Provisional Translation (as of April 2024)*

PSB/PED Notification No. 0116-1
PSB/MDED Notification No. 0116-1
January 16, 2024

To: Prefectural Health Departments (Bureaus)

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

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

Partial Revision of "Designation of Orphan Drugs etc."

Designation of orphan drugs, orphan medical devices, and orphan regenerative medicinal products (hereinafter referred to as "orphan drugs etc.") based on Article 77-2 (1) 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 "the Act") has been made in accordance with "Designation of Orphan Drugs etc." (Joint PSEHB/PED Notification No. 0831-7 issued by the Director, Pharmaceutical Evaluation Division and PSEHB/MDED Notification No. 0831-7 issued by the Director of Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated August 31, 2020, hereinafter referred to as the "Notification by Directors").

Designation of orphan drugs etc. has been revised as shown in the attached new/old comparison table based on the review at "Review Committee on Regulatory Affairs to Strengthen Drug Discovery and Development/Ensure Stable Supply," and it has been decided that the revision applies from today. We ask you to understand this revision and inform related parties under your jurisdiction of this matter.

In addition, with regard to Note 8 "Priority review and priority consultation," revision of its handling will be considered based on the number etc. of designations of orphan drugs approximately 1 year after the application of this notification.

The revised Notification by Directors is attached for reference.

Appendix

New/Old Comparison Table

(The underlined parts are revised)

New	Old
1 Designation Criteria Designation of orphan drugs etc. in accordance with Article 77-2 (1) of the Act shall be made for drugs, medical devices, and regenerative medicine products (hereinafter referred to as "drugs etc.") that are related to the application for designation and meet all of the following (1) to (3). (1) Number of subjects A Criteria for the number of subjects The number of subjects pertaining to the usage of the drugs etc. is less than 50,000 in Japan. However, if the usage is for a designated intractable disease (which refer to the designated diseases specified in Article 5 (1) of Act on Medical Care for Patients with Intractable Diseases [Act No. 50 of 2014, hereinafter referred to as "Designated Intractable Disease Act"], the same applies hereinafter), the number of subjects should be less than the number of subjects specified in the Article (approximately 1/1,000 of the population). B Method of estimation of the number of subjects It is necessary to estimate the number of subjects with the use of reliable results of surveys by Health and Labour Sciences Research Grants or related academic societies. However, if it is not possible to estimate a reliable number of subjects due to an insufficient survey on the number of patients, it is desirable to estimate it based on multiple statistical data etc. and by multiple methods. However, if the usage of the drugs etc. is for a designated intractable disease, the number of subjects is deemed to satisfy the requirements. It is therefore unnecessary to estimate the number of subjects separately. C Scope of diseases subject to designation The so-called "salami slicing" application in which the number of patients is calculated to be less than 50,000 by adding a prefix such as "serious," and a caveat etc. without any clear medical or pharmaceutical reasons	1 Designation of orphan drugs etc. (1) Designation Criteria Designation of orphan drugs etc. in accordance with Article 77-2 (1) of the Act shall be made for drugs, medical devices, and regenerative medicinal products (hereinafter referred to as "drugs etc.") that are related to the application for designation and meet all of the following. A Number of subjects (Article 250-2 and Article 251 of Regulation for Enforcement of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices [Order of the Ministry of Health and Welfare No. 1 of 1961, hereinafter referred to as "Enforcement Regulation"]) The number of subjects pertaining to the usage of the drugs etc. (for drugs or regenerative medicinal products to be used for prevention of infectious diseases, subjects who are expected, at the time of application for designation, to use the drug or regenerative medicinal product when marketing approval is granted) is less than 50,000 in Japan. However, if the usage is for a designated intractable disease (which refer to the designated diseases specified in Article 5 (1) of Act on Medical Care for Patients with Intractable Diseases [Act No. 50 of 2014, hereinafter referred to as "Designated Intractable Disease Act"] , the same applies hereinafter), the number of subjects specified in the Article (approximately 1/1,000 of the population) or less is the number of subjects to be covered. The following should be noted: - If the usage of the drugs etc. is for other diseases than the designated intractable diseases, it is necessary to estimate the number of patients with the use of survey results by Health and Labour Sciences Research Grants or reliable academic societies. However, if it is not possible to estimate a reliable number of patients due to an insufficient survey on the number of patients, the applicant should estimate it based on multiple statistical data and show that the estimated number of patients is less than 50,000. It is desirable to submit the results of estimation by

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is not acceptable in principle. On the other hand, if the applicant intends marketing drugs etc. for a restricted part of the target disease for which advancement in drug development is limited despite high unmet needs, and the restrisction is based on appropriate medical and pharmaceutical evidence including the age range (including pediatrics), treatment algorithm and line, risk classification, and the necessity of medication etc., the restricted part of disease is not deemed "salami slicing." However, if the number of patients with the overall disease largely exceeds 50,000, the number of patients should be carefully confirmed based on multiple pieces of evidence. D Use for prevention of infectious diseases For drugs or regenerative medicinal products to be used for prevention of infectious diseases, the estimated number of subjects who are expected, at the time of application for designation, to use the drug or regenerative medicine product in 1 year when marketing approval is granted, is regarded as the number of subjects. "Drugs to be used for prevention of infectious diseases" include but are not limited to drugs that satisfy any of the following: [1] Vaccines to be used for prevention of infectious diseases that are rare in Japan and epidemic in limited populations [2] Vaccines for travelers against infectious diseases that occur only in foreign countries to be used for visitors (travelers) who visit the epidemic area [3] Vaccines that are for emerging/re-emerging infectious diseases likely to have a significant impact on the life and health of the public, that are developed for the infectious disease before its epidemic, and that will not be used just after the approval	multiple methods. - If the usage of the drugs etc. is for a designated intractable disease, the number of subjects is deemed to satisfy the requirements. Therefore, submission of data for estimation of the number of patients may be replaced with a statement that the disease is a designated intractable disease. - The so-called "salami slicing application" in which the number of patients is calculated to be less than 50,000 by adding a prefix such as "serious" or a caveat etc. without any clear medical or pharmaceutical reasons is not acceptable in principle. - "Drugs to be used for prevention of infectious diseases" shall meet any of the following: - Vaccines to be used for prevention of infectious diseases that rarely occur in Japan or that occur only in foreign countries and occur only in a specific population such as visitors to the epidemic area - Vaccines to prevent possibly emerging or re-emerging infectious diseases due to gene mutation etc. which are likely to have a significant impact on the life and health of the public once it occurs but of which timing of occurrence and scale of epidemic are unknown, and which have not yet occurred at the time of application for designation

(2) Medical needs With marketing approval for the drugs etc. in application, those which are expected to have particularly excellent value for usage in its intended purpose. "Have particularly excellent value for usage" in Article 77-2 (1) (ii) of the Act, in principle, refer to drugs etc. with high medical needs that meet the following A and B: A Seriousness of the target disease In principle, the diseases to be designated are serious diseases or infectious diseases likely to have a significant impact on the life and health of the public. Serious diseases refer to diseases that are fatal as well as lead to the very low quality of life for a long time. B Effectiveness for the target disease Drugs etc. that meet any of the following [1] to [3] and that are effective for the target disease. [1] There are no approved drugs etc. (including treatment/ prophylaxis used as the standard but excluding unapproved or off-label use drugs etc.; the same applies to the following [2] to [3]). [2] There are approved drugs etc., however the prognosis of the target disease is poor even treated with those drugs etc. and, the existing treatment/prophylaxis options are not sufficient and thus multiple options are clinically needed (including cases where it is considered that there is a certain number of patients in whom treatment with approved drugs etc. is difficult due to the medical environment/treatment environment). Drugs etc. expected to be effective to a certain extent, for instance, those that have a novel mode of action and of which nonclinical study suggest the effect, or that can be administered to patients in whom administration of approved drugs etc. is difficult due to the medical environment/treatment environment. [3] Drugs etc. expected to be more effective and safer compared to approved drugs etc. based on clinical	B Medical needs With marketing approval for the drugs etc. in application, those which are expected to have particularly excellent value for usage in its intended purpose. "Have particularly excellent value for usage" in Article 77-2 (1) (ii) of the Act, in principle, refer to drugs etc. with high medical needs that are used for serious diseases and meet either of the following: (A) No appropriate alternative drugs etc. or treatments is available. (B) Expected to have significantly higher efficacy and safety compared to existing drugs etc.

study results etc. The following cases are considered as expected to be more effective and safer, although determination should be made by not only on the followings, but also case-by-case basis according to characteristics of the drug and disease. - Demonstrated to be superior in the efficacy or safety based on the results of head-to-head comparison with the approved drug in an appropriately designed comparative clinical study - Fully suggested significantly higher efficacy or safety compared to the approved drug based on the indirect comparison of multiple clinical studies etc. - Prioritized over the approved drug in Japanese or international major guidelines based on a certain extent of scientific evidence on efficacy or safety - High probability of being superior in safety because the safety profile is completely different and a certain number of patients who are difficult to receive approved drug can be treated by the drugs etc. For instance, in the case that degree of precautions in the package insert is significantly different (e.g. the boxed warning for the approved indication are different) etc.	
(3) Possibility of development Having organizations and plans that enable development in Japan. Specifically, the outline of a planned clinical studies to be conducted before the marketing application is clarified. In addition, nonclinical studies required to start a first-in human study have been mostly completed.	C Possibility of development There are rationales for the use of the drugs etc. for the target disease, and its development plan is recognized to be appropriate.
2 Method of designation (No change)	(2) Method of designation Designation of orphan drugs etc. are made after hearing the opinions of the Pharmaceutical Affairs and Food Sanitation Council. For designated drugs etc., the date of designation, name of drugs, target disease and the name and addresses of the applicant are published on the website of the Ministry of Health, Labour and Welfare.
3 Consultation on designation Before the application for the designation of	2 Consultation on designation Before the application for the designation of

orphan drugs etc., the applicant should consult with the person in charge of designation at Pharmaceutical Evaluation Division or Medical Device Evaluation Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare.	orphan drugs etc., the applicant should consult with the person in charge of designation at Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, or Office of Director, Medical Device and Regenerative Medicine Product Evaluation Division, Ministry of Health, Labour and Welfare.
4 Application for designation (1) Description in the application form Those who intend to apply for the designation of orphan drugs etc. should submit the application form using the Form No. 107 (1), Form No. 107 (2) or Form No. 107 (3) in the Enforcement Regulation. (2) Attachments to the application form (No change)	3 Application for designation (1) Description in the application form Those who intend to apply for the designation of orphan drugs etc. should submit the application form using the Form No. 107 (1), Form No. 107 (2) or Form No. 107 (3) in the Enforcement Regulation. However, those who have a foreign nationality and intend to obtain the designation of orphan drugs etc. should also notify the name, address, and contact information of the person in charge of development in Japan. (2) Attachments to the application form (No change)
5 Discontinuation of tests and research When a person designated (hereinafter referred to as "designation holder") pursuant to the provisions of Article 77-2, (1) of the Act intends to discontinue tests and research, marketing or manufacturing of orphan drugs etc. that pertain to the designation, they shall promptly notify the Minister of Health, Labour and Welfare thereof based on Article 77-5 of the Act. As a notification of discontinuation, Form No. 108 of the Enforcement Regulation should be submitted.	4 Discontinuation of tests and research When a person designated (hereinafter referred to as "designee") pursuant to the provisions of Article 77-2, (1) of the Act intends to discontinue tests and research, marketing or manufacturing of orphan drugs etc. that pertain to the designation, they shall promptly notify the Minister of Health, Labour and Welfare thereof based on Article 77-5 of the Act. As a notification of discontinuation, Form No. 108 of the Enforcement Regulation should be submitted.
6 Rescindment of designation The Minister of Health, Labour and Welfare, when receiving a notification of discontinuation under Article 77-5 of the Act, rescinds the designation based on Article 77-6 (1) of the Act. Based on Article 77-6 (2) of the Act, the Minister of Health, Labour and Welfare may rescind the designation in cases that fall under any of the following items: The public announcement of the rescindment of designation is made in accordance with 2. When rescinding based on A, the Minister will hear the opinion of the designation holder in advance. A The requirement of 1 is no longer met. B When unlawfulness such as false	5 Rescindment of designation The Minister of Health, Labour and Welfare, when receiving a notification of discontinuation under Article 77-5 of the Act, rescinds the designation based on Article 77-6 (1) of the Act. Based on Article 77-6 (2) of the Act, the Minister of Health, Labour and Welfare may rescind the designation in cases that fall under any of the following items: The public announcement of the rescindment of designation is made in accordance with 1 (2). A The requirement of 1(1) A is no longer met. B The requirement of 1 (1) B is no longer met due to approval of other drugs etc. C When unlawfulness such as false

descriptions in the application for designation is found. C When tests and research, or marketing is not provided for orphan drugs etc. without any legitimate grounds. D When a designation holder violates the Act or other pharmaceutical laws and regulations specified by Cabinet Order, or any of the dispositions thereupon.	descriptions in the application for designation is found. D When tests and research, or marketing is not provided for orphan drugs etc. without any legitimate grounds. E When a designee violates the Act or other pharmaceutical laws and regulations specified by Cabinet Order, or any of the dispositions thereupon.
7 Succession If the designation holder transfers the right of development in Japan to others, the designation holder should notify of discontinuation of tests and research in accordance with 5, and those receiving the right of development (hereinafter referred to as "appointed successor") should submit the data in E in 4 (1) and (2). However, if the contents of the documents have been changed since the time when the original designation holder receives the designation, data that show that the changes satisfy the requirements at the time of succession should also be submitted. Succession is approved with the letter of designation that is separately issued. Designation holders who consider succession should consult with the person in charge of designation specified in 3 in advance. In so doing, the designation holders should also submit a copy of the contract for succession and document that explain the background of succession.	6 Succession If the designee transfers the right of development in Japan to others (hereinafter referred to as "successor"), the designee should notify of discontinuation of tests and research in accordance with 4, and the successor should submit the data in E in 3 (1) and (2). However, if the contents of the documents have been changed since the time when the designee receives the designation, documents that show that the changes satisfy the requirements at the time of succession should also be submitted. Succession is approved with the letter of designation that is separately issued. Designees who consider succession should consult with the person in charge of designation specified in 2 in advance. In so doing, the designee should also submit a copy of the contract for succession and documents that explain the background of succession.
8 Priority review and priority consultation Orphan drugs subject to priority review/consultation are only those that satisfy the former designation criteria of orphan drugs for the time being. Therefore, those that have no sufficient evidence to meet the former designation criteria are not subject to priority review/consultation for orphan drugs. The eligibility for priority review/consultation will be described in Orphan Drug Designation Preliminary Evaluation Report. For orphan drugs that are considered to be not subject to priority review/consultation at the time of designation but later to fulfill the criteria of priority review/consultation as the development advances, the consultation service of Pharmaceuticals and Medical Devices Agency (PMDA) can be used (during consultation on how to summarize application dossier just before the marketing application in principle) to clarify the eligibility, by which priority reviewconsultation shall be applicable.	(New)

Reference

PSEHB/PED Notification No. 0831-7
PSEHB/MDED Notification No. 0831-7
August 31, 2020
[Partially revised] January 16, 2024

To: Prefectural Health Departments (Bureaus)

From: Director, Pharmaceutical Evaluation Division,
Pharmaceutical Safety and Environmental Health Bureau,
Ministry of Health, Labour and Welfare
(Official seal omitted)

Director of Medical Device Evaluation Division,
Pharmaceutical Safety and Environmental Health Bureau,
Ministry of Health, Labour and Welfare
(Official seal omitted)

Designation of Orphan Drugs etc.

Designation of orphan drugs, orphan medical devices, and orphan regenerative medicine products (hereinafter referred to as "orphan drugs etc.") based on Article 77-2 (1) of Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Act No. 145 of 1960, hereinafter referred to as "the Act") have been made conventionally in accordance with the "Criteria for Designation of Orphan Drugs" (PFSB Notification No. 0401-11 dated April 1, 2015 by Director, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, hereinafter referred to as "the former notification").

In association with regulation of the method of the public announcement for orphan drugs etc. by the Ministerial Ordinance on Maintenance, Etc. of Related Ministerial Ordinances in Association With Enforcement of the Act Partially Amending the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (MHLW Ordinance No. 155 of 2020), the handling of designation of orphan drugs etc. has been decided as shown below. We ask you to understand this revision and inform related parties under your jurisdiction of this matter.

This notification shall be applied from September 1, 2020, on and after which the

former notification is abolished.

Note

1 Designation Criteria

Designation of orphan drugs etc. in accordance with Article 77-2 (1) of the Act shall be made for drugs, medical devices, and regenerative medicine products (hereinafter referred to as "drugs etc.") that are related to the application for designation and meet all of the following (1) to (3).

(1) Number of subjects

A Criteria for the number of subjects

The number of subjects pertaining to the usage of the drugs etc. is less than 50,000 in Japan.

However, if the usage is for a designated intractable disease (which refer to the designated diseases specified in Article 5 (1) of Act on Medical Care for Patients with Intractable Diseases [Act No. 50 of 2014, hereinafter referred to as "Designated Intractable Disease Act"] , the same applies hereinafter), the number of subjects should be less than the number of subjects specified in the Article (approximately 1/1,000 of the population).

B Method of estimation of the number of subjects

It is necessary to estimate the number of subjects with the use of reliable results of surveys by Health and Labour Sciences Research Grants or related academic societies. However, if it is not possible to estimate a reliable number of subjects due to an insufficient survey on the number of patients, it is desirable to estimate it based on multiple statistical data etc. and by multiple methods.

However, if the usage of the drugs etc. is for a designated intractable disease, the number of subjects is deemed to satisfy the requirements. It is therefore unnecessary to estimate the number of subjects separately.

C Scope of diseases subject to designation

The so-called "salami slicing" application in which the number of patients is calculated to be less than 50,000 by adding a prefix such as "serious," and a caveat etc. without any clear medical or pharmaceutical reasons is not acceptable in principle.

On the other hand, if the applicant intends marketing drugs etc. for a restricted part of the target disease for which advancement in drug development is limited despite high unmet needs, and the restrisction is based on appropriate medical and pharmaceutical evidence including the age range (including pediatrics), treatment algorithm and line, risk classification, and the necessity of medication etc., the

restricted part of disease is not deemed “salami slicing.” However, if the number of patients with the overall disease largely exceeds 50,000, the number of patients should be carefully confirmed based on multiple pieces of evidence.

D Use for prevention of infectious diseases

For drugs or regenerative medicinal products to be used for prevention of infectious diseases, the estimated number of subjects who are expected, at the time of application for designation, to use the drug or regenerative medicine product in 1 year when marketing approval is granted, is regarded as the number of subjects. “Drugs to be used for prevention of infectious diseases” include but are not limited to drugs that satisfy any of the following:

[1] Vaccines to be used for prevention of infectious diseases that are rare in Japan and epidemic in limited populations

[2] Vaccines for travelers against infectious diseases that occur only in foreign countries to be used for visitors (travelers) who visit the epidemic area

[3] Vaccines that are for emerging/re-emerging infectious diseases likely to have a significant impact on the life and health of the public, that are developed for the infectious disease before its epidemic, and that will not be used just after the approval

(2) Medical needs

With marketing approval for the drugs etc. in application, those which are expected to have particularly excellent value for usage in its intended purpose.

“Have particularly excellent value for usage” in Article 77-2 (1) (ii) of the Act, in principle, refer to drugs etc. with high medical needs that meet the following A and B:

A Seriousness of the target disease

In principle, the diseases to be designated are serious diseases or infectious diseases likely to have a significant impact on the life and health of the public. Serious diseases refer to diseases that are fatal as well as lead to the very low quality of life for a long time.

B Effectiveness for the target disease

Drugs etc. that meet any of the following [1] to [3] and that are effective for the target disease.

[1] There are no approved drugs etc. (including treatment/prophylaxis used as the standard but excluding unapproved or off-label use drugs etc.; the same applies to the following [2] to [3]).

[2] There are approved drugs etc., however the prognosis of the target disease is poor even treated with those drugs etc. and, the existing treatment/prophylaxis options are not sufficient and thus multiple options are clinically needed (including cases where it is considered that there is a certain number of patients in whom treatment with approved drugs etc. is difficult due to the medical environment/treatment environment). Drugs etc. expected to be effective to a certain extent, for instance, those that have a novel mode of action and of which nonclinical study suggest the effect, or that can be administered to patients in whom administration of approved drugs etc. is difficult due to the medical environment/treatment environment.

[3] Drugs etc. expected to be more effective and safer compared to approved drugs etc. based on clinical study results etc.

The following cases are considered as expected to be more effective and safer, although determination should be made by not only on the followings, but also case-by-case basis according to characteristics of the drug and disease.

- Demonstrated to be superior in the efficacy or safety based on the results of head-to-head comparison with the approved drug in an appropriately designed comparative clinical study
- Fully suggested significantly higher efficacy or safety compared to the approved drug based on the indirect comparison of multiple clinical studies etc.
- Prioritized over the approved drug in Japanese or international major guidelines based on a certain extent of scientific evidence on efficacy or safety
- High probability of being superior in safety because the safety profile is completely different and a certain number of patients who are difficult to receive approved drug can be treated by the drugs etc. For instance, in the case that degree of precautions in the package insert is significantly different (e.g. the boxed warning for the approved indication are different) etc.

(3) Possibility of development

Having organizations and plans that enable development in Japan.

Specifically, the outline of a planned clinical studies to be conducted before the marketing application is clarified. In addition, nonclinical studies required to start a first-in human study have been mostly completed.

2 Method of designation

Designation of orphan drugs etc. are made after hearing the opinions of the Pharmaceutical Affairs and Food Sanitation Council.

For designated drugs etc., the date of designation, name of drugs, target disease and the name and addresses of the applicant are published on the website of the Ministry of Health, Labour and Welfare.

3 Consultation on designation

Before the application for the designation of orphan drugs etc., the applicant should consult with the person in charge of designation at Pharmaceutical Evaluation Division or Medical Device Evaluation Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare.

4 Application for designation

(1) Description in the application form

Those who intend to apply for the designation of orphan drugs etc. should submit the application form using the Form No. 107 (1), Form No. 107 (2) or Form No. 107 (3) in the Enforcement Regulation.

(2) Attachments to the application form

Article 250-2 of the Enforcement Regulation specifies the data to be attached to the application form, of which details are as shown below. Additionally, other data may be requested as necessary.

A Data on the number of subjects

Objective statistical data related to the number of subjects pertaining to the usage of the drugs etc.

B Data on medical needs

(A) Data on the target disease such as the cause and symptom

(B) Data on the current status of medical care such as the availability of similar drugs and availability of treatment

C Data serving as theoretical evidence for the use of the drugs etc.

(A) For drugs

Outline of data that are specified in Article 40 (1) (i) of the Enforcement regulations and that are available at the time of application for designation

(B) For medical devices and in vitro diagnostics

Outline of data that are specified in Article 114-19 (1) (i) or (ii) of the Enforcement regulations and that are available at the time of application for designation

(C) For regenerative medicine products

Outline of data that are specified in Article 137-23 of the Enforcement regulations and that are available at the time of application for designation

D Development plan

Data that show the outline of the development plan such as the planned endpoint and study period etc.

E Summary of orphan drugs etc.

Data for explanation at the committee and data for publication prepared using Attachment Form 1, Attachment Form 2 or Attachment Form 3 (that should include the name of orphan drugs etc., proposed indication, proposed intended usage or indication, proposed indication or performance and the name of applicant in English or the English name)

5 Discontinuation of tests and research

When a person designated (hereinafter referred to as "designation holder") pursuant to the provisions of Article 77-2, (1) of the Act intends to discontinue tests and research, marketing or manufacturing of orphan drugs etc. that pertain to the designation, they shall promptly notify the Minister of Health, Labour and Welfare thereof based on Article 77-5 of the Act.

As a notification of discontinuation, Form No. 108 of the Enforcement Regulation should be submitted.

6 Rescindment of designation

The Minister of Health, Labour and Welfare, when receiving a notification of discontinuation under Article 77-5 of the Act, rescinds the designation based on Article 77-6 (1) of the Act. Based on Article 77-6 (2) of the Act, the Minister of Health, Labour and Welfare may rescind the designation in cases that fall under any of the following items:

The public announcement of the rescindment of designation is made in accordance with 2. When rescinding based on A, the Minister will hear the opinion of the designation holder in advance.

A The requirement of 1 is no longer met.

B When unlawfulness such as false descriptions in the application for designation is found.

C When tests and research, or marketing is not provided for orphan drugs etc. without any legitimate grounds.

D When a designation holder violates the Act or other pharmaceutical laws and regulations specified by Cabinet Order, or any of the dispositions thereupon.

7 Succession

If the designation holder transfers the right of development in Japan to others, the designation holder should notify of discontinuation of tests and research in accordance with 5, and those receiving the right of development (hereinafter referred to as "appointed successor") should submit the data in E in 4 (1) and (2). However, if the contents of the documents have been changed since the time when the original designation holder receives the designation, data that show that the changes satisfy the requirements at the time of succession should also be submitted. Succession is approved with the letter of designation that is separately issued.

Designation holders who consider succession should consult with the person in charge of designation specified in 3 in advance. In so doing, the designation holders should also submit a copy of the contract for succession and document that explain the background of succession.

8 Priority review and priority consultation

Orphan drugs subject to priority review/consultation are only those that satisfy the former designation criteria of orphan drugs for the time being. Therefore, those that have no sufficient evidence to meet the former designation criteria are not subject to priority review/consultation for orphan drugs. The eligibility for priority review/consultation will be described in Orphan Drug Designation Preliminary Evaluation Report.

For orphan drugs that are considered to be not subject to priority review/consultation at the time of designation but later to fulfill the criteria of priority review/consultation as the development advances, the consultation service of Pharmaceuticals and Medical Devices Agency (PMDA) can be used (during consultation on how to summarize application dossier just before the marketing application in principle) to clarify the eligibility, by which priority review/consultation shall be applicable.

Attachment Form 1

Summary of Orphan Drug

Name	JAN should be accompanied with its English name such as INN.
Proposed indication	This should be accompanied by the English translation.
Name of applicant	This should be accompanied by the English name.
Target disease	Its summary and the number of patients should be explained.
Medical needs and development status etc.	Medical needs, clinical study results to date (including foreign clinical study) and development status should be explained.

(Note)
1. The forms should be in A4 size.
2. If a further explanation is required for the details, it may be described in an attachment.
3. This should be prepared with understanding that this will be used for publication.

Attachment Form 2

Summary of orphan medical device

Name	This should be accompanied by the English name.
Proposed intended usage or indication	This should be accompanied by the English translation.
Name of applicant	This should be accompanied by the English name.
Target disease	Its summary and the number of patients should be explained.
Medical needs and development status etc.	Medical needs, clinical study results to date (including foreign clinical study) and development status should be explained.

(Note)
1. The forms should be in A4 size.
2. If a further explanation is required for the details, it may be described in an attachment.
3. This should be prepared with understanding that this will be used for publication.

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Summary of orphan regenerative medicine product

Name	This should be accompanied by the English name.
Propose indication or performance	This should be accompanied by the English translation.
Name of applicant	This should be accompanied by the English name.
Target disease	Its summary and the number of patients should be explained.
Medical needs and development status etc.	Medical needs, clinical study results to date (including foreign clinical study) and development status should be explained.

(Note) 1. The forms should be in A4 size.
2. If a further explanation is required for the details, it may be described in an attachment.
3. These should be prepared with understanding that these will be used for publication.