PSB/MDED Notification No. 0112-1
January 12, 2024

To: Directors of Prefectural Health Departments (Bureaus)

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

Partial Revision of "Handling of Designation, etc. of Innovative Medical Devices, In Vitro Diagnostics, and Regenerative Medical Products under the SAKIGAKE system"

Designation of innovative medical devices, innovative in vitro diagnostics , and innovative regenerative medical products under the SAKIGAKE system (hereinafter referred to as "SAKIGAKE medical devices", "SAKIGAKE in vitro diagnostics", and "SAKIGAKE regenerative medical products", respectively) based on Article 77-2, Paragraph 2 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 handled in accordance with "Handling of Designation, etc. of Innovative Medical Devices, In Vitro Diagnostics, and Regenerative Medical Products under the SAKIGAKE system" (PSEHB/MDED Notification No. 0831-6 of the 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 "Director Notification"), etc.

We have recently decided to change the handling of designation of SAKIGAKE medical devices, in vitro diagnostics, and regenerative medical products as follows. Please be aware of these changes and inform related businesses under your jurisdiction of them.

Note

1. Requirements for designation

SAKIGAKE medical devices, in vitro diagnostics, or regenerative medical products (hereinafter referred to as "medical devices, etc.") shall meet all of the following four requirements.

Even if all four requirements are met, they are not designated if any of the following applies, in principle.

A When the intended use or effect based on the principle equivalent to that of a certain medical device previously designated as SAKIGAKE medical devices is to be added, or when other medical devices with the intended use or effect based on the principle equivalent to that of the medical device concerned have already been approved.

B When the intended use utilizing the principle or measurement item equivalent to that utilized for a certain in vitro diagnostic previously designated as SAKIGAKE in vitro diagnostics is to be added, or when other in vitro diagnostics with the intended use utilizing the same principle or measurement item as that utilized for the in vitro diagnostic concerned have already been approved.

C When the intended use or effect based on the mechanism of action equivalent to that of a certain regenerative medical product previously designated as SAKIGAKE revenerative medical products is to be added, or when other regenerative medical products with the indication or performance based on the mechanism of action equivalent to that of the regenerative medical product concerned have already been approved.

(1) Designation requirement 1: Innovativeness of treatment or diagnostic method

In principle, there should be a new principle for medical devices, a new principle or new measurement item for in vitro diagnostics, or a new mechanism of action for regenerative medical products.

(2) Designation requirement 2: Seriousness of the target disease

Any of the following diseases:

- A serious disease that significantly affects life
- Disease for which no curative therapy is available and the symptom (condition that makes it difficult to lead a social life) continues

(3) Designation requirement 3: Very high efficacy or safety for the target disease

There is no existing treatment or diagnostic method, substantial improvement of efficacy is expected compared to an existing treatment or diagnostic method, or significant improvement of safety is expected.

However, to claim that significant improvement of efficacy or safety is expected, the efficacy and safety in humans need to have been suggested at least in exploratory clinical studies, etc. either in Japan or abroad.

(4) Designation requirement 4: Willingness and system for early development and approval application in Japan ahead of other countries

Early development in Japan must be prioritized; the approval application in Japan ahead of or at the same time as applications in other countries (countries with an approval system at an equivalent level to that in Japan; the application within three months from the day of the first approval application in a country will be regarded as an application at the same time) should be planned; and there should be a system that allows for approval applications utilizing the SAKIGAKE comprehensive assessment consultation provided by the

Pharmaceuticals and Medical Devices Agency (hereinafter referred to as "PMDA") and a system that responds to prompt regulatory reviews.

It is desirable that a certain level of efficacy, etc. of the medical device, etc. can be expected based on nonclinical study results, etc. and that clinical trials are to be conducted in a way that includes Japan.

When filing an approval application for a medical device, etc. that requires a companion diagnostic, etc. for its use, there should be a system that enables an approval application for the diagnostic, etc. concerned in parallel (including a system for collaboration with other companies).

2. Method of designation

SAKIGAKE medical devices, SAKIGAKE in vitro diagnostics, and SAKIGAKE regenerative medical products (hereinafter referred to as "SAKIGAKE medical devices, etc.") shall be designated after hearing the opinions of the Pharmaceutical Affairs and Food Sanitation Council. For the time being, the designation will be made about twice a year (roughly in April and October), which will be changed according to the status of the review system in the future. However, special designation may be made if it is necessary from a public health perspective. For designated medical devices, etc., the date of designation, name of the medical device, etc., the target disease, and name of the applicant for designation are posted on the website of the Ministry of Health, Labour and Welfare.

3. Consultation on designation

Parties planning to apply for the designation as SAKIGAKE medical devices, etc. shall consult the Medical Device Evaluation Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare (hereinafter referred to as the "Medical Device Evaluation Division") in advance. Parties planning to apply for designation for medical devices or in vitro diagnostics shall request a consultation with PMDA according to the instructions of the Medical Device Evaluation Division. For regenerative medical products, instructions shall be given separately. In this consultation, the consulter, the Ministry of Health, Labour and Welfare, and PMDA will exchange opinions on whether or not the product discussed is subject to this system. Based on the exchange of opinions with the consulter, the Ministry of Health, Labour and Welfare and PMDA will comprehensively consider whether designation requirements are met and examine whether or not the product discussed is subject to this system. If it is judged possible for the product to be subject to this system, it will be described in the consultation record that it is acceptable to take the procedure for the application for designation. If it is impossible to judge whether or not it is appropriate to consider that the product is subject to this system by the time of preparation of the consultation record (within about 30 business days after the face-to-face advice), the Ministry of Health, Labour and Welfare and PMDA shall separately contact the consulter.

4. Procedures for designation

(1) Application for designation of target product

If designation of a target product is desired, an application for designation shall be made to the Medical Device Evaluation Division by attaching the submission data in (2) to the Form No. 107-2 specified in the Regulation for Enforcement of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Ministry of Health and Welfare Ordinance No. 1 of 1961; hereinafter referred to as the "Regulation"). In principle, data shall be submitted in an electronic file.

(2) Submission data for the application form for designation

Data to be attached to an application for designation are specified in the provisions of Article 251-2, Paragraph 2 of the Regulation. The specific contents are as follows. For designation applications for medical devices and in vitro diagnostics, C does not have to be attached. In addition, submission of other data may be requested as necessary.

A Data on mechanism of action or principle

B Data on medical needs

(a) Data on the target disease such as etiology and symptoms

(b) Data on the current status of medical care, such as presence or absence of similar medical devices, etc., and of treatment methods

C Summary of study results on toxicity, pharmacological action, etc.

D Summary of clinical study results

E Outline of development plan in Japan and overseas

F Summary of fulfillment of requirements for designation as SAKIGAKE medical devices, etc.

Summary prepared in accordance with either of Attached Forms 1 to 3 as data for explanation to a committee and data for publication

5. Priority handling of designated medical devices, etc. and points to consider

(1) Priority consultation

Designated products can be handled in priority to other medical devices, etc. in the face-to-face advice, etc. provided by PMDA. Consult PMDA on the timing of consultation.

(2) Enhanced prior assessment

Consult the concierge described later and use all consultation categories of SAKIGAKE comprehensive assessment consultation provided by PMDA, in principle, during the period after designation up to the approval application, because these frameworks need to be utilized proactively from before the approval application in order to reduce the time from the approval application to approval (e.g., within six months for medical devices).

For example, regarding quality management and GLP/GCP/GPSP compliance assessment, it is considered significant to proactively utilize frameworks of consultation, etc. including preparation of information, etc. necessary for such assessment from an early stage so that scheduling/assessment can be implemented promptly after approval application.

If the prior assessment by the SAKIGAKE comprehensive assessment consultation described above is insufficient (including the cases where some data necessary for evaluation are not available or responses to the content of advice, etc. by PMDA have been insufficient), the time from the approval application to approval may be set individually based on the status of evaluation of medical devices, etc.

(3) Priority review

Designated products shall be reviewed as a priority review pursuant to the provisions of Article 23-2-5, Paragraph 10 of the Act and Article 23-25, Paragraph 9 of the Act.

(4) Concierge

As an appropriate person who can communicate and coordinate with the Ministry of Health, Labour and Welfare and PMDA, a person appointed by PMDA (hereinafter referred to as “concierge”) shall provide consultation on the progress management of the development of the target product and make adjustments with the approval applicant and departments related to regulatory review. At an early stage after the designation, the

concierge for the target product shall contact the party to which designation was granted pursuant to the provisions of Article 77-2, Paragraph 2 of Act (hereinafter referred to as the "designated party") regarding the target product.

6. Discontinuation of study/research, etc.

When intending to discontinue the study/research, marketing, or manufacturing of a SAKIGAKE medical device, etc. related to the designation concerned, the designated party shall promptly notify the Minister of Health, Labour and Welfare pursuant to the provisions of Article 77-5 of the Act.

The notification of discontinuation shall be made by submitting a notification form using Form No. 108 of the Regulation.

7. Cancellation of designation

If a notification of discontinuation is made pursuant to the provisions of Article 77-5 of the Act, the Minister of Health, Labour and Welfare shall cancel the designation pursuant to the provisions of Article 77-6, Paragraph 1 of the Act. In addition, in the case where any of the following applies, the designation may be canceled pursuant to the provisions of Paragraph 2 of the same article.

When designation is canceled, the Medical Device Evaluation Division shall report it to the Pharmaceutical Affairs and Food Sanitation Council and post it on the website in accordance with 2.

(1) The designation requirement 1 or 2 is not considered to be met because of the approval of another medical device, etc. in Japan before the approval of the designated medical device, etc.

(2) Based on the confirmatory clinical study results, etc., an extremely high level of efficacy or significant improvement of safety can no longer be expected, and the designation requirement 3 is not considered to be met.

(3) The designated medical device, etc. no longer meets the designation requirement 4 for any of the following reasons.

- The approval application was not filed in Japan ahead of, or at the same time with other countries.
- It is no longer possible to achieve early development in Japan because the approval application was filed without sufficient prior assessment or because considerable defects were discovered in the application data.

(4) The same medical device, etc. was approved overseas earlier.

(5) Any fraud such as false description was recognized in the designation application form.

(6) When study/research or marketing of the SAKIGAKE medical device, etc. is not implemented without any justifiable reason.

(7) The designated party violates the provisions of the Act or other laws and regulations related to pharmaceutical affairs or punishment based on them.

8. Handling of succession

When transferring the development right in Japan from the designated party to another party (hereinafter referred to as "successor"), the designated party shall submit a notification of discontinuation of the study/research, etc. in accordance with 6, and the successor shall submit the application form in 4 (1) and the data in (2) F. If any change has been made since the time when the designation was granted to the designated party, data showing that the designation requirements are still met at the time of succession shall also be submitted for the changed part. Succession shall be approved with the written designation separately issued.

The designated party considering succession should consult the Medical Device Evaluation Division in advance. At that time, a copy of the contract related to the succession, documents that clearly present the background, etc. of succession, etc. shall be also submitted.

9. Effective date

This notification shall apply from January 12, 2024.

10. Other

A companion diagnostic, etc. (in vitro diagnostic or medical device) used for the purposes including the improvement of the efficacy or safety of SAKIGAKE medical devices, etc. or SAKIGAKE pharmacetucial products designated based on the "Handling of Designation of Innovative Pharmacetucial products under the SAKIGAKE system" (PSEHB/PED Notification No. 0831-6, dated August 31, 2020) may be designated as a SAKIGAKE medical device, etc. regardless of the designation requirements in 1. and the procedures for designation in 4. so that there will be no delay in the development/approval of the SAKIGAKE medical device, etc. or pharmaceutical product concerned. In this case, cancellation of designation in 7. shall be handled in accordance with the handling of SAKIGAKE pharmaceutical products.

Attached Form 1

Summary of Fulfillment of Requirements for Designation as SAKIGAKE Medical Devices

<table>
<tr><td colspan="2">Name of applicant</td><td></td></tr>
<tr><td rowspan="2">Name</td><td>Generic name[*1]</td><td></td></tr>
<tr><td>Brand name[*2]</td><td></td></tr>
<tr><td rowspan="2">Designation requirement 1</td><td>Innovativeness of the treatment method[*3]</td><td>☐ Having a new principle
☐ Other (　　)</td></tr>
<tr><td colspan="2">(Summary of judgment that the above requirement is met)</td></tr>
<tr><td rowspan="2">Designation requirement 2</td><td>Seriousness of the target disease[*3]</td><td>☐ A serious disease that significantly affects life
☐ Disease for which no curative therapy is available and the symptom (condition that makes it difficult to lead a social life) continues</td></tr>
<tr><td colspan="2">(Outline of the target disease[*4])</td></tr>
<tr><td rowspan="2">Designation requirement 3</td><td>Very high efficacy or safety for the target disease[*3]</td><td>☐ There is no existing treatment method.
☐ Substantial improvement of efficacy or safety is expected compared to an existing treatment method.[*5]</td></tr>
<tr><td colspan="2">(Summary of current treatment method for the target disease and study results, etc. suggesting efficacy)</td></tr>
<tr><td rowspan="3">Designation requirement 4</td><td>Willingness/system for early development/ application in Japan ahead of other countries[*3]</td><td>☐ Approval applications are planned in Japan (alone) ahead of other countries.
☐ Japan is to be included in the area (limited to the cases where multiple countries/regions are involved) where approval applications are filed for the first time in the world.
☐ There is a system that enables the approval application and responses to prompt regulatory reviews.</td></tr>
<tr><td>Planned timing of approval application</td><td></td></tr>
<tr><td colspan="2">(Overview of progress status/schedule of development[*6*7])</td></tr>
</table>

*1: If the generic name has not been determined, enter "New."
*2: Enter if it has already been determined. If approved in Japan, enter the Japanese name. Otherwise, enter in English. If the name has not been determined, enter a tentative name.
*3: Fill the applicable ☐.
*4: Describe the patient background and estimated number of target patients for the application product.
*5: If this item is selected, briefly describe the reason why substantial improvement in efficacy or safety is expected.
*6: The planned timing of utilization of a SAKIGAKE comprehensive assessment consultation should be included in the description.
*7: For a pharmaceutical product that requires a companion diagnostic, etc. for its use, describe the cooperation system with the company of the diagnostic agent, etc. concerned and the progress status, etc. of development.

(Other points to consider)
1 Use an A4 size form.
2 If a more detailed explanation is necessary, it is acceptable to attach it as an attachment.
3 Prepare this form assuming its use as published material.

Attached Form 2

Summary of Fulfillment of Requirements for Designation as SAKIGAKE In Vitro Diagnostics

<table>
<tr><td colspan="2">Name of applicant</td><td></td></tr>
<tr><td rowspan="2">Name</td><td>Generic name*1</td><td></td></tr>
<tr><td>Brand name*2</td><td></td></tr>
<tr><td rowspan="2">Designation requirement 1</td><td>Innovativeness of diagnostic method*3</td><td>☐ Having a new principle
☐ Having a new measurement item
☐ Other (　　)</td></tr>
<tr><td colspan="2">(Summary of judgment that the above requirement is met)</td></tr>
<tr><td rowspan="2">Designation requirement 2</td><td>Seriousness of the target disease*3</td><td>☐ A serious disease that significantly affects life
☐ Disease for which no curative therapy is available and the symptom (condition that makes it difficult to lead a social life) continues</td></tr>
<tr><td colspan="2">(Outline of target disease*4)</td></tr>
<tr><td rowspan="2">Designation requirement 3</td><td>Very high efficacy or safety for the target disease*3</td><td>☐ There is no existing diagnostic method.
☐ Substantial improvement of efficacy or safety is expected compared to the existing diagnostic method.*5</td></tr>
<tr><td colspan="2">(Summary of the current treatment method for the target disease and study results, etc. suggesting efficacy)</td></tr>
<tr><td rowspan="3">Designation requirement 4</td><td>Willingness/system for early development/application in Japan ahead of other countries*3</td><td>☐ Approval applications are planned in Japan (alone) ahead of other countries.
☐ Japan is to be included in the area (limited to the cases where multiple countries/regions are involved) where approval applications are filed for the first time in the world.
☐ There is a system that enables the approval application and responses to prompt regulatory reviews.</td></tr>
<tr><td>Planned timing of approval application</td><td></td></tr>
<tr><td colspan="2">(Overview of progress status/schedule of development*6)</td></tr>
</table>

*1: If the generic name has not been determined, enter “New.”
*2: Enter if it has already been determined. If approved in Japan, enter the Japanese name. Otherwise, enter in English. If the name has not been determined, enter a tentative name.
*3: Fill the applicable ☐.
*4: Describe the patient background and estimated number of target patients for the application product.
*5: If this item is selected, briefly describe the reason why substantial improvement in efficacy is expected.
*6: The planned timing of utilization of a SAKIGAKE comprehensive assessment consultation should be included in the description.

(Other points to consider)
1 Use an A4 size form.
2 If a more detailed explanation is necessary, it is acceptable to attach it as an attachment.
3 Prepare this form assuming its use as published material.

Attached Form 3

Summary of Fulfillment of Requirements for Designation as SAKIGAKE Regenerative Medical Products

<table>
<tr><td colspan="2">Name of applicant</td><td></td></tr>
<tr><td rowspan="2">Name</td><td>Generic name[*1]</td><td></td></tr>
<tr><td>Brand name[*2]</td><td></td></tr>
<tr><td rowspan="2">Designation requirement 1</td><td>Innovativeness of the treatment method[*3]</td><td>☐ Having a new mechanism of action
☐ Other (　　)</td></tr>
<tr><td colspan="2">(Summary of judgment that the above requirement is met)</td></tr>
<tr><td rowspan="2">Designation requirement 2</td><td>Seriousness of the target disease[*3]</td><td>☐ A serious disease that significantly affects life
☐ Disease for which no curative therapy is available and the symptom (condition that makes it difficult to lead a social life) continues</td></tr>
<tr><td colspan="2">(Outline of the target disease[*4])</td></tr>
<tr><td rowspan="2">Designation requirement 3</td><td>Very high efficacy or safety for the target disease[*3]</td><td>☐ There is no existing treatment method.
☐ Substantial improvement of efficacy or safety is expected compared to an existing treatment method.[*5]</td></tr>
<tr><td colspan="2">(Summary of the current treatment method for the target disease and study results, etc. suggesting efficacy)</td></tr>
<tr><td rowspan="3">Designation requirement 4</td><td>Willingness/system for early development/application in Japan ahead of other countries[*3]</td><td>☐ Approval applications are planned in Japan (alone) ahead of other countries.
☐ Japan is to be included in the area (limited to the cases where multiple countries/regions are involved) where approval applications are filed for the first time in the world.
☐ There is a system that enables the approval application and responses to prompt regulatory reviews.</td></tr>
<tr><td>Planned timing of approval application</td><td></td></tr>
<tr><td colspan="2">(Overview of progress status/schedule of development[*6*7])</td></tr>
</table>

*1: If the generic name has not been determined, enter “Clinical trial identification code, etc.”
*2: Enter if it has already been determined. If approved in Japan, enter the Japanese name. Otherwise, enter in English. If the name has not been determined, enter a tentative name.
*3: Fill the applicable ☐.
*4: Describe the patient background and estimated number of target patients for the application product.
*5: If this item is selected, briefly describe the reason why substantial improvement in efficacy is expected.
*6: The planned timing of utilization of a SAKIGAKE comprehensive assessment consultation should be included in the description.
*7: For a pharmaceutical product that requires a companion diagnostic, etc. for its use, describe the cooperation system with the company of the diagnostic agent, etc. concerned and the progress status, etc. of development.

(Other points to consider)
1 Use an A4 size form.
2 If a more detailed explanation is necessary, it is acceptable to attach it as an attachment.
3 Prepare this form assuming its use as published material.