Review Regulations for the Registration of Orphan Drugs

Article 1

These Regulations are established pursuant to the stipulations of Articles 15 to 22 in the Rare Disease and Orphan Drug Act (hereinafter referred to as the Act).

Article 2

Pharmaceutical companies applying for registration of orphan drugs shall fill out the application form and submit it, along with the application fee and the following documents, to the central competent authority for review:

I. Label, package insert and license.
II. Data related to efficacy, quality and safety.
III. For applications for registration of an imported orphan drug, approval for manufacture and sales issued by the country of origin and the document stating the manufacturer's authorization for registration.
IV. Other documents designated by the central competent authority, as shown in Table 1 and Table 2.

Article 3

With applications for manufacture or import of orphan medicaments, such as new drugs, new medical devices or medical devices for new medical efficacy, the following documents shall be attached in addition to the documents prescribed in the stipulations of the preceding Article.

I. Academic theories and related research reports and data.
II. Safety test reports and clinical trial reports

Article 4

If the pharmaceutical company is unable to attach the certificate of approval for manufacture and sale issued by the country of origin as stipulated in Article 3, Paragraph 3 at the time of application, it should supplement the document before collecting the permit.

Article 5

When applying for registration of import or manufacture of orphan drugs, the pharmaceutical company shall attach the approval documents issued by the central competent authority for its manufacturing sites or the documents certifying its compliance with the Good Manufacturing Practice (GMP) and relevant documents for such drugs. If necessary, the central competent authority may send staff to investigate.

Article 6

For those applying for registration in accordance with the Act, Article 18, Paragraph 1, Subparagraphs 2 to 4, in addition to the certificates and documents stipulated in Article 3, the relevant materials stipulated in the Act, Article 18, Paragraph 1, Subparagraphs 2 to 4 shall be submitted.

Article 7

The fee for applications for registration of orphan drugs is subject to the fee standards set by the central competent authority.

Article 8

These Regulations take effect August 9, 2000.

Table 1 Documents to Be Attached for Registration of Orphan Drugs

Materials to be submitted	Orphan drug		Orphan medical device	
	Local products	Imported products	Local products	Imported products
Fee	○	○	○	○
Original and duplicate copy of the Drug Registration Application Form	○	○	○	○
Relevant affidavit as stipulated for trademark and patent (A)	○	○	○	○
Relevant affidavit as stipulated for test failure (B)	○	○		
Form for sticking label and package insert (two copies)	○	○	○	○
Form for sticking license	○	○	○	○
Manufacture and control standards or batch	○	○		

manufacture records				
Two copies of testing specifications, methods and results for the active pharmaceutical ingredient (API)	◯	◯		
Two copies of testing specifications, methods and results for the excipient(s)		△		
Two copies of testing specifications, methods and results for the final products	◯	◯	◯	◯
Documents of stability study	◯	◯	△	△
Certificates Adopted				
Certificate of approval for manufacture and sale from the country of origin	△	◯		◯
Authorization letter		◯		◯
Drug prescription basis/medical device specification basis	△		△	△
Photocopy of the latest approval letter for drug GMP follow-up factory inspection/photocopy of GMP Approval and Registration Certificate	◯		◯	◯

Good Manufacturing Practice Certificate for the site of manufacture		◯		
Three copies of sterile preparation validation report		△		
Technical data for medical devices, such as physical, chemical, biocompatibility or electrical properties, according to product characteristics			△	△
Efficacy, quality and safety data	See Table 2			
Medical device clinical trial reports (at least three reports, along with Chinese translation)			△	△
Drug testing	◯	◯	△	△

◯ indicates item is required; △ indicates depends on case

Table 2 Information on Efficacy, Quality and Safety for Examination and Registration of Orphan Drugs

Clinical trial report
Absorption, distribution, metabolism, excretion, bioavailability/bioequivalence test report
Pharmacological effects
Safety test report
Stability test report
Physicochemical properties, test methods, specifications
Origin, discovery, and usage status in other countries

Medical journal	○	○	
Clinical trial	○	○	
Bioequivalence	△	×	
Bioavailability	△	○	
Excretion	△	△	
Metabolism	△	△	
Distribution	△	△	
Absorption	△	△	
General pharmacological properties	○	×	
Proof of efficacy	○	○	
Local irritation	△	×	
Carcinogenicity	△	×	
Variability	△	×	
Antigenicity	△	×	
Dependence	△	×	
Embryo testing	△	△	
Chronic toxicity	△	△	
Subacute toxicity	○	○	
Acute toxicity	○	○	
	○	○	
Inspection specifications & method	○	○	
Physical and chemical properties	○	×	
Structural formula	○	×	
Property comparison	○	○	
Usage status in other countries	△	△	
Origin and discovery	○	○	
New ingredient			
Similar medical product	New administration route		

	New therapeutic effect		○	△	○	×	×	×	×	×	×	×	×	×	×	×	×	×	○	×	△	△	△	△	△	×	○	○
	New compound		○	△	○	×	×	○	○	○	○	△	×	×	×	×	×	△	○	○	△	△	△	△	○	×	○	△
	New dosage form	Controlled release preparation	○	△	○	×	×	○	○	△	△	△	×	×	×	×	×	×	×	×	×	×	×	×	○		○	△
		Immediate release preparation	○	△	○	×	×	○	○	×	×	×	×	×	×	×	×	×	×	×	×	×	×	×	◎	◎	◎	△

	New administration dose	◯	△	◯	×	×	×	×	△	△	△	×	×	×	×	×	×	◯	×	△	△	△	△	△	×	◯	△
	New unit strength	◯	△	◯	×	×	◯	◯	△	△	△	×	×	×	×	×	×	△	×	×	×	×	×	◎	◎	◎	×
	Vaccine	◯	△	◯	×	×	◯	◯	△	△	△	×	×	◯	△	×	△	×	×	×	×	×	×	×	×	◯	◯

Note: ◯ indicates materials that must be submitted

◎ indicates one of the options below:

(1) Bioequivalence test (2) Bioavailability and clinical **trial**

× indicates materials that are not required

△ indicates depends on case