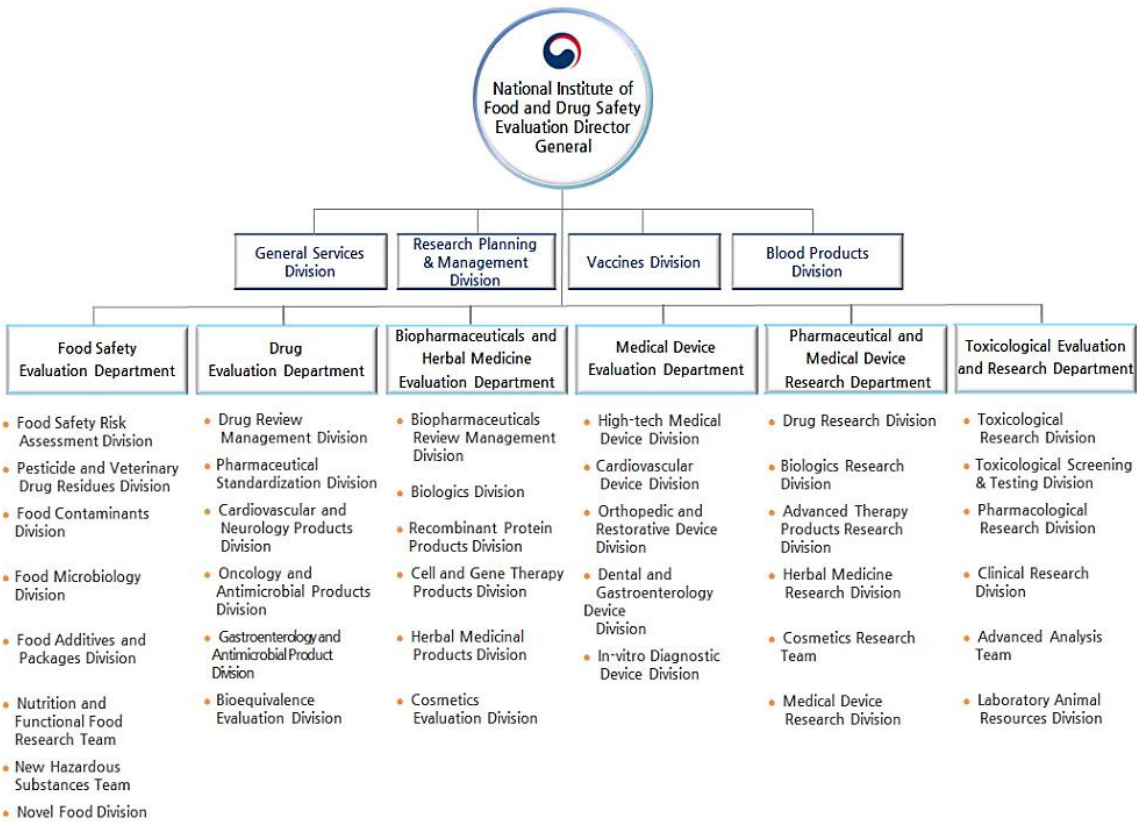


[Figure 1] Organization of Ministry of Food and Drug Safety

2. National Institute of Food and Drug Safety Evaluation

2.1 Organization

As an affiliate of the MFDS, the National Institute of Food and Drug Safety Evaluation (NIFDS) is responsible for conducting review, test, analysis, research, and risk assessment of food, drugs, cosmetics, and medical devices. The organization of the NIFDS is shown in Figure 2 as below:



[Figure 2] Organization of National Institute of Food and Drug Safety Evaluation

2.2 Task

The Drug Evaluation Department of the NIFDS consists of Drug Review Management Division; Pharmaceutical Standardization Division; Cardiovascular and Neurology Products Division; Oncology and Antimicrobial Products Division; Gastroenterology and Metabolism Products Division; and Bioequivalence Evaluation Division. Regarding drug review, each Division is responsible for reviewing and managing drug approval and review data; and establishing guidelines as below:

(1) Drug Review Management Division:

- Manages overall review of drug marketing approval and notification
- Establishes and revises guidelines and guides on drug approval and review
- Conducts prior review of pharmaceuticals
- Discloses drug review information
- Manages and improves Good Review Practice (GRP)
- Conducts safety and efficacy review on off-label use of approved/notified drugs
- Supports registration of drug patent information
- Supports international cooperation by operating the APEC Harmonization Center (AHC) and other activities

(2) Pharmaceutical Standardization Division:

- Establishes drug standards and specifications
- Collects information on recently developed drug standards and specifications from international organizations and other economies; and compares and reviews such information
- Reviews Drug Master File (DMF) data
- Reviews quality of drug substances
- Reviews quality data of generic drugs
- Establishes and revises guidelines and guides on concerned drug approval and review

(3) Cardiovascular and Neurology Products Division:

- Conducts quality, safety, and efficacy review of cardiovascular, respiratory, central nervous, and peripheral nervous drugs and narcotics
- Reviews clinical trial protocols for concerned drugs
- Reviews changes to concerned drug data after approval/notification
- Reviews re-evaluation and reassessment data for concerned drugs
- Establishes and revises guidelines and guides on concerned drug approval and review

(4) Oncology and Antimicrobial Products Division:

- Conducts quality, safety, and efficacy review of antibiotics, chemotherapeutic agents, anti-cancer drugs, anthelmintics, anti-allergy drugs, radiopharmaceuticals, and diagnostic drugs
- Reviews clinical trial protocols of concerned drugs
- Reviews changes to concerned drug data after approval/notification
- Establishes and revises guidelines and guides on concerned drug approval and review

(5) Gastroenterology and Metabolism Products Division:

- Conducts quality, safety, and efficacy review of gastrointestinal, urogenital organ, hormone, sensory organ, and metabolic drugs
- Reviews clinical trial protocols of concerned drugs
- Reviews changes to concerned drug data after approval/notification
- Reviews re-evaluation and reassessment data for concerned drugs
- Establishes and revises guidelines and guides on concerned drug approval and review

(6) Bioequivalence Evaluation Division:

- Reviews bioequivalence test protocol, result report, and reassessment
- Reviews equivalence test result report
- Reviews bioequivalence of generic substitution
- Establishes and revises guidelines and guides on concerned drug approval and review

2.3 Website

National Institute of Food and Drug Safety Evaluation (NIFDS):
http://www.nifds.go.kr/en

Ⅱ. Related Laws and Regulations

1. Pharmaceutical Affairs Act

The 「Pharmaceutical Affairs Act (hereinafter referred to as "Act")」 prescribes requirements for pharmaceutical affairs such as license of pharmacist and drug marketing business and consists of nine (9) Chapters and 98 Articles as below:

(1) Chapter I. General Provisions

(2) Chapter II. Pharmacists and Oriental Pharmacists

(3) Chapter III. Pharmaceutical Affairs Council

(4) Chapter IV. Pharmacies and Dispensing Drugs

(5) Chapter V. Manufacture, Importation, etc. of Drugs, etc.
Chapter V-2. Patent Lists, Prohibition of Sale, etc. of Drugs

(6) Chapter VI. Handling of Drugs, etc.

(7) Chapter VII. Supervision

(8) Chapter VIII. Supplementary Provisions

(9) Chapter IX. Penalty Provisions

**As of December 2016*

In addition, there are the 「Enforcement Decree on the Pharmaceutical Affairs Act」 (Presidential Decree) and the 「Enforcement Regulation on the Pharmaceutical Affairs Act」 (Ministerial Decree of the Ministry of Health and Welfare) that prescribe the matters delegated by the Act and the matters required for its enforcement.

2. Regulation on Safety of Medicinal Products, etc.

The 「Regulation on Safety of Medicinal Products, etc.」 (Ordinance of the Prime Minister) stipulates the matters delegated by the Act and Enforcement Decree on the Act to be prescribed by Ordinance of the Prime Minister regarding drug manufacturing, approval, and follow-up actions, including drug manufacture, entrustment, drug approval/notification, safety/efficacy data, specification and test method, renewal, clinical trial application, institutions for clinical and non-clinical studies, and GMP.

3. Related laws and Notifications

Other laws and notifications on drug approval or notification, including related regulations, eligible products, required dossiers, and considerations for approval data preparation are as follows:

- Laws: 「Enforcement Decree on the Standards of Facilities of Manufacturers and Importers of Medicinal Products, etc.」 (Presidential Decree); 「Enforcement Regulation of the Enforcement Decree on the Standards of Facilities of Manufacturers and Importers of Medicinal Products, etc.」 (Ordinance of the Prime Minister)
- MFDS Notifications: 「Regulation on Pharmaceuticals Approval, Notification, and Review」 ; 「Regulation on Prior Review of Pharmaceuticals」 ; 「Regulation on Registration of Drug Substances (DMF)」 ; 「Regulation on Approval for Investigational New Drug Application of Drugs」

More notifications and guidelines related to drug approval are available at the MFDS website.[2)]

2) Home > DRUGS > Regulations (http://www.mfds.go.kr/eng/index.do?nMenuCode=128)

Ⅲ. Classification of Pharmaceutical Products

1. New drug

According to the 「Pharmaceutical Affairs Act」, "new drug", designated by the MFDS, is a drug of novel materials with the new chemical structure or construction of substance, or a combination drug containing novel materials as active substance. However, drugs listed in the 「Korean Pharmacopoeia (PK)」 or foreign pharmaceutical compendia/pharmacopoeia, recognized by the MFDS shall be excluded.

*** List of official compendia/pharmacopoeia recognized by the MFDS:**

(1) U.S. Pharmacopoeia National Formulary
(2) Japanese Pharmacopoeia
(3) British Pharmacopoeia
(4) European Pharmacopoeia
(5) Deutsches Arzneibuch (Germany)
(6) Pharmacipee Francaise (France)

2. Drug requiring data submission

According to the 「Regulation on Pharmaceuticals Approval, Notification, and Review」 (MFDS Notification), "drug requiring the safety/efficacy review data submission (hereinafter referred to as "drug requiring data submission")" shall refer to the following pharmaceutical drug that is not classified as a new drug, but requires the safety/efficacy review:[3)]

3) Paragraph 8, Article 2 (Definitions) of the 「Regulation on Pharmaceuticals Approval, Notification, and Review」 (MFDS Notification)

(1) Drugs containing new salt (isomer, etc.) as active substance

(2) Drugs with new indications

(3) Drugs with new composition of active substance or only with changes in strength

(4) Drugs with new route of administration

(5) Drugs with new administration/dosage

(6) Enzyme, yeast, or bacterial preparations with new origin that is almost pharmacologically equivalent to the previously approved drugs

(7) Drugs with new dosage form, but with the same route of administration

3. Generic drug

"Generic drug" means pharmaceutical drugs of which type of active substance, strength, dosage form, efficacy/effectiveness, administration/dosage, and route of administration are identical to those of the previously approved drugs. However, "generic drug" is not specifically defined by Korean regulations.

4. Orphan drug

"Orphan drug" refers to a pharmaceutical drug designated by the MFDS, for which introduction is urgently required since there is no alternative drug, and meets the following criteria[4]:

(1) Drugs that are used to treat diseases affecting 20,000 patients or less (prevalence) in Korea

(2) Drugs that are used to treat diseases, for which appropriate therapies and pharmaceutical drugs have not been developed, or that have been significantly improved in terms of safety and/or efficacy, compared to the existing alternatives

---

4) 「Regulation on Designation of Orphan Drugs」 (MFDS Notification)

Ⅳ. Drug Approval System

1. Investigational new drug approval application

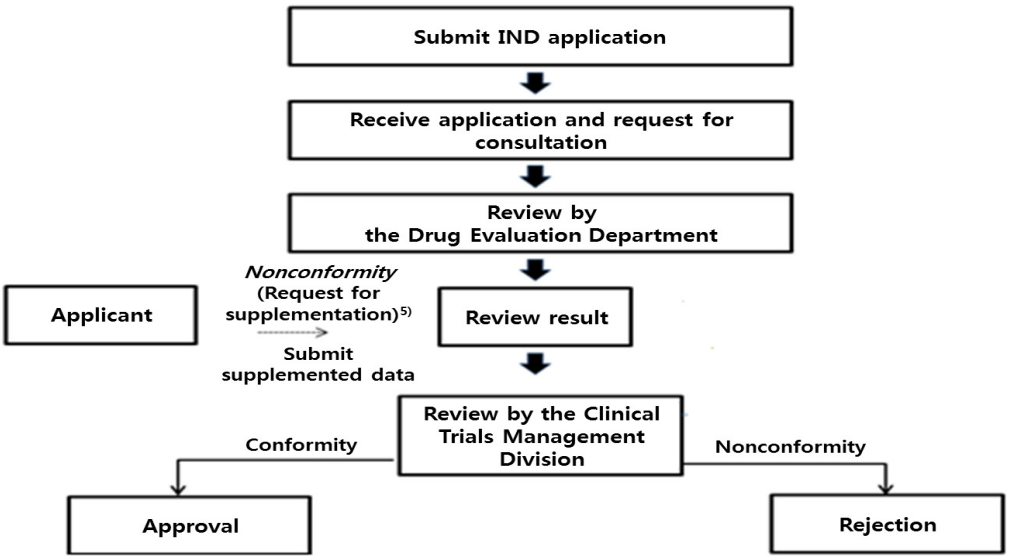
"Investigational New Drug (IND) Application" refers to the process through which an applicant who intends to execute a clinical trial using a drug in order to demonstrate the safety and efficacy of the drug on humans applies for an approval from the MFDS. The following drugs require IND application: new drugs under development; or drugs with new formulation, route of administration, indication, or administration/dosage. However, if a clinical trial is executed to observe clinical effectiveness and adverse reaction of approved drugs marketed in Korea, the clinical trial is not subject to the IND approval by the MFDS.

1.1 IND Procedure

The review process for IND application shall follow five (5) steps: (1) Receipt of IND application dossiers; (2) Request for consultation of the Drug Evaluation Department; (3) Review of submitted data (including safety data); (4) Notification of review result; (5) Request for supplementation or final decision

- Reception (Clinical Trials Management Division) → Review of submitted dossiers (Drug Evaluation Department) → Final decision (Clinical Trials Management Division)[5)]

5) If submitted data are insufficient at the review stage, applicants are requested to supplement the data up to two times. If the data are still insufficient even after that, such application will be rejected.



[Figure 3] Procedure of Investigational New Drug Application

1.2 Review period

IND review period: 30 days

1.3 Required dossiers

An applicant for investigational new drug application shall submit the following data:[6)]

(1) IND application

(2) Development plan

(3) Investigator's Brochure (IB)

(4) Documentation or data that prove the investigational drug is manufactured in compliance with [Appendix 1] (Good Manufacturing Practice) or [Appendix 4-2] (Good Manufacturing Practice for investigational drug) of the 「Regulation on Safety of Medicinal Products, etc.」 (Ordinance of the Prime Minister)

6) Article 24 (Approval of clinical trial protocol, etc.) of the 「Regulation on Safety of Medicinal Products, etc.」 (Ordinance of the Prime Minister); Article 5 (Requirements of Submission Data) of the 「Regulation on Approval for Investigational New Drug Application of Drugs」 (MFDS Notification)

(5) Data on manufacturing and quality of the investigational drug:
Data on drug substance and its quantity, manufacturing method, and manufacturer of the investigational drug

(6) Data of nonclinical test results:
Toxicity, pharmacological, and ADME (Absorption, distribution, metabolism, and excretion) data

(7) Data on the prior clinical use of the investigational product (if available)

(8) Data on clinical trial institution, investigator, and contract research institute according to Article 34-2 (2) of the Act

(9) Rules on compensation for victims of clinical trial

(10) Trial subject's informed consent form

(11) Clinical trial protocol

1.4 Use of foreign clinical data[7)]

Foreign clinical data that meet any of the following requirements may be substituted for drug safety/efficacy data:

(1) Documents or notarial writings which confirm that submitted clinical study data were already submitted to or approved by competent regulatory authorities (of approval or registration) in other economies

(2) Data that are published in a specialized academic journal listed in the Science Citation Index (SCI)

(3) Data that verify the reliability of clinical trial institution and compliance with Good Clinical Practice (GCP)

7) Article 7 (Requirements for Review Data) of the 「Regulation on Pharmaceuticals Approval, Notification, and Review」 (MFDS Notification)

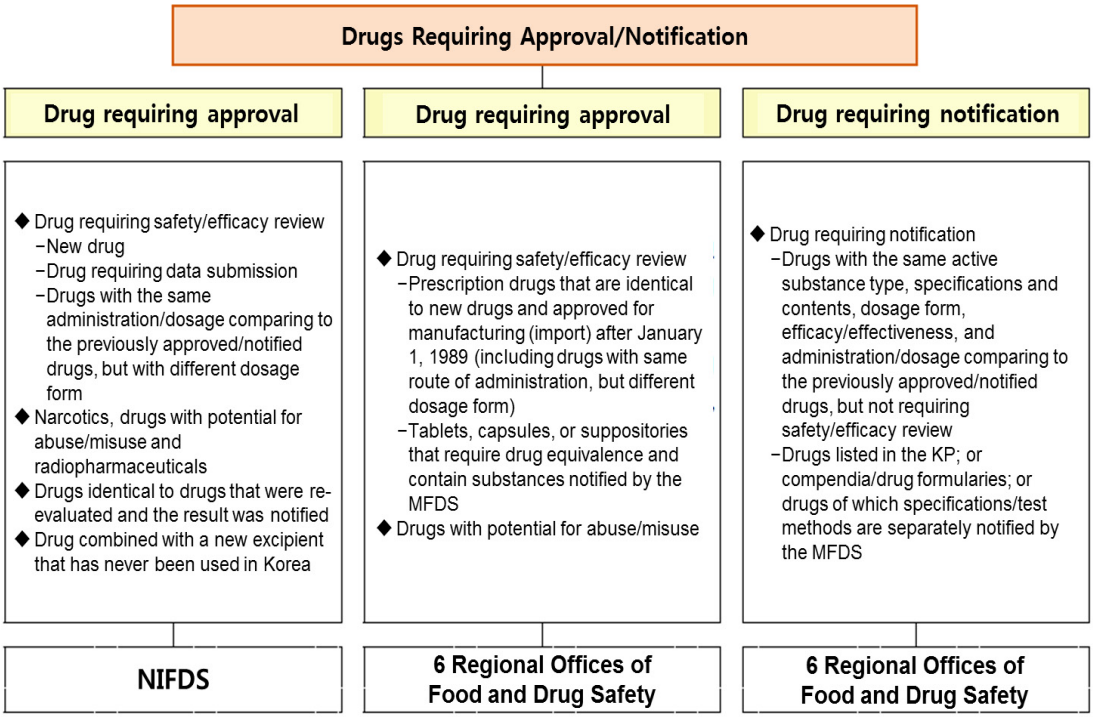
2. Drug approval and notification

2.1 Drug requiring approval and notification[8)]

Depending on the type of review and submitted data, the NIFDS or the Regional Office shall conduct a review as shown below:

(1) Review by the NIFDS: Approval and post-approval change of drug manufacturing/ marketing and import (excluding drugs requiring approval by the Regional Office)

(2) Review by the Regional Office: Approval (post-approval change) and notification of drug that requires drug equivalence



[Figure 4] Drugs Requiring Approval/Notification and Responsible Organizations

8) 「Guide for Pharmaceuticals Approval and Notification」 (2015)

2.2 New Drug Application (NDA)

2.2.1 Procedure

Drug manufacturers, contract manufacturers/distributors, and importers with legitimate facilities may apply for approval of new drug manufacturing/marketing (import) to the NIFDS according to the following process. A review of such application shall be conducted by the Drug Evaluation Department.

(1) Reception and pre-review of application

- Application shall be submitted by visiting the NIFDS or via e-Drug Service (ezdrug).
- After pre-review of the submitted application data to confirm whether they meet the data requirements, such application shall be sent to the responsible Division.

(2) Review

- Scope and requirements of the submitted data are re-confirmed and reviewed.
- An applicant for a new drug or incrementally modified drug (IMD) may request product briefing, if necessary.
- Respective Divisions shall review the application data and report the result to the Drug Review Management Division.
  - Drug Review Management Division evaluates the review result of the safety/efficacy data, and specifications/test methods.
  - Pharmaceutical Quality Division reviews GMP assessment data.
  - Pharmaceutical Approval and Patent Management Division confirms any patent relations and reviews application for generic exclusivity.
- If submitted data are insufficient, the applicant is requested to supplement data up to two times. If the data are still insufficient even after that, such application shall be rejected.

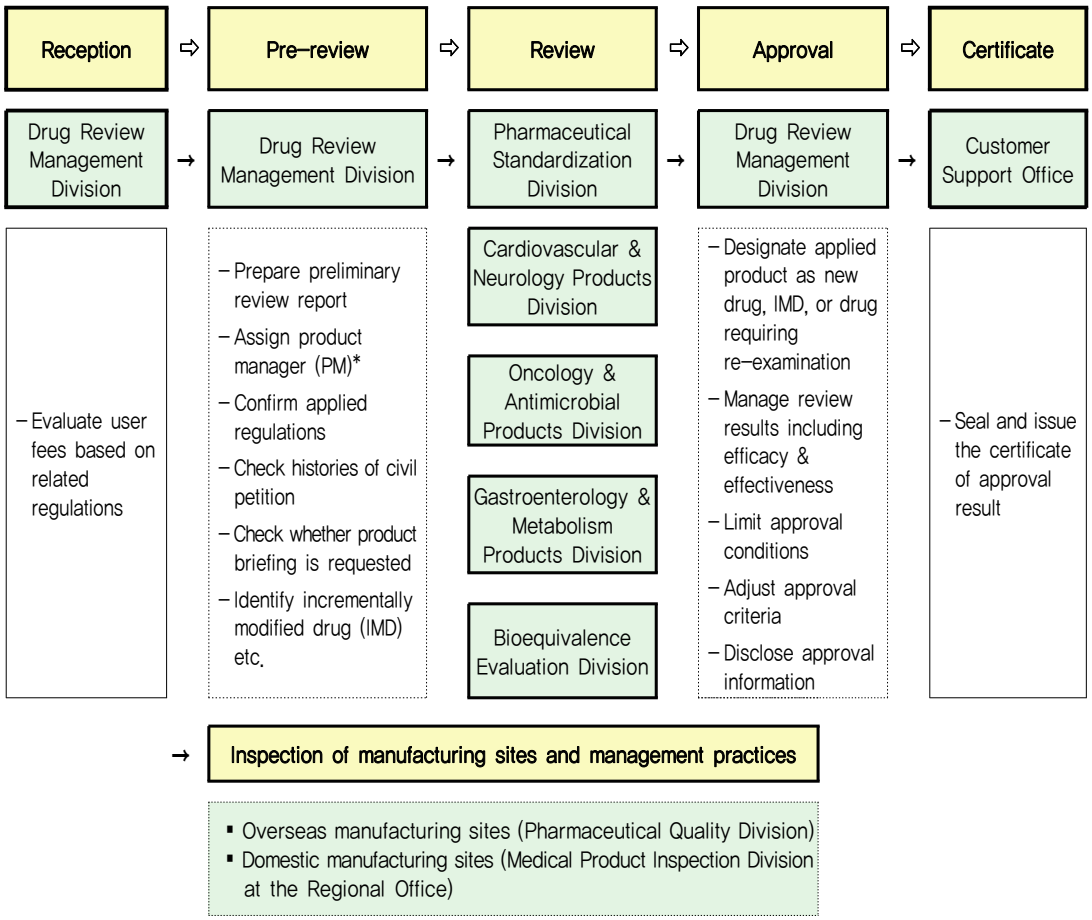
(3) Report of review result

- The Drug Review Management Division shall receive and review the result of review from each Division and then notify the result to the applicant.

(4) Drug approval

(5) Disclosure of information

- After completion of drug approval, the applicant is requested to consent to information disclosure including review result of safety/efficacy, specifications/test methods, and bioequivalence test. If the applicant consents to the request, review result shall be made public through the MFDS website.



[Figure 5] Procedure of New Drug Manufacturing/Marketing Approval

2.2.2 Review period

Review period shall be either:

- 90 days when DMF review is not included; or
- 120 days when DMF review is included.

**Note: If a request for supplementation of data is made, the review period shall be extended based on the period taken to supplement necessary data.*

2.2.3 Required dossiers

2.2.3.1 Required application data for new drug approval

The new drug application data shall be prepared in Common Technical Documents (CTD) format.

(1) Application for drug manufacturing/marketing (import)

(2) Safety and efficacy data
  ① Origin or discovery, and development history
  ② Structure elucidation and physiochemical properties
  ③ Stability data
  ④ Toxicity data
  ⑤ Pharmacological data
  ⑥ Clinical test result
  ⑦ Data on current status of use in other economies
  ⑧ Comparative review with similar drugs in Korea and data on their properties of relevant drugs

(3) Specifications and test methods

(4) For imported drugs, the following certificates that are related to pharmaceutical manufacturing/marketing:
  ① Certificate of manufacturing issued by the government or public agencies of the manufacturing economy, indicating that such product is legitimately manufactured in accordance with the laws and regulations of the economy

② Certificate of marketing issued by the government or public agencies of the economy that granted approval or registration of such product, indicating that such product is legitimately marketed in accordance with the laws and regulations of the economy[9)]

(5) Data required for the evaluation of GMP inspection

(6) DMF application and attached data (if DMF[10)] is used)

(7) Name and address of API manufacturer

(8) Agreement for contract manufacturing including name and address of subcontractors, in case of drugs subject to contract manufacturing/marketing

(9) Patent certificates and supporting documents/data (in case where an applicant applied for approval of drug manufacturing/marketing and import based on safety/efficacy data of drugs listed on the Pharmaceutical Patent List

9) If the certificate cannot be submitted with application, the applicant may submit the explanatory statements including expected submission date within the process period. Once the preparation of the required data is completed, the applicant may submit the data within the aforementioned submission date.

10) Drug substance requiring registration under the 「Regulation on Registration of Drug Substances」 (MFDS Notification). For more information, refer to "2. Drug Master File" under "Part V. Others" and "Appendix 2" of this Guideline.

2.2.3.2 Scope of review data submission: safety/efficacy data and specifications/ test methods

- Type of drugs and scope of required data[11)]

Classification \ Required Data	Data Number																																			
	1	2																		3				4						5					6		7	8
		A								B								A		B																
		1)	2)	3)	4)	5)	6)	7)	8)	1)	2)	3)	4)	5)	6)	7)		1)	2)	1)	2)	A	B	C	D	E	F	A	B	C	D	A	B		
I. New drugs																																				
1. Pharmaceutical drug containing new chemical entity (NCE) with novel chemical structure or composition	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	△	△	○	○	○	○	○	○	○	○	○
2. Combination drug containing NCE as an active substance with novel chemical structure or composition	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	*○	*○	○	○	△	•△	*○	*○	*○	○	○	○	○	○	○
3. Radiopharmaceutical drug among pharmaceutical drugs that fall under subparagraphs 1 & 2	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	×	×	×	×	×	△	△	○	○	○	○	○	○	○
4. Over-the-Counter (OTC) drug with sufficient experience of use in and out of Korea	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	△	△	△	△	△	△	△	△	△	△	△	△	△	○	○

○ : Data submission is required.
△ : Data submission may be exempted since the data submission is meaningless or impossible based on justification on individual pharmaceuticals.
× : Data submission is exempted.
※ : Data submission is required in case of new isomers and salts, etc.
** For details on required data per data number, refer to Appendix 1 of this document.*

[Table 1] Type of New Drugs and Scope of Required Data

2.2.3.3 Required data for GMP inspection

For a specific data required for GMP inspection, refer to "1. GMP Compliance Assessment" under "Part V. Others" of this guideline.

11) Article 5 (Requirements for Submissions) of the 「Regulation on Pharmaceuticals Approval, Notification, and Review」 (MFDS Notification)

2.3 Application for approval of drug requiring data submission

2.3.1 Procedure

The approval process of "drug requiring data submission" is the same to that as shown in Figure 4.

2.3.2 Review period

Type of drug		Data for review	Responsible organization	Review period
Drugs requiring approval	Drugs requiring data submission	– Specifications/test methods – Safety/efficacy data – GMP assessment and on-site inspection data	NIFDS (Drug Evaluation Department) Drug Review Management Division	120 days
		– Specifications/test methods – Safety/efficacy data – GMP assessment and on-site inspection data – DMF assessment data		

2.3.3 Required dossiers

The application data for "drug requiring data submission" shall be prepared in CTD format and required dossiers shall be the same to NDA. For scope of data required for review of safety/efficacy and specifications/test methods, refer to Table 2.

Classification \ Required data	Data Number																																				
	1	2																	3				4										5			6		7	8
		A								B									A		B		A	B	C	D	E	F				A	B	C	A	B		
		1)	2)	3)	4)	5)	6)	7)	8)	1)	2)	3)	4)	5)	6)	7)			1)	2)	1)	2)						1)	2)	3)									
Ⅱ. Drugs requiring data submission																																					
1. Drugs containing new salt (isomer, etc.) as an active substance	○	○	○	○	○	○	○	○	×	△	△	○	○	○	○	×	×	×	○	×	△	×	×	×	×	△	△	△	△	△	△	○	×	○	○
2. Drugs with new indication	○	×	×	×	×	×	×	×	×	×	×	×	×	×	×	×	×	×	○	×	×	×	×	×	×	×	×	△	△	△	○	△	△	○	×	○	○
3. Drugs with new composition of active substance or only with changes in strength																																					
Drugs for review	Ground for exemption (examples of use in Korea)																																				
New composition (multiple preparations)	Single preparations or multiple preparations	○	※	※	△	○	○	○	△	△	△	△	○	○	○	△	△	×	×	○	×	△	•△	×	×	×	•△	×	×	○*	※	※	○	×	○	○
Multiple preparations, with changes in strength	Multiple preparations	○	※	※	△	○	○	○	△	△	△	△	○	○	○	△	△	×	×	○	×	△	×	×	×	×	△	×	×	※	※	※	○	×	○	○
Single preparations	Single preparations or multiple preparations	○	※	※	△	○	○	○	△	△	△	△	○	○	○	△	△	×	×	○	×	※	×	×	×	×	△	×	×	○	※	※	○	×	○	○
4. Drugs with new route of administration																																					
Drugs for review	Ground for exemption (examples of use in Korea)																																				
Subcutaneous (SC), intramuscular (IM)	Intravenous injection (IV)	○	△	△	△	○	○	○	△	△	△	△	○	○	○	△	△	×	×	○	×	×	×	×	×	×	×	×	×	○	×	×	○	×	○	○
IV	SC, IM	○	△	△	△	○	○	○	△	△	△	△	○	○	○	△	△	×	×	○	×	○	△	×	○	×	×	×	×	○	×	○	○	×	○	○
Oral	Injection	○	△	△	△	○	○	○	△	△	△	△	○	○	○	△	△	×	×	○	×	×	×	×	×	×	×	×	×	△	×	×	○	×	○	○
Inhalation	SC, IM	○	△	△	△	○	○	○	△	△	△	△	○	○	○	△	△	×	×	○	×	○	○	×	×	×	×	×	×	○	×	○	○	×	○	○
External	Oral or injection	○	△	△	△	○	○	○	△	△	△	△	○	○	○	△	△	×	×	○	×	×	×	×	×	×	×	△	×	×	○	×	×	○	×	○	○
External	External	○	△	△	△	○	○	○	△	△	△	△	○	○	○	△	△	×	×	○	×	×	×	×	×	×	×	△	×	×	○	×	○	○	×	○	○
Radiopharmaceuticals		○	△	△	△	○	○	○	△	△	△	△	○	○	○	△	△	×	×	○	×	×	×	×	×	×	×	×	×	×	×	×	○	○	×	○	○
Others (not listed above)		○	△	△	△	○	○	○	△	△	△	△	○	○	○	△	△	×	×	○	×	△	△	×	△	×	△	×	△	○	×	○	○	×	○	○
5. Drugs with new administration/ dosage		○	△	△	△	○	○	○	△	△	△	△	○	○	○	△	△	×	×	△	×	×	×	×	×	×	×	×	×	△	×	△	○	×	○	○
6. Enzyme, yeast, or bacterial preparations with new origin (almost pharmacologically equivalent)		○	△	△	△	○	○	○	△	△	△	△	○	○	○	△	△	×	×	○	×	○	×	×	×	×	×	×	×	○	×	△	△	×	○	○
7. Drugs with new dosage form (same route of administration)		○	△	△	△	○	○	○	△	△	△	△	○	○	○	△	△	×	×	○	×	×	×	×	×	×	×	△	×	×	×	×	△	△	×	○	○

○ : Data submission is required.

△ : Data submission may be exempted since the data submission is meaningless or impossible based on justification on individual pharmaceuticals.

× : Data submission is exempted.

※ : Data submission is required in case of new isomers and salts, etc.

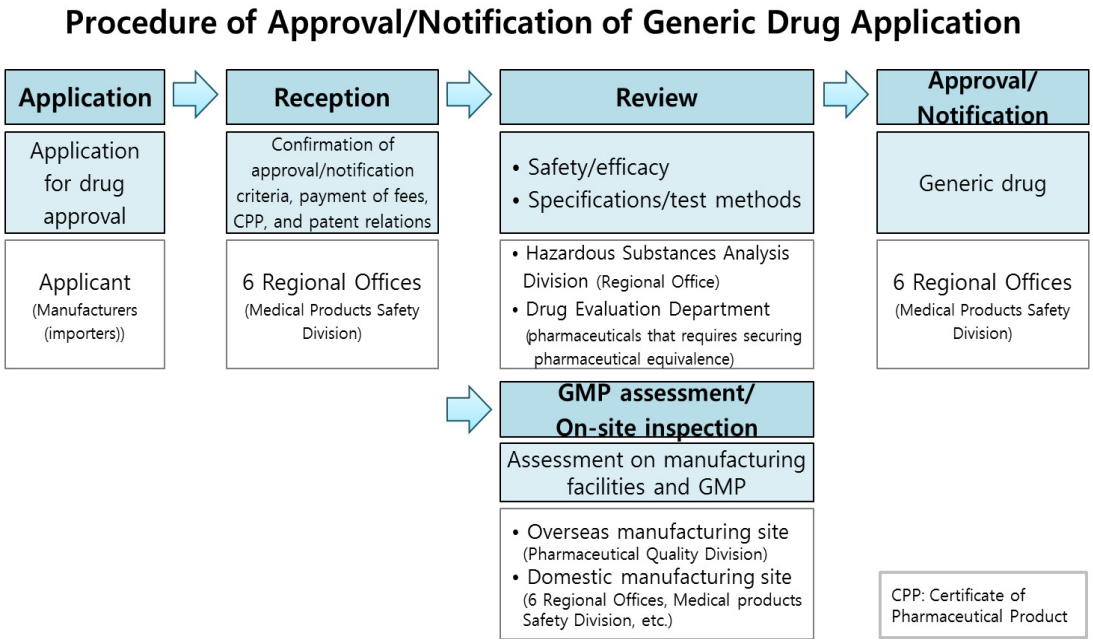
** For details on required data per data number, refer to Appendix 1 of this document.*

[Table 2] Type of Drug Requiring Data Submission and Scope of Required Data

2.4 Generic drug application for approval/notification

2.4.1 Procedure

The procedure of approval/notification of generic drug application is as shown in Figure 5 below:



[Figure 6] Procedure of Approval/Notification of Generic Drug Application

2.4.2 Review Period

Type of drug		Data for review	Responsible organization	Review period
Drugs requiring approval	Generic drugs	– Specifications/test methods – Safety/efficacy data(i.e. bioequivalence data) and stability data – GMP assessment and on-site inspection data ※ *A separate review is required if DMF is necessary*	Regional Office or Drug Review Management Division	90 days
Drugs requiring notification		– Specifications/test methods – Drug equivalence data and stability data (injections) – GMP assessment and on-site inspection data	Regional Office	90 days

2.4.3 Required dossiers[12)]

For scope of data required for application for generic drug approval/notification, refer to Table 3.

The application data for approval of following drugs shall be prepared in CTD format and bioequivalence test or comparative clinical study data for review of safety/efficacy shall be submitted together with stability data:[13)]

(1) Prescription drugs that obtained manufacturing/marketing and import approval since January 1, 1989, falling under new drug (including drugs with the same route of administration, but different dosage form)

(2) Prescription drugs (tablets, capsules, and suppositories) with substances identical to drugs previously approved for manufacturing/marketing and import; provided that such drugs need to secure pharmaceutical equivalence as notified by the 「Designation of Pharmaceuticals Required Securing Pharmaceutical Equivalence」[14)]

For application of the special dosage form, it is necessary to confirm a change of internal absorption amount or speed because drug release or dissolution mechanism is different due to changes of preparation technology even if the administration/dosage is identical to that of drugs which are already approved/notified (e.g. transdermal patch, implant, extended-release preparations, sublingual tablet, inhaler applied to lung (metered spray), suspension injection). In this case, bioequivalence test or comparative clinical study data for review of safety/efficacy shall be submitted together with stability data.

---

12) [Appendix 14] of the 「Regulation on Pharmaceuticals Approval, Notification, and Review」 (MFDS Notification)

13) 「Regulation on Safety of Medicinal Products, etc.」 (Ordinance of the Prime Minister)

14) Commercial drugs, expensive drugs, drugs with single substance, and others that require securing pharmaceutical equivalence, etc.

Classification \ Required data	Data Number															
	1	2	3							4						5
			A	B	C	D	E	F	G	A	B	C	D	E	F	
1. Drugs with the same APIs, their quantities, and dosage form comparing to the previously approved drugs																
1) Drugs subject to bioequivalence test under Article 3-1 of the 「Standard on Pharmaceutical Equivalence Study	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○
2) Injections	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○	○
3) Other generic drugs except for subparagraph 1) and 2)	×	○	×	×	×	○	○	△	△	△	△	△	○	△	△	△
2. Drugs manufactured under the OTC monographs	△	△	×	×	×	○	○	△	×	×	×	△	○	△	×	×
3. Drugs approved (notified) as drug substance (excluding new drugs)	△	○	○	○	○	○	○	△	△							

○ : Data submission is required.

△ : Data submission may be exempted since the data submission is meaningless or impossible based on justification on individual pharmaceuticals

× : Data submission is exempted.

[Table 3] Type of Generic Drugs and Scope of Required Data

[Required data per data number]

1. Origin or discovery and development history
2. Data on current status of use in Korea and other economies
3. Drug substance data
   - A. Structure elucidation
   - B. Physiochemical properties
   - C. Manufacturing methods
   - D. Supporting data for specifications and test methods
   - E. Test results
   - F. Reference standard, reagents, and test solutions
   - G. Container and packaging
4. Drug product data
   - A. Drug ingredients and quantities
   - B. Manufacturing methods
   - C. Supporting data for specifications and test methods
   - D. Test results
   - E. Reference standard, reagents, and test solutions
   - F. Container and packaging
5. Stability Data

3. Orphan drug

3.1 Required dossiers for orphan drug designation

Since orphan drugs are to meet urgent medical needs without an alternative treatment, time to review orphan drug designation may be reduced with high priority. To be designated as orphan drug:

- the number of patients must be 20,000 or less in Korea; and drugs must be used to treat diseases, for which appropriate therapies and drugs have not developed; or
- drugs should demonstrate a significant improvement in safety or efficacy compared with the existing alternative drugs.[15)]

Required dossiers for orphan drug designation shall include:

- Data that prove the product meets the aforementioned designation criteria
- A recommendation letter for orphan drug designation from relevant associations[16)] including Korean Medical Association (KMA); or a copy of written opinion on the designation of orphan drugs in the development stage[17)]
- Comprehensive drug safety management plan (risk management plan) including risk evaluation and mitigation strategy (REMS) such as patient information leaflet and Elements to Assure Safe Use (ETASU)[18)]

---

15) 「Regulation on Designation of Orphan Drugs」 (MFDS Notification)

16) A recommendation letter from Korean Medical Association (KMA), Korean Dental Association, Korean Hospital Association, or affiliated association of Korean Academy of Medical Sciences related with the disease concerned. Refer to the 「Regulation on Designation of Orphan Drugs」 (MFDS Notification).

17) Submission of the recommendation letter may be exempted if there are clear supporting data verifying that relevant drugs are designated as orphan drugs in other economies or may be used to treat rare diseases.

18) Article 4 (Application for Approval of Drug Manufacturing, Marketing, and Import) of the 「Regulation on Safety of Medicinal Products, etc.」 (Ordinance of the Prime Minister)

3.2 Incentives

If a drug is designated as orphan drug, the drug shall be approved by expedited review process. Regardless that clinical trials were conducted in Korea or not, all orphan drugs shall be subject to re-evaluation. Re-evaluation period of orphan drugs shall be 10 years, and if safety and efficacy of orphan drugs have been improved comparing to alternatives, such period shall be four (4) or six (6) years.[19)]

For approval of orphan drug, an applicant may submit one (1) batch manufacturing record for GMP assessment (for non-orphan drugs, submission of three (3)-batch records is required). Moreover, duplicating GMP assessment shall be exempted if manufacturing process is the same with the existing drugs manufactured by a subcontractor and such drugs have already undergone GMP assessment under approval process.[20)]

The MFDS is currently facilitating development of orphan drugs by exempting prior review fees including review of orphan drug specification and test methods and GMP assessment.[21)]

3.3 Procedure and review period

Orphan drugs are subject to expedited review (refer to “5.1 Expedited Review”).

---

19) Article 2 and Article 22 of the 「Regulation on Pharmaceuticals Approval, Notification, and Review」 (MFDS Notification)

20) Article 4 and [Appendix 1] of the 「Regulation on Safety of Medicinal Products, etc.」 (Ordinance of the Prime Minister)

21) 「Regulation on Fees for Pharmaceutical Approval, etc.」 (MFDS Notification)

4. Prior review[22)]

"Prior review" is review of documentation required for drug approval and notification by the MFDS prior to the submission for approval or notification of pharmaceuticals or approval of clinical trials and bioequivalence test.

4.1 Subject and scope of prior review[23)]

Subject and scope of prior review shall be as follows:

(1) Safety/efficacy data

(2) Specification and test methods

(3) GMP data

(4) Clinical trial protocol

(5) Bioequivalence test protocol

(6) Pharmaceutical development plan

(7) Other required data for drug approval/notification, IND approval, and approval of bioequivalence test protocol

4.2 Procedure[24)]

Once an applicant submits application for prior review of pharmaceuticals and required data via e-Drug Service (http://ezdrug.mfds.go.kr), the MFDS shall temporarily organize prior review team and conduct prior review as below. If required, the team may receive advice from external experts in writing or through meeting.

(1) The prior review team shall review submitted data and if required, the team may request a detailed explanation on the product and the application.

---

22) Article 35-2 (Prior Review of Pharmaceuticals Approval, etc.) of the 「Pharmaceutical Affairs Act」

23) Article 41 (Subject of Prior Review, etc.) of the 「Regulation on Safety of Medicinal Products, etc.」 (Ordinance of the Prime Minister)

24) Article 7 (Prior Review Process) of the 「Regulation on Prior Review of Pharmaceuticals」 (MFDS Notification)

(2) After reviewing the submitted data, the prior review team shall prepare the primary review result and notify the applicant of the result. If submitted data for prior review satisfy the criteria, prior review result notification may be issued at the time of notifying the primary review result. In case of "clinical trial protocol", in principle, face-to-face meeting shall be substituted for notification of primary review result.

(3) Face-to-face meeting shall be held with prior review team, applicant, head of responsible department (if necessary), and external experts.

(4) An applicant who has any opinion on the result of primary review result or face-to-face meeting may send an opinion letter to the responsible department within 14 days from the date of notification. During this period, the applicant may submit supplementary data. However, if data cannot be submitted within such period, the applicant may request an extension of period to a maximum of 60 days.

(5) Within the processing period, primary review result, applicant's opinion letter, and face-to-face meeting result. shall be comprehensively reviewed and then notification of the prior review result will be issued.

4.3 Review period

- Clinical trial data: 30 days
- Safety/efficacy data: 45 days (New drug: 60 days)
- Specification and test methods (excluding biologics and diagnostic drugs)
  - New drugs and antibiotics: 90 days
  - Drugs requiring data submission: 55 days
  - Previously approved drugs: 45 days
  - Changes made to the specification and test methods: 30 days
- Specification and test methods (diagnostic drugs)
  - Diagnostic drugs: 45 days
  - Changes made to the specification and test methods: 32 days
- Other data except as above: 50 days

5. Expedited review[25)]

5.1 Drugs subject to expedited review

In case of the following pharmaceuticals for which clinical effectiveness is expected to treat life-threatening diseases or irreversible diseases, the MFDS may allow an applicant to submit the part of required data after placing the product on the market in order to expedite review process:

- Pharmaceuticals intended to treat life-threatening diseases such as AIDS and cancers
- Pharmaceuticals for which urgent introduction is necessary because it is impossible to treat with currently existing therapies
- Pharmaceuticals such as orphan drug, cancer drug, or DNA chip that are considered to be necessary for patient treatment or industrial development
- Natural new drugs that are used for AIDS and cancers.
- New drugs (including IMDs) or drugs for which Korean clinical investigation records were submitted

5.2 Procedure

There is no specific regulation for expedited review. For procedure, refer to review process for drug approval.

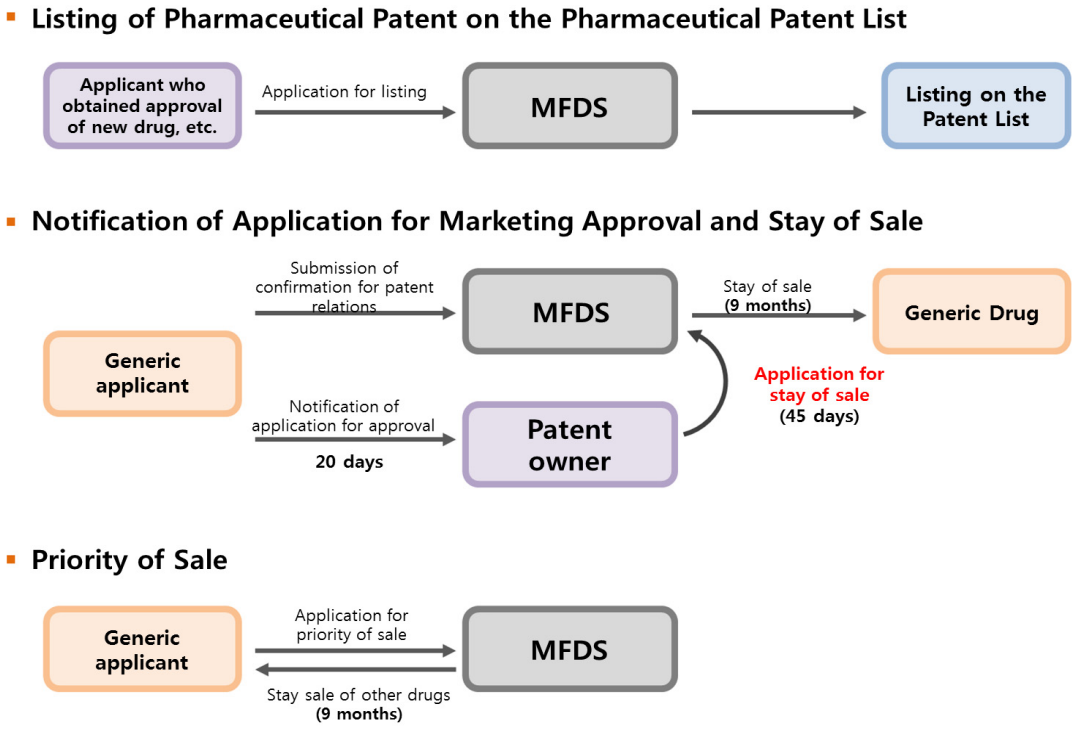
25) Article 58 (Expedited Review, etc.) of the 「Regulation on Pharmaceuticals Approval, Notification, and Review」 (MFDS Notification)

6. Patent-approval linkage system[26)]

6.1 Overview

To list a pharmaceutical patent (substance, composition, formulation, and medical use of pharmaceutical products, which have obtained approval of manufacturing/marketing and import) on the Patent List, an application shall be submitted to the MFDS. If such patent satisfies the relevant criteria, the MFDS shall list the patent on the List and open to the public.

If an application for drug approval is submitted relied on the safety/efficacy data of the listed drugs on the Patent List, the applicant shall notify the marketing approval holder and patentee of such application.



[Figure 7] Overview of Patent-Approval Linkage System

26) 「Guide for Patent-approval Linkage System」

6.2 Application for listing

(1) Applicant for listing

- A party that has obtained product marketing approval of a pharmaceutical product (including importers) and holds the patent right regarding the pharmaceutical product

(2) Period of application for listing

- The application shall be submitted to the MFDS within 30 days from the date of marketing approval
- If the patent had not been existed at the time of approval, but has been (newly) registered after the date of such approval, the application shall be submitted to the MFDS within 30 days from the patent listing date.

(3) Requirements for listing

Under Article 50-2(4) of the Act, a patent which has satisfied the following requirements may be listed:

- A patent should be about substance, composition, formulation, and medical use of pharmaceutical product;
- A patent should be directly related to the subject of marketing approval or change approval;
- Application for listing should be made prior to the date of marketing approval or post-approval change of the pharmaceutical product according to Article 42 of the 「Patent Law」 ;
- A patent should not be expired; and
- The marketing approval or change approval of the pharmaceutical product is valid.

(4) Preparation of Pharmaceutical Patent List

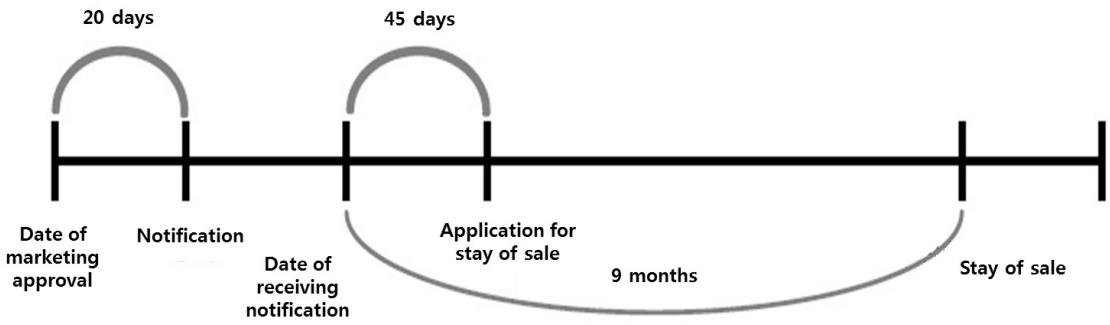
- If the listing of patent on the Patent List is decided, the following matters are opened to the public: i) product name; ii) identity information of marketing approval holder; iii) identity information of the patentee; iv) identity information of attorney (if any); v) patent number; vi) listing date and expiry date of patent; and vii) patent claims.

6.3 Notification of application for approval and stay of sales

Generic applicant who applied for marketing approval relying on the safety/efficacy data submitted for a listed drug on the Patent List or post-approval change in terms of efficacy/effectiveness of the listed drug shall notify a party who listed the patent and patentee of the following within 20 days from the date of such application: application for marketing approvals, application date, and reason of patent invalidity or non-infringement of the listed drugs.[27] If the patent term has expired or an applicant wishes to sell drugs after patent expiry date, notification of the application shall not be necessarily required. The notifying party shall submit the notification data to the MFDS.

Patentees of listed drugs may file a patent litigation against the applicant within 45 days from the date of receiving notification and apply for stay of sale against the generic drug to the MFDS. The sale is stayed during nine (9) months from the date on which the patentee receives the notification. However, the decision or ruling that the listing of the patent on the Patent List is invalid or the patent is not infringed by the generic drug shall be grounds for cancellation of a stay of sale.

27) Article 50-4 (Prior Review of Pharmaceuticals Approval, etc.) of the 「Pharmaceutical Affairs Act」



[Figure 8] Marketing Approval Application Date and Period of Stay of Sale

6.4 Priority of sale

Requirements for obtaining the priority of sale shall be as follows:

- The person who applied for marketing approval relying on the safety and efficacy data of listed drug on the earliest day; and
- Obtained favorable decision or ruling with respect to the listed patent in question; and
- As the filer of the patent action prior to applying for marketing approval, first files the patent action or obtains a favorable decision or ruling before the first filer

The sales of other generic drugs may be stayed for nine (9) months from the effective sales date for a generic drug with priority of sale.

Ⅴ. Others

1. GMP compliance assessment[28),29)]

1.1 Drugs subject to GMP compliance assessment

Manufacturers shall ensure that drugs are manufactured and marketed in compliance of Good Manufacturing Practice (GMP) specified in [Appendix 1] of the 「Regulation on Safety of Medicinal Products, etc.」 (Ordinance of the Prime Minister) depending on pharmaceutical forms (solid oral dosage forms, injections, eye drops, oral solutions, ointments, and other dosage forms).

In case of application for drug manufacturing/marketing approval, relevant data shall be submitted for GMP compliance assessment except the following cases:

- Drug substances do not include medicinal herb and do not have pharmacological activity (pharmacologically affecting the human body) (e.g. excipients, etc.).
- Drug products do not directly affect the human body (e.g. disinfectant, etc.) and drug substances are used for such product.
- Manufacturing sites have a valid GMP certificate which is previously issued and valid for three (3) years from the issuance date.

Moreover, depending on manufacturing methods (synthesis, fermentation, extraction, and other methods), drug substances shall be in compliance of Good Manufacturing Practice (GMP) for Drug Substance specified in [Appendix 1-2] of the 「Regulation on Safety of Medicinal Products, etc.」 (Ordinance of the Prime Minister).

---

28) 「Guidance on Good Manufacturing Practice for Drug Product」 (March 2015)

29) Article 4 (Application for Drug Manufacturing/Marketing and Import Approval), Article 5 (Notification of Drug Manufacturing/Marketing and Import), Article 48 (Compliance of Manufacturers, etc.), and [Appendix 1] (Good Manufacturing Practice) of the 「Regulation on Safety of Medicinal Products, etc.」 (Ordinance of the Prime Minister)

1.2 GMP compliance assessment and decision[30)]

1.2.1 On-site inspection

GMP compliance assessment and decision shall be both based on desk-top review of the submitted documents and if required, on-site inspection shall be conducted.

(1) On-site inspection is required for the following cases:

- The manufacturing site is subject to the GMP compliance assessment for the first time.
- GMP certificate for the manufacturing site has expired (During the term of validity, on-site inspection is not required).
- Other cases with reasonable reasons to carry out on-site inspection

(2) Criteria for assessment result and decision criteria

Category	Findings	Decision (Principle)
Critical	• Issues with significant risk(s) that have produced or will produce products harmful to human; or equivalent issues • False documentations	Non-conformity
Major	• Products have been produced or have possibility to be produced differently from the approved requirements • Issues caused by major deviation from GMP criteria or conditions for manufacturing approval • Issues with batch release process or negligence of duties by personnel • Issues that are not "Major" independently, but become "Major", considering together with "Minor" issues found	Supplementation
Minor/Others	• Issues not classified as "Critical" or "Major", but deviated from GMP criteria	Supplementation or Warning for corrective action

30) 「Operation Guideline for Prior GMP Assessment by Pharmaceuticals, etc.」

1.3 Required dossiers

For GMP compliance assessment, the following data shall be submitted. In principle, when data are from other economies, a summary written in Korean (main abstract) shall be submitted with the original document. In case of foreign languages except English, translation of whole documents shall be attached thereto, if required. However, raw data including validation result report in this case are not necessarily required to be translated.

(1) Floor plan of manufacturing site

(2) Data on manufacturing facility associated with the drug application

(3) Data on facilities and environmental management associated with the drug application

(4) GMP organization chart and quality control (assurance) system

(5) Regulation of document management and list of documents

(6) Copy of Master Formula and GMP records
** manufacturing records of not less than three (3) batches*

(7) Validation data associated with the drug application

2. Drug Master File[31)]

Drug Master File (DMF) is a system where manufacturers are required to submit application for drug substance designated by the MFDS and detailed data for overall management; and if appropriate, the MFDS registers drug substances on the system so that manufacturers utilize such data from the system for the drug product application.[32)]

(1) Drug substances for DMF

- New entity drug substance that is used for active substance of new drugs approved by the MFDS since July 1, 2002
- Drug substances specified in Appendix 2 and their salts and hydrates
- Human placental drug substances (including drugs under final bulk process)

  ** Orphan drugs, radiopharmaceuticals, drugs manufactured for import, and substances without pharmacological activity (excipients) shall be excluded.*

(1) Required dossiers

If previously registered and publicly notified drug substances subject to DMF are used, submission is not required and list for such notification is available at the MFDS website.[33)]

- Data on facilities required for drug manufacturing and quality control
- Physicochemical properties and stability data
- Manufacturing methods, packages, containers, and cautions in the use of product
- Data that the product satisfies GMP to the equivalent or higher level
- Certificate of Analysis (CoA) of drug substance, analytical methods, solvents used
- Investigational drug substance for quality test

  ** Data may be submitted in CTD format.*

---

31) 「Regulation on Registration of Drug Substances (DMF)」 (MFDS Notification)

32) 「Registration Process of Drug Substances (Guideline)」

33) MFDS website: http://www.mfds.go.kr/index.do?mid=1030&cd=168 (in Korean)

3. Labeling and package inserts[34)]

(1) Labeling of drug container and package

The following information shall be indicated on a drug container and package. If all the information is specified in the package inserts, either some of the information shall be summarized or "See package inserts." shall be indicated.

① Trade name and address of authorized manufacturer or importer
② Drug name
③ Manufacturing number and shelf-life or date of expiration
④ Weight or dose/quantity
⑤ Words of "Prescription drug" or "OTC drug"
⑥ Mandatory information prescribed by the Korean Pharmacopoeia or the Central Pharmaceutical Affairs Council (CPAC)
⑦ Other following information prescribed by the 「Regulation on Safety of Medicinal Products, etc.」 [35)]

- Appearance
- Efficacy/effectiveness
- Storage conditions
- Name and strength of preservatives (if any)
- Name and address of subcontractors (in case of contract manufacturing)
- Trade name and address of original manufacturer (in economy of origin) in case of imported product or imported and dispensed product
- Mark of "Standardized product" and economy of origin (economy name, etc.) in case of standardized herbal product
- In case of Press-through-pack (PTP) where products are packaged individually, product name, name of authorized manufacturer or trade name of importer, manufacturing number, shelf-life or date of expiration shall be indicated on each PTP. However, shelf-life or date of expiration may be indicated as year/month unless it exceeds such shelf-life or date of expiration.
- Barcode or radio frequency identification (RFID) tag prescribed by the Minister of Health and Welfare in consultation with the MFDS
- Name of substance, animal origin, and the part to be used if animal-derived substances (including excipients) are used; except the case where such substance does not cause any concerns of bovine spongiform encephalopathy (BSE) infection from manufacturing process (e.g. empty capsule)
- Name of excipients as prescribed by the MFDS in case of products including injections, dermatologic agents, etc. notified by the MFDS
- Words of "Product likely to cause drug abuse and misuse" if such product is recognized to have a significant risk of causing drug abuse and/or drug misuse and notified by the MFDS
- Name of tar color (if any)
- Print of "National batch release drug" per every package unit in case of national batch release product

34) Article 56 (Labeling of Drug Containers, etc.) of the 「Pharmaceutical Affairs Act」

35) Article 69 (Labeling of Medicinal Products), Article 70 (Information on Package Inserts), and Article 77 (Labeling Format) of the 「Regulation on Safety of Medicinal Products, etc.」 (Ordinance of the Prime Minister)

(2) Information on package inserts

Subparagraphs ① through ⑦ under the above "(1) Labeling of drug container and package" shall be specified. In addition, the following information shall be required:

① Administration/dosage and cautions in the use or handling of drug

② Description specifying that a drug has passed shelf-life or date of expiration, or adulterated/contaminated or damaged will only be exchanged through pharmacies, sellers of general sales list medicines, and drug distributors; and instructions for exchange of such drugs

③ Year/Month/Date of package inserts preparation or final revision

(3) Language of labeling

The drug labeling shall be written in Korean, but Chinese character or another foreign language may be used in the same font size, in parallel with Korean.

4. Certificate of a Pharmaceutical Product for approval of new drug import[36),37)]

In case of an imported new drug, the Certificate of a Pharmaceutical Product (CPP) issued by the manufacturing economy shall be submitted. However, if the CPP is not available at the time of application, an applicant may submit the Certificate during the review period within the year.

Each CPP document shall be issued within two (2) years from the date of submission (if the cycle of CPP issuance by government or public agency from the economy of production/registration is more than two (2) years, such period shall be observed). If a drug has ever been marketed in other economies other than the economy where it is manufactured and is listed in pharmaceutical compendia[38)] published within three (3) years including the year in question, a certificate signed by a responsible person of the manufacturer and notarized by a public agency may be submitted, in lieu of the CPP.

5. Approval of drug manufacturing/marketing[39)]

An applicant who has conducted clinical tests with approved protocol and obtained drug marketing approval ("contract manufacturing/marketing business"), but with no manufacturing site may produce or sell drugs with other subcontractors through contract manufacturing/marketing.

---

36) Article 4 (Preparation of Application for Drug Approval or Notification, etc.) of the 「Regulation on Pharmaceuticals Approval, Notification, and Review」 (MFDS Notification)

37) Article 4 (Application for Approval Drug Manufacturing, Marketing, and Import) of the 「Regulation on Safety of Medicinal Products, etc.」 (Ordinance of the Prime Minister)

38) U.S. Physicians' Desk Reference (PDR); Drugs in Japan; ABPI Data Sheet Compendium; Rote Liste; VIDAL; L'iniformatore Farmaceutico; Arzneimittel Kompendium der Schweiz; and Compendium of Pharmaceuticals and Specialties

39) Article 31 (Approval of Manufacturing Business, etc.) of the 「Pharmaceutical Affairs Act」

6. Fees[40)]

Refer to "Application Fees for Pharmaceutical Approval/Notification" (Appendix 2).

Unit: KRW (₩)

Category	Types of drugs	Online application	Application in person/by mail
Pharmaceutical approval	New drug	6,177,850	6,828,150
	Orphan drug	3,398,150	3,755,850
	Drug requiring data submission; and Generic drug	2,007,350	2,218,650
	Provided that if the following review process is completed or unnecessary, respective fees (see Appendix 1) shall be excluded: safety/efficacy review, specifications and test methods review, and GMP data review		
Pharmaceutical notification	Pharmaceuticals	1,544,700	1,707,300
	Provided that if the following review process is completed or unnecessary, respective fees (see Appendix 1) shall be excluded: safety/efficacy review, specification and test methods review, and GMP data review		
If a review is separately conducted	Request for safety/efficacy review of drug A. New drug B. Drug requiring data submission	 3,080,000 771,400	 3,405,000 852,600
	Request for specifications and test methods review of drugs A. New drug B. Drug requiring data submission	 1,860,000 462,650	 2,060,000 511,350

**As of November 2016*

40) 「Regulation on Fees for Pharmaceutical Approval, etc.」 (MFDS Notification)

Ⅵ. References

1. Pharmaceutical Affairs Act

2. Enforcement Regulation on the Pharmaceutical Affairs Act

3. Regulation on Safety of Medicinal Products, etc.

4. Guide for Pharmaceuticals Approval and Notification, MFDS

5. National Law Information Center: http://www.law.go.kr/main.html

Appendix 1 Required data per data number

1. Origin or discovery and development history
2. Elucidation of structure and physiochemical properties (quality data)
   - A. Drug substance data
     - 1) Structure elucidation
     - 2) Physiochemical properties
     - 3) Manufacturing methods
     - 4) Data indicating specifications and test methods
     - 5) Supporting data for specifications and test methods
     - 6) Test results
     - 7) Reference standard, reagents, and test solutions
     - 8) Container and packaging
   - B. Drug product data
     - 1) Drug ingredients and quantities
     - 2) Manufacturing methods
     - 3) Data indicating specifications and test methods
     - 4) Supporting data for specifications and test methods
     - 5) Test results
     - 6) Reference standard, reagents, and test solutions
     - 7) Container and packaging
3. Stability data
   - A. Drug substance data
     - 1) Long-term or accelerated stability test
     - 2) Stress test
   - B. Drug product data
     - 1) Long-term or accelerated stability test
     - 2) Stress test
4. Toxicity data
   - A. Single dose toxicity test
   - B. Repeated dose toxicity test
   - C. Genotoxicity test
   - D. Reproductive and development toxicity test

E. Carcinogenicity test

F. Other toxicity test

1) Topical toxicity test (including topical tolerance test)

2) Dependence

3) Antigenicity and immunotoxicity

4) Mechanism of toxic action

5) Metabolites

6) Impurities

7) Others

5. Pharmacological data

A. Efficacy test

B. General pharmacological test data or safety pharmacological test data

C. Absorption, distribution, metabolism, and excretion (ADME) data

1) Analysis methods and validation report

2) Absorption

3) Distribution

4) Metabolism

5) Excretion

D. Drug interactions

6. Clinical test result data

A. Investigator's Brochure

1) Biopharmaceutics test report

2) Report of test pertinent to Pharmacokinetics (PK) using human biomaterials

3) PK test report

4) Pharmacodynamics (PD) test report

5) Efficacy and safety test report

6) Report on experience in postmarket use

7) Case report forms (CRF) and list of individual patients

B. Bridging data

7. Data on current status of use in other economies

8. Comparative review with similar drugs in Korea and data on properties of relevant drugs

Appendix 2 Application Fees for Pharmaceutical Approval/Notification

- Related regulation: 「Regulation on Fees for Pharmaceutical Approval, etc.」 (MFDS Notification)

**As of November 2016*

Unit: KRW (₩)

Type	Online	In person/ by mail
1. Application for drug manufacturing business license or conditional manufacturing business license; notification of quasi-drug manufacturing business; and notification of contract manufacturing/marketing business	385,700	426,300
2. Application for drug approval or conditional drug manufacturing		
(1) New drug (including new biological drug)	6,177,850	6,828,150
(2) Orphan drug[41]	3,398,150 (1,699,070)	3,755,850 (1,877,920)
(3) Pharmaceuticals except for subparagraphs (1) and (2)	2,007,350	2,218,650
(4) Fees shall be excluded, if review of subparagraphs (1) through (3) is completed or unnecessary with respect to any of the following:		
1) Safety/efficacy review of new drug	3,080,000	3,405,000
2) Specifications and test methods review of new drug	1,860,000	2,060,000
3) Safety/efficacy review of orphan drug[42]	1,544,700 (772,350)	1,707,300 (853,650)
4) Specifications and test methods review of orphan drug[42]	1,310,000 (655,000)	1,450,000 (725,000)
5) Safety/efficacy review of pharmaceuticals except for new drug and orphan drug	771,400	852,600
6) Specifications and test methods review of pharmaceuticals except for new drug and orphan drug	462,650	511,350
(5) Fees shall be excluded if GMP compliance assessment of subparagraphs (1) and (3) is unnecessary.	617,500	682,500
(6) Fees shall be excluded if GMP compliance assessment of orphan drug is unnecessary[42]	235,000 (117,500)	260,000 (130,000)
3. Pharmaceutical notification		
(1) Pharmaceuticals	1,544,700	1,707,300
(2) Fees shall be excluded if review or examination of subparagraphs (1) through (3) is completed or unnecessary with respect to any of the following:		
1) Specifications and test methods review	462,650	511,350
2) Bioequivalence test data review	308,750	341,250
3) GMP compliance assessment	617,500	682,500

Type	Online	In person/ by mail
4. Prior review of pharmaceuticals		
(1) Application for safety/efficacy review		
1) New drugs (including new biological product)	2,317,050	2,560,950
2) Other drugs except for new drug (including orphan drug)	772,350	853,650
3) Quasi-drugs containing new entity	1,588,000	1,755,000
4) Other quasi-drugs	385,700	426,300
(2) Application for specifications and test methods review		
1) New drugs (including new biological product)	926,250	1,023,750
2) Other drugs	463,600	512,400
3) Quasi-drugs containing new entity	850,000	940,000
4) Other quasi-drugs	231,800	256,200
(3) Application for review of GMP data	250,000	280,000
(4) IND application of pharmaceuticals	772,350	853,650
(5) Application for approval of bioequivalence test protocol	772,350	853,650
(6) Application for pharmaceuticals development plan	1,853,450	2,048,550
(7) Other data required for pharmaceutical approval and/or notification (Provided that if such product is designated as domestically developed orphan drug, fees from subparagraphs (1) 2), (4), and (6) shall be exempted)	231,800	256,200
5. IND application[42)]	772,350	853,650
6. Application for approval of bioequivalence test protocol	308,750	341,250

41) If an application for drug approval is submitted with clinical test result, prepared by obtaining approval of clinical trial protocol and conducting clinical trial, some of fees are exempted. For more information, refer to the related regulation.

42) Fees shall be exempted if a clinical test is conducted for the purpose of academic research without any request from outside.

Application fees for listing of pharmaceutical patent

Unit: KRW (₩)

Type	Online	In person/ by mail
1. Application for listing of pharmaceutical patent		
(1) Basic fees (if there is one (1) patent claim for listing of pharmaceutical patent)	81,000	90,000
(2) Additional fees (if there are two (2) or more patent claims for listing of pharmaceutical patent, such fees shall be added per claim)	32,000	36,000
2. Application for stay of sale	341,000	379,000
3. Application for priority of sale	1,125,000	1,250,000

Appendix 3 Drug Substance Requiring Registration

- Related regulation: 「Regulation on Registration of Drug Substances (DMF)」 (MFDS Notification)

**As of December 2015*

1. Gliclazide
2. Nabumetone
3. Lansoprazole
4. Rebamipide
5. Levosulpiride
6. Loratadine
7. Lovastatin
8. Loxoprofen
9. Roxythromycin
10. Risperidone
11. Domperidone
12. Enalapril
13. Trimebutine
14. Doxazocin
15. Bucillamine
16. Cimetropium
17. Biphenyl dimethyl dicarboxylate
18. Cyclosporine
19. Cefadroxil
20. Cefaclor
21. Cefodizime
22. Cefuroxime axetil
23. Cefradine
24. Cefminox
25. Cefpodoxime proxetil
26. Cefixime
27. Cimetidine
28. Cilostazol
29. Simvastatin
30. Amoxicillin
31. Aceclofenac
32. Acetaminophen
33. Acyclovir
34. Atenolol
35. Ranitidine
36. Lomefloxacin
37. Metformin
38. Bambuterol
39. Sertraline
40. Cetirizine
41. Pseudoephedrine
42. Amitriptyline
43. Acetyl-l-carnitine
44. Azelastine
45. Ambroxol
46. Eperisone
47. Ondansetron
48. Terazosin
49. Terbinafine
50. Tiropramide
51. Fluoxetine
52. Omeprazole
53. Oxatomide
54. Oxaprozin
55. Ibuproxam
56. Itraconazole

57. Vinorelbine
58. Medroxy progesterone
59. Terlipressin
60. Carvedilol
61. Ketorolac
62. Clarithromycin
63. Teicoplanin
64. Tofisopam
65. Triamcinolone
66. Triflusal
67. Famotidine
68. Paclitaxel
69. Felodipine
70. Pravastatin
71. Prednisolone
72. Flomoxef
73. Flumazenil
74. Fluconazole
75. (Deleted)
76. Astromycin
77. Isepamicin
78. Glimepiride
79. (Deleted)
80. Diclofenac
81. Methocarbamol
82. Cefbuperazone
83. S-carboxymethyl cysteine
84. Cefepime
85. Ciprofloxacin
86. Gemcitabine
87. Carteolol
88. Phenylephrine
89. Ofloxacin
90. Somatostatin
91. Tobramycin
92. Ketotifen
93. Clobetasol
94. Finasteride
95. Piperacillin
96. Hyaluronic acid
97. Diethylpropion
98. Phentermine
99. Phendimetrazine
100. Norfloxacin
101. Doxycycline
102. Levofloxacin
103. Rifampicin
104. Metronidazole
105. Sulfasalazine
106. Cefatrizine propylene glycol
107. Erythromycin
108. Bacampicillin
109. Midecamycin
110. Pyrazinamide
111. Mazindol
112. (Deleted)
113. Clavulanic acid
114. Cefmetazole
115. Ceftizoxime
116. Ceftriaxone
117. Cefotiam
118. Cefotaxime
119. Talniflumate
120. Streptokinase/Streptodornase
121. Risedronic acid
122. Losartan
123. Heparin
124. Sulpiride
125. S-atenolol
126. Levocetirizine

127. S-omeprazole
128. Lercanidipine
129. Clopidogrel
130. Amlodipine
131. S-amlodipine
132. Atorvastatin
133. Irbesartan
134. Nifedipine
135. Valsartan
136. Dropropizine
137. Levodropropizine
138. Erdosteine
139. Acetylcysteine
140. Tibolone
141. (Deleted)
142. Gabapentin
143. Naproxen
144. Nizatidine
145. Dexibuprofen
146. Lactobacillus acidophillus
147. Mesoglycan
148. Meloxicam
149. Sulodexide
150. Sulbactam
151. Cefalexin
152. Acebrophylline
153. Acarbose
154. Afloqualone
155. Alibendol
156. Ebastine
157. Epirubicin
158. Donepezil
159. Vancomycin
160. Imidapril
161. Tramadol
162. Propiverine
163. Oxiracetam
164. Iopamidol
165. Zaltoprofen
166. Thioctic acid
167. Ketoconazole
168. Choline alfoscerate
169. Teprenone
170. Topiramate
171. Pranlukast
172. Quetiapine
173. Chondroitin
174. Gatifloxacin
175. Tandospirone
176. Naloxone
177. Granisetron
178. Nebivolol
179. Desloratadine
180. Dexketoprofen trometamol
181. Estradiol
182. Ramosetron
183. Levetiracetam
184. Rivastigmine
185. Miconazole
186. Beclomethasone
187. Formoterol
188. Ipratropium
189. Xylometazoline
190. Sirolimus
191. Azithromycin
192. Atosiban
193. Fondaparinux
194. Epinastine
195. Procaterol
196. Pioglitazone

197. Oxaliplatin
198. Paricalcitol
199. Polydeoxyribonucleotide
200. Brimonidine
201. Timolol
202. Clevudine
203. Tadalafil
204. Tacrolimus
205. Theobromine
206. Tosufloxacin
207. Topotecan
208. Travoprost
209. Drugs that require securing pharmaceutical equivalence as per Article 4 ① 3 B of the 「Regulation on Safety of Medicinal Products, etc.」
210. Drug substance of injections
211. Drug substance to be registered by a person/company who wishes to manufacture/market or import drug substance

Guide to Drug Approval System in Korea

Date of Issue	April 2017
Issued by	Yeowon Sohn
Executive Editor	Sun Hee Lee
Translation proofread by	(Drug Review Management Division, Drug Evaluation Department, National Institute of Food and Drug Safety Evaluation) Youngju Choi, Heesung Kim, Eunhee Kim, Yoonsook Lee, Yongseok Ko, Daehyun Baek, Myung Ah Chung, Sook Lim, Su-kyoung Seong, Wook-Jin Chung, Ju-kyoung Song, Bong Seo Park, Cheulho Cho, Sang-A Yoo, Sun Young Chang,Yoonjung Choi, Eunkyoung Lee, Minyoung Lim, Ji-na Lee,
Published by	National Institute of Food and Drug Safety Evaluation

※ If you have any comment or inquiries on this Guide, please contact the Drug Review Management Division (International Cooperation), Drug Evaluation Department, National Institute of Food and Drug Safety Evaluation, Ministry of Food and Drug Safety, Korea.

TEL : +82-43-719-2874~77

FAX : +82-43-719-2870

Guide to Drug Approval System in Korea

MINISTRY OF FOOD AND DRUG SAFETY
National Institute of Food and Drug Safety Evaluation