Orphan Designation System in Japan

10, March 2014

Ministry of Health,
Labour and Welfare

Background of the Orphan Designation System

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Ministry of Health, Labour and Welfare

- Before the system had been implemented, the R&D on medicines for rare diseases including HIV infection had not been enough in Japan
- It was needed to provide the people with the safe and effective medicines/medical devices answering the needs from the people.

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in 1993, the PAA had been amended based on these backgrounds.

The contents of the system

- ✓Priority consultation and on clinical trials and review
- ✓Discount of the fee for review
- ✓Extension of re-examination period
- ✓Grant for R&D
- ✓Tax incentives

Pharmaceutical Affairs Act (Low. No. 145 dated August 10, 1960)

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(Designation)

Article 77-2:

When an application is made from a person (including those who manufacture etc. In foreign countries with respect to a product to be exported to Japan) The minister of Health, Labour and Welfare may designate the drug or medical device in the application as an orphan drug or orphan medical device in the application as an orphan drug or orphan medical device after seeking the opinion PAFSC

(1)The number of patients using such a drug or medical devices does not exceed the number specified by MHLW Ministerial Ordinance

(2)A drug or medical devices, if approved for marketing, is expected to prove especially valuable when the drug or medical device is used in the medical practice

2. When the Minister designates pursuant to the provisions of the preceding paragraph, this designation shall be published.

(Notification of suspension of research and development etc.)

Article 77-2-4

When a person obtaining the designation specified under Article 77-2, Paragraph 1, intends to suspend the research and development, or manufacturer or import of the designated orphan drug or medical device, she/he shall submit notification of the suspension to the minister beforehand.

(Cancellation etc. of Designation)

Article 77-2-5

When the notification pursuant to the provisions of the preceding article has been submitted, the Minister shall cancel the designation specified under Article 77-2, Paragraph 1 (hereinafter referred to as “designation” in this article).

2.The minister may cancel the designation when any one of the following items is met.

(1) The orphan drug or medical device has not fallen under any one of the items, Paragraph 1, Article 77-2;
(2) Any improper action is taken in designation.
(3) The orphan drug or orphan medical devices is not developed or marketed without proper reason.
(4) The person obtaining the designation has violated this law or other laws and ordinances related pharmaceutical affairs or the measured taken in accordance with the laws and ordinances.

3.When the designation has been cancelled pursuant to the provisions of the two preceding paragraphs, the Minister shall publish the cancellation.

Notification on the Act to Amend the PAA etc.

(Bureau of Pharmaceutical Affairs, Notification Number 725dated 25th August, 1993)

(Designation of orphan drugs/medical devices)

Designation Criteria

The designation of orphan drugs/medical devices, specified under Article 77-2, should be done for the products fulfilling all of the following requirements

(1) Number of patients

The number of patients who may use the drug or medical device should be less than 50000 in Japan.

(2) Medical needs

The drugs or medical devices should be indicated for the treatment of serious diseases, including difficult-to-treat diseases. In addition, they must be drugs or medical devices for which there are high medical needs satisfying one of the following criteria.

(3) Possibility of development

There should be a theoretical rationale for the use of the product for the target disease, and the development plan should be appropriate.

Designation Criteria 1/2

（1） The number of the patients

・The number of the patients for the proposed orphan product is to be under 50,000 in Japan.

○The estimation of the number of patients:
Health and Labour Sciences Research Grant
Academic Societies
○Desirable to have multiple statistical data.

・From 2006, the following products can be the subject of the orphan designation, as long as the number of the expected patients is under 50,000 **at the time of the application**

○A vaccine for the infectious disease which is rare in Japan, or only observed in other than Japan, and the indication of the vaccine is for prevention purpose with specified group such as those who are planning to go to the place of epidemic area
○A vaccine to prevent new infectious disease which results from gene mutation, and has not yet emerged, but has a big impact on people's health and life once emerges

Designation Criteria 2/2

（2） The necessity in medical needs

- Drugs for rare diseases
  - ・No medical treatment so far
  - ・Significant effectiveness and safety when compared with existing medical products

（3） Feasibility of development to a product

- Evidence that the product can be used for the diseases
- Feasible plan for the development of the products

Preparation for the Consultation the Application of Designation

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（1） Appointment of the consultation

- ○ The consultation is held by MHLW (Evaluation and Licensing Division: ELD)
- ○ On an as-needed basis
- ○ The arrangement should be done by facsimile and/or postal basis
  - ・ The format and its instruction available through the URL below: http://www.mhlw.go.jp/english/policy/health-medical/pharmaceuticals/dl/20120618_02.pdf
  - ・ The summary/brochure on the product is desirable

（2） The date of the consultation

- ○ The date of the consultation is to be notifies from the responsible officials once determined.

The Consultation on the Application

（1） How to conduct?

- ○ Prior to submission of the application
- ○ Applicant is required to come to MHLW (ELD)
- ○ Allotted time is approximately 30 mins
- ○ No Specific limit on the number of visitor: (request to make it appropriate number always)

（2） Materials required for the consultation:

- ○ The **draft application** and **its attachments** should be ready.
- ○ Reference documents can be attached if necessary.
- ○ 5 copies of the document
- ○ The documents to be presented should be sent 1 week of the consultation beforehand

Applications of Orphan Drug/Medical Device Designation

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○Application form

- Article 250, Ministerial Ordinance for Enforcement of the Pharmaceutical Affairs Act
  - Application for Orphan Drug Designation [Form 107(1)],
  - Application for Orphan Medical Device Designation [Form 107(2)]
- Number of copies to be submitted: One original and two copies
- Submit to:
  Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW

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Attachments to the Application

- Data on the number of patients
  - Objective statistical data on the number of patients in Japan for whom the drug or medical device will be indicated.
- Data on medical needs
  - Data on the diseases such as etiology and symptom
  - Data on the current status such as availability of similar drugs/medical devices and treatment
- Data on the theoretical rationale for the use of the drugs/medical devices
  - Related data in a draft dossier of application for marketing authorization, which is available at the time of application for orphan drug/medical device
- Development plan (data on the possibility of development)
  - Data on the outline of the development plan, including the current development status, expected test items, duration of the study and necessary expenses
- Preparation of Summary of the Orphan Drug/Medical Device
  - The Summary of the Orphan Drug/Medical Device should be prepared for Committee meetings and publication.

Orphan Drug/Device Designation Procedure

Required data (for drugs)

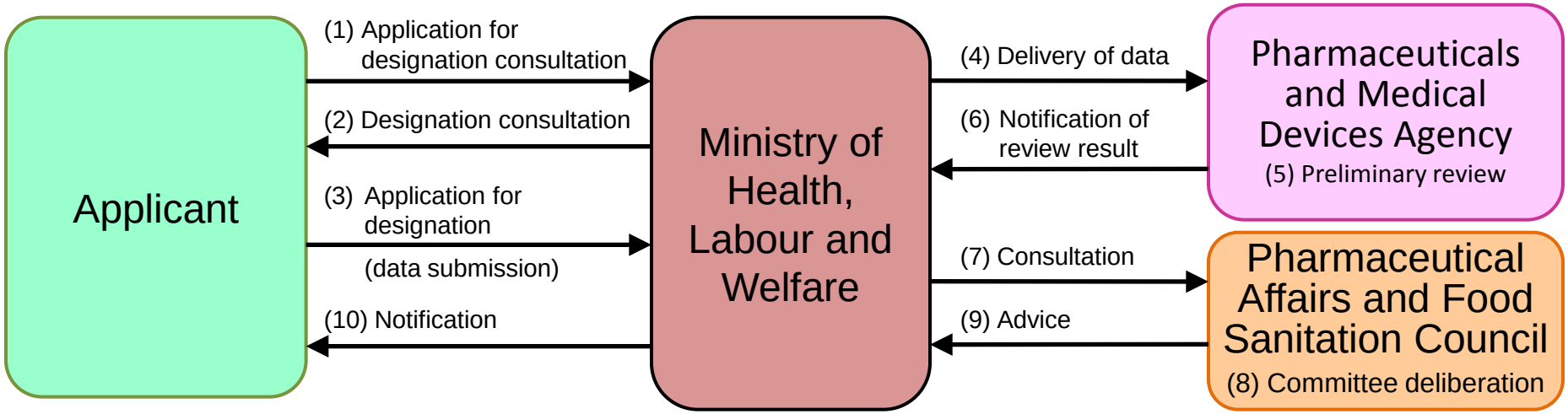
Number of patients
- Objective statistical data on the number of patients who will use the drug in Japan

Medical needs
- Indication (e.g., cause and symptoms)
- Current clinical situation, such as the availability of similar drugs or treatment

Rationale (subject to availability)
- Origin or history of discovery and usage conditions in foreign countries etc.
- Manufacturing method, specifications and test procedures
- Stability
- Pharmacological effects
- Absorption, distribution, metabolism and excretion
- Toxicity
- Clinical data

Development plan
- Summary of development plan, such as the expected test items, laboratories and necessary expenses

Designation procedure



Cancellation of Designation

The sponsor of the designated orphan drug/medical device must notify the Minister of Health, Labour and Welfare of its intention to discontinue the research, marketing or manufacturing of the product at least 1 year before the expected discontinuation. Contact the administrator of orphan drug/medical device designation at the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW and the NIBIO when submitting a notice.

○Forms to be filled

- ◆ (Article 252, Ministerial Ordinance for Enforcement of the Pharmaceutical Affairs Act)
- ◆ Orphan Drug/Medical Device Research/Marketing/Manufacturing Discontinuation Notice (Form 108)

○Number of copies to be submitted: One original and two copies

○To be submitted to:

Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW

The withdrawal of orphan drug/medical device designation will be notified after the Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, MHLW receives the discontinuation notice and reports to Pharmaceutical Affairs and Food Sanitation Council (PAFSC).