PSB/MDED Notification No. 0329-5
March 29, 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, etc. of Notifications of Clinical Trial Plans, etc. Related to Equipment/Devices, etc."

Handling of notifications, etc. of clinical trial plans related to drugs by persons who intend to sponsor clinical trials has been shown in "Handling, etc. of Notifications of Clinical Trial Plans, etc. Related to Equipment/Devices, etc." (PSEHB/MDED Notification No. 0831-8 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 changed part of the handling of the notifications of clinical trial plans in the Director Notification as follows. Please inform related businesses, etc. under your jurisdiction of the change.

The revised Director Notification is shown in the attachment.

Please note that a copy of this notification will be sent to the related organizations in the attached list.

Note

Corresponding part	New	Old
1. (8) B [1]	[1] Except for the cases of [2], [3], or [4], a notification shall be submitted for each clinical trial notification before changes in notified items, in principle. Any change of the notifier that changes the actual condition in clinical trials sponsored by companies requires a new notification, not a notification of changes in a clinical trial plan. Any change of the representative notifier in clinical trials conducted by persons who intend to be sponsor-investigators requires a new notification, not a notification of changes in clinical trial plan (excluding changes in the affiliated organization of the representative notifier). Also for changes in investigational devices (including addition of a shape), it is acceptable to submit a clinical trial notification before making changes, in principle. However, in cases including those where the results of a clinical trial cannot be regarded as continuous results based on the details of changes in the investigational devices (when it is judged impossible to evaluate the results as those of a continuous clinical trial in the regulatory review), a new notification is required instead of a notification of changes because it is appropriate to discontinue the clinical trial based on the protocol before the changes and conduct a new clinical trial. As to whether or not the results can be regarded as those of a continuous clinical trial after the changes to investigational devices, Office of Medical Devices I or II, or Office of Software as a Medical Device shall be consulted using the face-to-face advice, etc. provided by PMDA as necessary.	[1] Except for the cases of [2], [3], or [4], a notification shall be submitted for each clinical trial notification before changes in notified items, in principle. Any change of the representative notifier requires a new notification, not a notification of changes in clinical trial plan. Also for changes in investigational devices (including addition of a shape), it is acceptable to submit a clinical trial notification before making changes, in principle. However, in cases including those where the results of a clinical trial cannot be regarded as continuous results based on the details of changes in the investigational devices (when it is judged impossible to evaluate the results as those of a continuous clinical trial in the regulatory review), a new notification is required instead of a notification of changes because it is appropriate to discontinue the clinical trial based on the protocol before the changes and conduct a new clinical trial. As to whether or not the results can be regarded as those of a continuous clinical trial after the changes to investigational devices, Office of Medical Devices I or II shall be consulted using the face-to-face advice, etc. provided by PMDA as necessary.
1. (8) B [2]	[2] When a new test device is to be added to the clinical trial notification, the notification shall be submitted at the same timing as A, [1] or [2] above, depending on the test device to be added. If the objective or the target disease is changed, the notification of the change must be submitted by about two weeks before the implementation of the clinical trial	[2] When a new test device is to be added to the clinical trial notification, the notification shall be submitted at the same timing as A, [1] or [2] above depending on the test device to be added. If the objective or the target disease is changed, the protocol with the changed objective or target disease must be submitted by about two weeks before the implementation of the clinical trial.

	according to the protocol with the changed objective or target disease.	
1. (8) B [3]	[3] In clinical trials by sponsors, the notification of the following matters may be made collectively in about six months after the change. If a clinical trial completion notification or clinical trial discontinuation notification is submitted before six months pass after the last notification of changes in the clinical trial plan, it is acceptable to enter any changes occurring up to that point in the clinical trial completion notification or clinical trial discontinuation notification as a means of notification.	[3] In clinical trials by sponsors, the notification of the following matters may be made collectively in about six months ~~(one year for the change or only the addition or deletion of the names of subinvestigators)~~ after the change. ~~For the quantity of study devices, study drug equivalents, and study product equivalents to be delivered (received) and the planned number of subjects, changes in the quantity or number of subjects occurring in association with the conduct of the clinical trial do not need to be reported in notifications, but may be reported collectively in a clinical trial completion notification or clinical trial discontinuation notification.~~ If a clinical trial completion notification or clinical trial discontinuation notification is submitted before six months pass after the last notification of changes in the clinical trial plan, it is acceptable to enter any changes occurring up to that point in the clinical trial completion notification or clinical trial discontinuation notification as a means of notification.
	・ (Omitted) ・ A change in manufacturing method that does not change the actual condition such as a change of only the name of the manufacturer in an exporting country and a change of the brand name in an exporting country ・ A change in the generic name that does not change the actual condition ・ A minor change of the study period due to the different date of conclusion of the contract compared with the medical institution with the earliest conclusion of the clinical trial contract (if the latest scheduled date of completion of observation at a medical institution is extended, a prior notification is necessary) ・ Deletion of the investigator due to deletion of the medical institution that failed to conclude the contract ・ Deletion of the coordinating investigator or a member physician of the coordinating committee, and changes in the affiliated organization, affiliation, and name of the	・ (Omitted) ・ A change in manufacturing method that does not change the actual condition such as a change of only the name of the manufacturer in an exporting country and a change of the brand name in an exporting country ・ A minor change of the study period due to the different date of conclusion of the contract compared with the medical institution with the earliest conclusion of the clinical trial contract (if the latest scheduled date of completion of observation at a medical institution is extended, a prior notification is necessary) ・ Deletion of the investigator due to deletion of the medical institution that failed to conclude the contract ・ ~~Change, addition, and deletion of the names of subinvestigators~~ ・ Deletion of the coordinating investigator or a member physician of the coordinating committee, and changes in the affiliated organization, affiliation, and name of the

	coordinating investigator or a member physician of the coordinating committee ・ (Omitted)	coordinating investigator or a member physician of the coordinating committee ・ (Omitted)
1. (8) B [4]	[4] In clinical trials by sponsor-investigators, the notification of the following matters may be made collectively in about six months after the change. If a clinical trial completion notification or clinical trial discontinuation notification is submitted before six months pass after the last notification of changes in the clinical trial plan, it is acceptable to enter any changes occurring up to that point in the clinical trial completion notification or clinical trial discontinuation notification as a means of notification.	[4] In clinical trials by sponsor-investigators, the notification of the following matters may be made collectively in about six months ~~(one year for the change or only the addition or deletion of the names of subinvestigators)~~ after the change. ~~For the quantity of study devices, study drug equivalents, and study product equivalents to be delivered (received) and the planned number of subjects, changes in the quantity or number of subjects occurring in association with the conduct of the clinical trial do not need to be reported in notifications, but may be reported collectively in a clinical trial completion notification or clinical trial discontinuation notification.~~ If a clinical trial completion notification or clinical trial discontinuation notification is submitted before six months pass after the last notification of changes in the clinical trial plan, it is acceptable to enter any changes occurring up to that point in the clinical trial completion notification or clinical trial discontinuation notification as a means of notification.
	・ (Omitted) ・ A change in manufacturing method that does not change the actual condition such as a change of only the name of the manufacturer in an exporting country and a change of the brand name in an exporting country ・ <u>A change in the generic name that does not change the actual condition</u> ・ A change of the name, clinical department, address, or main phone number of the medical institution ・ A change of the name of investigator ・ Deletion of the coordinating investigator (except for the representative notifier) or a member physician of the coordinating committee and changes in the affiliated organization, affiliation, and name of the coordinating investigator or a member physician of the coordinating committee ・ (Omitted)	・ (Omitted) ・ A change in manufacturing method that does not change the actual condition such as a change of only the name of the manufacturer in an exporting country and a change of the brand name in an exporting country ・ A change of the name, clinical department, address, or main phone number of the medical institution ・ A change of the name of investigator ・ ~~Change, addition, and deletion of the names of subinvestigators~~ ・ Deletion of the coordinating investigator (except for the representative notifier) or a member physician of the coordinating committee and changes in the affiliated organization, affiliation, and name of the coordinating investigator or a member physician of the coordinating committee ・ (Omitted)

1. (8) B [8]	[8] The following matters do not need to be reported in notifications of changes in clinical trial plans, but may be reported collectively in a clinical trial completion notification or clinical trial discontinuation notification. ・ Changes in the quantity of study devices, study drug equivalents, and study product equivalents to be delivered (received) and the number of subjects ・ A change, addition, and deletion of the name of a subinvestigator (However, the names of all subinvestigators including those who are no longer subinvestigators should be reported; for a change in the name of a subinvestigator during the clinical trial, it is sufficient to report the name after the change) The information on subinvestigators should be appropriately managed so that it can be submitted if submission is requested during the clinical trial.	-
1. (8) E	E If a clinical trial notification is submitted within 30 days after the start of an urgently conducted clinical trial specified in Article 80-2, Paragraph 2 of the Act, the first report should be made by the start date of the clinical trial using the Attached Forms 1 or 2 of the Director-General Notification. If there is any change before the submission of the clinical trial notification, it should be reported appropriately to the Medical Device Evaluation Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare.	E If a clinical trial notification is submitted within 30 days after the start of an urgently conducted clinical trial specified in Article 80-2, Paragraph 2 of the Act, the first report should be made by the start date of the clinical trial using the Attached Forms 1 or 2 of the Director-General Notification. If there is any change before the submission of the clinical trial notification, it should be reported appropriately to the Medical Device Evaluation Division, Pharmaceutical Safety ~~and Environmental Health~~ Bureau, Ministry of Health, Labour and Welfare.
3.	3. Notification of discontinuation of development of the investigational device If it is decided to discontinue the development of the test device for which a clinical trial notification has been submitted, a notification on the decision shall be made to the Director, Medical Device Evaluation Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare using the Attached Form 1 without delay after it is made. Discontinuation of development in this case refers to, for example, discontinuation of development for all of the indications of equipment/device, etc. for which the clinical trial was originally conducted for its multiple indications. The reason for	3. Notification of discontinuation of development of the investigational device If it is decided to discontinue the development of the test device for which a clinical trial notification has been submitted, a notification on the decision shall be made to the Director, Medical Device Evaluation Division, Pharmaceutical Safety ~~and Environmental Health~~ Bureau, Ministry of Health, Labour and Welfare using the Attached Form 1 without delay after it is made. Discontinuation of development in this case refers to, for example, discontinuation of development for all of the indications of equipment/device, etc. for which the clinical trial was originally conducted for its multiple indications. The

	discontinuation of development should be explained in detail.	reason for discontinuation of development should be explained in detail.
Attached Form 1	To: Director of Medical Device Evaluation Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare	To: Director of Medical Device Evaluation Division, Pharmaceutical Safety ~~and Environmental Health~~ Bureau, Ministry of Health, Labour and Welfare

End of Document

Attachment

PSEHB/MDED Notification No. 0831-8
August 31, 2020
[Partially revised] March 31, 2023
[Partially revised] March 29, 2024

To: Directors of Prefectural Health Departments (Bureaus)

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

Handling, etc. of Notifications of Clinical Trial Plans, etc. Related to Equipment/Devices, etc.

Handling, etc. of notifications of clinical trial plans, etc. related to equipment/devices, etc. has been handled in accordance with ”Notifications of Clinical Trial Plans, etc. Related to Equipment/Devices, etc.” (PFSB Notification No. 0709004, the Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated July 9, 2007; hereinafter referred to as the “previous Director-General Notification”) and “Handling, etc. of Notifications of Clinical Trial Plans, etc. Related to Equipment/Devices, etc.” (PFSB/ELD/OMDE Notification No. 0329-10 of the Office of Medical Device Evaluation, Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated March 29, 2013; hereinafter referred to as the “previous Office Director Notification”).

With the enforcement of the Ministerial Ordinance on the Development of Related Ministerial Ordinances in Accordance with Enforcement of the Act Partially Amending the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Ministry of Health, Labour and Welfare Ordinance No. 155 in 2020), “Notifications, etc. of Clinical Trial Plans, etc. Related to Equipment/Devices, etc.” (PSEHB Notification No. 0831-6 of the Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated August 31, 2020; hereinafter referred to as the “Director-General Notification”) has recently been issued, and the handling, etc. of its details has been specified as follows. Please inform related businesses and medical institutions, etc. under your jurisdiction of this.

With the application of this notification, the previous Office Director Notification shall be abolished as of August 31, 2022.

Note

1 Notification of clinical trial plans, etc.

(1) The person who intends to sponsor a clinical trial or the person who intends to be a sponsor-investigator must notify the Pharmaceuticals and Medical Devices Agency (hereinafter referred to as "PMDA") of plans of clinical trials on the test devices specified in 1., (1), A to F of the Note for the Director-General Notification pursuant to the provisions of Article 80-2, Paragraph 2 and Article 80-3, Paragraph 4 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 "Act") and Article 274 of 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").

(2) The terms in Article 269 of the Regulation that are applied with modifications in Article 275 of the Regulation are defined as follows.

[1] Test device*

An equipment/device that is investigated in a clinical trial, and use of the results of the clinical trial concerned as approval application data is intended. A main test device refers to the test device when there is one test device at the time of the clinical trial notification. When there are multiple test devices, it refers to one test device selected by the notifier.

The drugs and processed cells, etc. for which use of the results of the clinical trial concerned as approval application data is intended shall be handled in the same manner as "test devices" in this notification.

*: Among the equipment/devices, etc. described in the clinical trial notification, the main test device and other concomitantly used equipment/devices, etc. for which approval application is planned are included.

[2] Study device

The term refers to the test device as well as the comparator, concomitant device, etc. specified in the clinical trial notification and the protocol to be used for evaluation of the efficacy and safety of the test device. A study device can be used regardless of whether it has been approved in Japan or overseas.

The drugs and regenerative medical products specified in the clinical trial notification and the protocol to be used for the evaluation of efficacy and safety of the test device (hereinafter referred to as "study drug equivalents" and "study product equivalents," respectively) shall be handled in the same manner as "study devices" in this notification.

(3) In a multicenter clinical trial conducted by a person who intends to be a sponsor-investigator, a representative notifier shall, in principle, make arrangements with each medical institution before submitting a clinical trial notification. In this case, only the representative notifier can be specified in the notifier column, and it is not necessary to enter the investigator. If there are special circumstances in which the coordinating investigator cannot submit the clinical trial notification as a representative, each investigator shall submit the notification by entering a statement indicating that the trial is a multicenter study in the remarks column.

(4) If the notifier of a clinical trial plan has changed matters related to the notification in (1) pursuant to the provisions of Article 270 of the Regulation applied with modifications in Article 275 of the Regulation, or if the notifier has discontinued or completed the clinical trial

related to the notification in (1), the notifier shall make a notification of the content, reason, etc.

(5) The notification of clinical trial plans, etc. shall be submitted according to the following methods.

[1] Online submission using the electronic study data system

Submit the notification using the electronic study data system.

[2] Submission at the reception or by postal mail

Electronically record the plan in CD-R or DVD-R (hereinafter collectively referred to as the "electronic media") and submit it.

In the submission method in [1], the notification submitted to PMDA and the receipt e-mail from PMDA shall be retained as clinical trial-related documents.

In the submission method in [2], bring two copies of only the notification (excluding appendices and submission data) in paper media. In the submission by postal mail, enclose two copies of only the notification (excluding appendices and submission data) in paper media and a return envelope. One of the copies of the notification in paper media will be returned to the clinical trial notifier with PMDA's receipt stamp. Retain this copy with a copy of the set of data submitted to PMDA as clinical trial-related documents.

(6) Refer to the description guideline in Attachment 1 for details of the notification items and Attachment 2 for the input format for electronic media.

(7) When multiple test devices are used in a clinical trial, one notification shall be made for one protocol identification code, in principle. In the case of joint development, make a notification in joint names, in principle.

(8) The timing of submission shall be as follows, in principle, depending on the type of notification.

A Clinical trial notifications (Attached Forms 1 and 2 of the Director-General Notification)

[1] Notifications of clinical trial plans by persons who intend to sponsor clinical trials

If the clinical trial plan in the notification concerned is subject to an investigation pursuant to the provisions of the latter part of Article 80-2, Paragraph 3 of the Act, the notification must be submitted at least 30 days before the scheduled date of conclusion of the contract with the medical institution conducting the clinical trial. The clinical trial contract must not be concluded unless 30 days have passed since the date of the notification.

If the clinical trial plan is not subject to the investigation concerned, the notification must be submitted at least about two weeks before the scheduled date of conclusion of the contract with the medical institution conducting the clinical trial.

[2] Notifications of clinical trial plans by persons who intend to be sponsor-investigators

If the clinical trial plan in the notification concerned is subject to an investigation pursuant to the provisions of the latter part of Article 80-2, Paragraph 3 of Act, the notification must be submitted at least 30 days before the scheduled date of obtaining investigational devices from the investigational device provider or the scheduled date of implementation of the clinical trial. The investigational devices must not be obtained from the investigational device provider or the clinical trial must not be conducted unless 30 days have passed since the date of the notification.

If the clinical trial plan is not subject to the investigation concerned, the notification must be submitted at least about two weeks before the scheduled date of obtaining investigational devices from the investigational device provider or the scheduled date of implementation of the clinical trial.

B Notifications of changes in clinical trial plans (Attached Forms 3 and 4 of the Director-General Notification)

[1] Except for the cases of [2], [3], or [4], a notification shall be submitted for each clinical trial notification before changes in notified items, in principle. Any change of the notifier that changes the actual condition in clinical trials sponsored by companies requires a new notification, not a notification of changes in the clinical trial plan. Any change of the representative notifier in clinical trials conducted by persons who intend to be sponsor-investigators requires a new notification, not a notification of changes in the clinical trial plan (excluding changes in the affiliated organization of the representative notifier). Also for changes in investigational devices (including addition of a shape), it is acceptable to submit a clinical trial notification before making changes, in principle. However, in cases including those where the results of a clinical trial cannot be regarded as continuous results based on the details of changes in the investigational devices (when it is judged impossible to evaluate the results as those of a continuous clinical trial in the regulatory review), a new notification is required instead of a notification of changes because it is appropriate to discontinue the clinical trial based on the protocol before the changes and conduct a new clinical trial. As to whether or not the results can be regarded as those of a continuous clinical trial after the changes to investigational devices, consult the Office of Medical Devices I or II, or Office of Software as a Medical Device using the face-to-face advice, etc. provided by PMDA as necessary.

[2] When a new test device is to be added to the clinical trial notification, the notification shall be submitted at the same timing as A, [1] or [2] above depending on the test device to be added. If the objective or the target disease is changed, the notification of the change must be submitted by about two weeks before the implementation of the clinical trial according to the protocol with the changed objective or target disease.

[3] In clinical trials by sponsors, the notification of the following matters may be made collectively in about six months after the change. If a clinical trial completion notification or clinical trial discontinuation notification is submitted before six months pass after the last notification of changes in the clinical trial plan, it is acceptable to enter any changes occurring up to that point in the clinical trial completion notification or clinical trial discontinuation notification.

- A change in the name (a change in the name of the corporation and a change in the representative that do not change the actual condition), address, and vendor code of the clinical trial notifier
- A change, addition, and deletion of the name, affiliation, phone number, and fax number or e-mail address of the person in charge of notification (an in-house system should be established so that the person in charge after the change can be contacted)
- A change in the name, address, and vendor code of the manufacturing site or sales office that does not change the actual condition
- A change in the name (a change in the name of the corporation and a change in the representative that do not change the actual condition) and address of a foreign manufacturer
- A change in the name (a change in the name of the corporation and a change in the representative that do not change the actual condition) and address of the clinical trial in-country representative (if there is no change in a foreign manufacturer and the clinical trial in-country representative is to be changed to another corporation, prior notification is necessary)

- A change in a manufacturing method that does not change the actual condition such as a change of only the name of a manufacturer in an exporting country and a change of a brand name in an exporting country
- A change in the generic name that does not change the actual condition
- A minor change of the study period due to the different date of conclusion of the contract compared with the medical institution with the earliest conclusion of the clinical trial contract (if the latest scheduled date of completion of observation at a medical institution is extended, a prior notification is necessary)
- Deletion of the medical institution that failed to conclude the contract and a change of the name, clinical department, address, and main phone number of a medical institution
- A change of the name of an investigator
- Deletion of an investigator due to deletion of the medical institution that failed to conclude the contract
- Deletion of a coordinating investigator or a member physician of the coordinating committee, and change in the affiliated organization, affiliation, and name of a coordinating investigator or a member physician of the coordinating committee
- A change, addition, and deletion of the name, address, and scope of entrusted operations of a party entrusted with the entire or partial operation related to the request and management of the clinical trial (Contract Research Organization [CRO])
- A change, addition, and deletion of the name, address, and scope of entrusted operations of a party entrusted with a part of operations related to the conduct of the clinical trial (Site Management Organization [SMO]) by the medical institution
- A change, addition, and deletion of the name and address of the founder of the institutional review board (IRB)

[4] In clinical trials by sponsor-investigators, the notification of the following matters may be made collectively in about six months after the change. If a clinical trial completion notification or clinical trial discontinuation notification is submitted before six months pass after the last notification of changes in the clinical trial plan, it is acceptable to enter any changes occurring up to that point in the clinical trial completion notification or clinical trial discontinuation notification.

- A change of the affiliation (only within the same affiliated organization) and name of the clinical trial notifier
- A change, addition, and deletion of the name, affiliation, phone number, and fax number or e-mail address of the person in charge of notification (a system should be established so that the person in charge after the change can be contacted)
- A change in the name (a change in the name of the corporation and a change in the representative that do not change the actual condition) and address of the investigational device provider
- A change in a manufacturing method that does not change the actual condition such as a change of only the name of a manufacturer in an exporting country and a change of a brand name in an exporting country
- A change in the generic name that does not change the actual condition
- A change of the name, clinical department, address, or main phone number of the medical institution
- A change of the name of an investigator

- Deletion of a coordinating investigator (except for the representative notifier) or a member physician of the coordinating committee and a change in the affiliated organization, affiliation, and name of a coordinating investigator or a member physician of the coordinating committee
- A change, addition, and deletion of the name, address, and scope of entrusted operations of a party entrusted with the entire or partial preparation and management of the clinical trial (Contract Research Organization [CRO])
- A change, addition, and deletion of the name, address, and scope of entrusted operations of a party entrusted with a part of operations related to the conduct of the clinical trial (Site Management Organization [SMO]) by the medical institution
- A change, addition, and deletion of the name and address of the founder of the IRB

[5] It is desirable to periodically review the notification items of the clinical trial plan approximately once every six months after the date of notification in order to confirm the necessity of update.

[6] If an investigator is added after the representative notifier submits the notification for a multicenter clinical trial to be conducted by a sponsor-investigator, it is acceptable for the representative notifier to submit a notification of changes in the clinical trial plan.

[7] Changes related to submission data are not subject to the notification of changes. However, if any change is to be made to matters that may affect the safety of subjects or the results of the clinical trial other than the change of the objective or the target disease of the clinical trial, its notification shall be made as an attachment to the notification of changes or the Office of Review Management, PMDA shall be notified in advance.

[8] The following matters do not need to be reported in notifications of changes in the clinical trial plan, but may be reported collectively in a clinical trial completion notification or clinical trial discontinuation notification.

- Changes in the quantity of study devices, study drug equivalents, and study product equivalents to be delivered (received) and the number of subjects
- A change, addition, and deletion of the name of a subinvestigator (However, the names of all subinvestigators including those who are no longer subinvestigators should be reported; for a change in the name of a subinvestigator during the clinical trial, it is sufficient to report the name after the change)

The information on subinvestigators should be appropriately managed so that it can be submitted if submission is requested during the clinical trial.

C Clinical trial discontinuation notifications (Attached Forms 5 and 6 of the Director-General Notification)

A clinical trial discontinuation notification shall be submitted without delay for each clinical trial notification whenever the clinical trial is discontinued.

D Clinical trial completion notifications (Attached Forms 7 and 8 of the Director-General Notification)

In a clinical trial by a sponsor, a notification shall be submitted without delay at the time when a notification of completion of the clinical trial is received from all medical institutions for each clinical trial notification and collection of investigational devices is completed.

In a clinical trial by a sponsor-investigator, the clinical trial completion notification shall be submitted without delay for each clinical trial notification whenever the clinical trial is completed. In a multicenter clinical trial, a clinical trial completion notification or a clinical

trial discontinuation notification shall be submitted when the clinical trial is completed or discontinued at all medical institutions.

E If a clinical trial notification is submitted within 30 days after the start of an urgently conducted clinical trial specified in Article 80-2, Paragraph 2 of the Act, the first report should be made by the start date of the clinical trial using Attached Forms 1 or 2 of the Director-General Notification. If there is any change before the submission of the clinical trial notification, it should be reported appropriately to the Medical Device Evaluation Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare.

(9) Submission data shall be as follows, in principle, depending on the type of notification.

A Clinical trial notifications

[1] Data to be attached to a notification subject to a 30-day investigation shall be as follows. In clinical trials by sponsor-investigators, the written opinion of the IRB, approval document from the head of the medical institution, etc. do not need to be attached, but the conduct of the clinical trial should be approved by the head of the medical institution in advance based on the provisions of Article 21 of the Ministerial Ordinance on Good Clinical Practice (GCP) for Medical Devices (MHLW Ordinance No. 36 of 2005).

- Document stating the reason why the conduct of the clinical trial concerned is scientifically justified
- Protocol
- Written information and informed consent form used for informed consent (If those with the same contents are used at multiple medical institutions, one of them may be attached.)
- Sample case report form (If the items to be entered in the case report form are clearly shown in the protocol, the submission is not required.)
- The latest Investigator's Brochure (In clinical trials by sponsor-investigators, it can be in English if a Japanese summary of the items necessary for the conduct, etc. of the clinical trial is attached. In cases where a person who intends to sponsor a clinical trial is going to conduct a clinical trial using more than one test device and cannot obtain the Investigator's Brochures of the test devices to be concomitantly used with the test device the person is planning to market because the former test devices are marketed by other companies or for other reasons, or a person who intends to conduct a clinical trial cannot obtain the Investigator's Brochures of the test devices, it is acceptable to attach the documents describing the latest scientific findings regarding the test devices concerned [instructions for use, academic papers, etc.] instead of the Investigator's Brochures, only if the test devices have already been approved in Japan and the person who intends to sponsor the clinical trial or the person who intends to conduct the clinical trial considers that the safety of the test devices concerned can be ensured when they are used in the clinical trial. When submitting academic papers, etc., a document summarizing them should also be attached.)
- Documents describing the latest scientific findings related to the study devices other than the test device, study drug equivalents, and study product equivalents (package inserts/instructions for use, interview forms [in cases of study drug equivalents], academic papers, etc.). When submitting academic papers, etc., a document summarizing them should also be attached.

[2] Data to be attached to a notification that should be submitted at least about two weeks before the scheduled date of implementation (notifications in (8), A, [1] and [2] and B, [2] that are

not subject to a 30-day investigation) shall be as follows. In clinical trials by sponsor-investigators, the written opinion of the IRB, approval document from the head of the medical institution, etc. do not need to be attached, but the conduct of the clinical trial should be approved by the head of the medical institution in advance based on the provisions of Article 21 of the Ministerial Ordinance on Good Clinical Practice (GCP) for Medical Devices (Ministry of Health, Labour and Welfare Ordinance No. 36 of 2005).

- Document stating the reason why the conduct of the clinical trial concerned is scientifically justified (including the description of the outline of new study results and information after the previous notification)
- Protocol
- Written information and informed consent form used for informed consent (If those with the same contents are used at multiple medical institutions, one of them may be attached.)
- Sample case report form (If the items to be entered in the case report form are clearly shown in the protocol, the submission is not required.)
- The latest Investigator's Brochure (In clinical trials by sponsor-investigators, it can be in English if a Japanese summary of the items necessary for the conduct, etc. of the clinical trial is attached. In cases where a person who intends to sponsor a clinical trial is going to conduct a clinical trial using more than one test device and cannot obtain the Investigator's Brochures of the test devices to be concomitantly used with the test device the person is planning to market because the former test devices are marketed by other companies or for other reasons, or a person who intends to conduct a clinical trial cannot obtain the Investigator's Brochures of test devices, it is acceptable to attach the documents describing the latest scientific findings regarding the test devices concerned [instructions for use, academic papers, etc.] instead of the Investigator's Brochures, only if the test devices have already been approved in Japan and the person who intends to sponsor the clinical trial or the person who intends to conduct the clinical trial considers that the safety of the test devices concerned can be ensured when they are used in the clinical trial. When submitting academic papers, etc., a document summarizing them should also be attached.)
- Documents describing the latest scientific findings related to the study devices other than the test device, study drug equivalents, and study product equivalents (package inserts/instructions for use, interview forms [in cases of study drug equivalents], academic papers, etc.). When submitting academic papers, etc., a document summarizing them should also be attached.

B Notifications of changes in clinical trial plan (except for A, [1] and [2])

- Data related to changes as needed

C Clinical trial discontinuation notifications

- Data related to the reason for discontinuation (including information on patients who used up to the time of discontinuation) as needed

2. Investigations of clinical trial plans

The equipment/devices, etc. subject to a 30-day investigation are shown in 2 of the Note for the Director-General Notification. However, if a plan of a clinical trial with the same structure and principle as well as the same form of use with those of an already-conducted clinical trial is

to be submitted by a different notifier, these devices, etc. will not be subject to a 30-day investigation only if the investigational device provider is the same.

3. Notification of discontinuation of development of the investigational device

If it is decided to discontinue the development of the test device for which a clinical trial notification has been submitted, a notification on the decision shall be made to the Director, Medical Device Evaluation Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare using Attached Form 1 without delay after it is made. Discontinuation of development in this case refers to, for example, discontinuation of development for all of the indications of equipment/device, etc. for which the clinical trial was originally conducted for its multiple indications. The reason for discontinuation of development should be explained in detail.

4. Points to consider when clinical trial notification is not required

(1) The clinical trials of equipment/devices, etc. not requiring clinical trial notifications include the clinical trials related to the following equipment/devices, etc.

A Equipment/devices, etc. considered to have the same structure, directions for use, indications, and performance, etc. as those of the medical devices that have already been approved or certified (those corresponding to generic medical devices)

B Equipment/devices, etc. not used directly on the human body (excluding the cases where approved medical devices used concomitantly or in a control group are used directly on the human body with the directions for use or indications are outside the scope of the approved or certified directions for use or indications; excluding equipment/devices, etc. that affect human body through generated substances, electromagnetic waves, output information, etc.)

C General medical devices specified in Article 23-2-12, Paragraph 1 of the Act (however, general medical devices with the structure, instructions for use, indications, and performance, etc. that are obviously different from those of existing medical devices are excluded)

D Controlled medical devices meeting the criteria specified by the Minister of Health, Labour and Welfare pursuant to the provisions of Article 23-2-23, Paragraph 1 of the Act (however, controlled medical devices with the structure, instructions for use, indications, and performance, etc. that are obviously different from those of existing medical devices are excluded)

E Equipment/devices, etc. in accordance with A through D that are expected to correspond to improved medical devices and have been considered not requiring the submission of results of clinical studies in the consultation with PMDA

(2) When conducting clinical trials of equipment/devices, etc. in cases where notification of a clinical trial plan of equipment/devices, etc. is not required, attention shall be paid to the following points.

A The description, quality, or performance of the investigational device shall meet the criteria for medical devices specified by the Minister of Health, Labour and Welfare pursuant to the provisions of Article 41, Paragraph 3 of the Act.

B In cases of medical devices for which the criteria are specified in the provisions of Article 42, Paragraph 2 of the Act, the criteria (excluding those related to labels and instructions for use) shall be met.

C Based on the provisions of Article 80-2, Paragraphs 1, 4, and 5 of the Act, the clinical trials shall be conducted in accordance with the Ministerial Ordinance on Good Clinical Practice (GCP) for Medical Devices (Ministry of Health, Labour and Welfare Ordinance No. 36 of

2005) and PSEHB/MDED Notification No. 0831-12 of the Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated August 31, 2020, "Partial Revision of the 'Guidance on Ministerial Ordinance on Good Clinical Practice (GCP) for Medical Devices'" (hereinafter referred to as "GCP Ministerial Ordinance for Medical Devices, etc."). In clinical trials of drugs or regenerative medical products, when investigational devices are concomitantly used as clinical trials of equipment/devices, etc. in cases where clinical trial notifications for equipment/devices, etc. are not required, it is acceptable to prepare the protocol, Investigator's Brochure, written information, and other documents required by the GCP Ministerial Ordinance for Medical Devices, etc. as a part of the documents related to clinical trials of drugs.

D In clinical trials of drugs or regenerative medical products, when investigational devices are concomitantly used as clinical trials of equipment/devices, etc. in cases where clinical trial notifications for equipment/devices, etc. are not required, the category, generic name, classification, and other necessary matters to identify the investigational devices as well as the quantity shall be entered in the section, "Description of equipment/devices, etc. to be concomitantly used in the clinical trial related to this notification," in the clinical trial notification (including a notification of changes in the clinical trial plan) for drugs pursuant to the provision of the former part of Article 80-2, Paragraph 2 of the Act.

E Based on the provisions of Article 80-2, Paragraph 6 of the Act and Article 274-2 of the Regulation, malfunctions, etc. related to clinical trials of equipment/devices, etc. shall be reported. This reporting obligation is related to a person who sponsors a clinical trial of a equipment/device, etc. and provides the equipment/device, etc. to medical institutions in cases where notifications of clinical trial plans for equipment/devices, etc. is not required.

F For equipment/devices for which matters, etc. to be described in precautions, etc. are specified in the notification of the Safety Division, such as vacuum blood collection tubes (test tubes), appropriately reflect them in the Investigator's Brochure, protocol, etc. that are required to be prepared by the GCP Ministerial Ordinance for Medical Devices, etc. (if they are prepared as a part of documents related to clinical trials of drugs according to the latter part of C, such documents).

G In clinical trials of drugs or regenerative medical products, when investigational devices are concomitantly used as clinical trials of equipment/devices, etc. in cases where clinical trial notifications for equipment/devices, etc. are not required (including the cases where intended use and indications are different from those of existing medical devices), approval or certification of the concomitantly used medical devices needs to be obtained or their marketing notifications need to be made by the time of or at the same time with the approval of the drugs or regenerative medical products. However, this does not apply to the case where other medical devices that can be used concomitantly with the drugs concerned have already been approved or certified or their marketing notifications have been made and they have been supplied.

H If a clinical trial is conducted without submitting the required clinical trial notification for the equipment/device, etc. requiring submission of data related to clinical study results at the time of approval application, the clinical trial cannot be used as submission data for approval application based on the Act and the case may be regarded as a violation of Article 55, Paragraph 2 of the Act that is applied with modifications in Article 64 of the Act. For the scope of the cases where data related to the results of clinical studies need to be submitted,

see PFSB/ELD/OMDE Notification No. 0804001 of the Office of Medical Device Evaluation, Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated August 4, 2008, "Scope, etc. of Cases Where Medical Device Clinical Study Data Are Necessary." In addition, it should be confirmed appropriately through face-to-face advice, etc. with PMDA in advance where necessary.

5. Registration of study implementation status, etc.

After submitting a clinical trial notification, the information related to the clinical trial shall be registered at the domestic clinical study information registration center (Japan Registry of Clinical Trials [jRCT]) for the purpose of revealing the implementation status, etc. of the clinical trial to third parties, ensuring the transparency of the clinical trial, thereby contributing to protection of subjects, assurance of access of healthcare professionals and Japanese citizens to clinical trial information, and activation, etc. of clinical trials. Pay attention to the following points at the time of registration.

(1) Scope of the clinical trials to be registered

Clinical studies using investigational devices shall be registered. However, this does not apply to early-stage exploratory studies in healthy subjects and studies in humans required by the Japan Industrial Standards (JIS) cited in certification standards.

(2) Registration languages

Trials shall be registered in Japanese and English from the viewpoint of securing access of healthcare professionals in Japan and Japanese citizens to clinical trial information, and of international sharing of clinical trial information (registration with Primary Registry on the World Health Organization [WHO] Registry Network).

(3) Information to be registered

In principle, items for which WHO requires registration/publication in the International Clinical Trials Registry Platform (ICTRP) (see Attachment 3) should be registered according to the format of the clinical study information registration center.

In particular, in order to ensure the access of Japanese citizens to clinical trial information, physicians who represent clinical trials, investigational device, target diseases, main inclusion/exclusion criteria, current status of the clinical trial (ongoing, completion, etc.), medical institutions, contact information for inquiries on clinical trials, etc. should be registered/updated in a timely manner.

In this notification, "physicians who represent clinical trials" among the matters for which WHO requires registration/publication in ICTRP refer to the persons who are responsible for responding to inquiries to the "contact for scientific queries" and are assumed to be, for example, investigators who are taking initiative in clinical trial plans concerned from a scientific standpoint, coordinating investigators, or persons at sponsors who are responsible for clinical trial plans from a medical standpoint.

(4) Timing and update of registration

A Registration of clinical trial information

In principle, clinical trial information should be registered before participation of the first subject and updated if the subject recruitment status changes.

B Registration of outline of clinical trial results

In principle, the results should be registered within one year after completion of clinical trials. However, if it is difficult, registration should be made within one year after approval or marketing in any country. If there is any conflict with the laws or regulations of each country

where the clinical trial is conducted or if publication in a peer-reviewed medical journal is hindered, registration should be made by a method conforming to the laws or regulations concerned.

6. Application timing

This notification shall apply to clinical trial notifications, etc. submitted on or after September 1, 2020. Until August 31, 2022, notifications may be submitted according to the previous rules.

Attachment 1

Description Guidelines for Clinical Trial Notifications, etc.

Description in each notification shall be as follows, in principle.

1. Common items for clinical trial notifications
   (1) Clinical trial identification code of the main test device
      [1] Enter the clinical trial identification code determined by the company itself, the investigational device provider or the sponsor-investigator (no more than 20 alphanumeric characters) in half-width characters.
      [2] When changing the clinical trial identification code reported in the first notification, clarify the date of change and the reason for change in the notification of changes.
      [3] Different codes should be used for test devices with different structure and principle. Even if the structure and principle are the same, a different clinical trial identification code may be used, for example, for an equipment/device, etc. with a different form of use.
      [4] A single clinical trial identification code should be used across a series of clinical trials.
   (2) Type of clinical trial
      Specify whether the clinical trial is a company-sponsored clinical trial or an investigator-initiated clinical trial.
   (3) Date of initial notification for the main test device
      Enter the date on which the first clinical trial notification related to the same clinical trial identification code was submitted.
   (4) Category of the main test device
      It should be entered in accordance with Section 2, 1 of the Note for PFSB/MDRMPED Notification No. 1120-1, dated November 20, 2014, “Points to Consider When Preparing Marketing Approval Applications for Medical Devices” (hereinafter referred to as “Counsellor Notification”).
   (5) Generic name and classification of the main test device
      The generic name should be entered in accordance with Section 2, 2, (1) of the Note for the Counsellor Notification. The classification should be described according to the Attached Table 1 of PFSB Notification No. 0720022 of the Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated July 20, 2004, “Enforcement of Specially Controlled Medical Devices, Controlled Medical Devices, and General Medical Devices Designated by the Minister of Health, Labour and Welfare Pursuant to the Provisions of Article 2, Paragraphs 5 to 7 of the Pharmaceutical Affairs Act (Ministerial Announcement) and Specially Designated Maintenance-and-management-required Medical Devices Designated by the Minister of Health, Labour and Welfare Pursuant to the Provisions of Article 2, Paragraph 8 of the Pharmaceutical Affairs Act (Ministerial Announcement).”
   (6) Remarks column
      Make sure to enter the name, affiliation, phone number, and fax number or e-mail address of the person in charge. Enter the phone number, fax number, and e-mail address in half-width characters.
   (7) Other
      Enter the vendor code (9 digits) in parentheses under the name of the notifier. Enter “999999999” if there is no vendor code.

2. Clinical trial notifications (related to Attached Forms 1 and 2 of the Director-General Notification)

(1) Number of notifications for the main test device

The cumulative number of clinical trial notifications (not including notifications of changes in clinical trial plans, etc.) related to the same clinical trial identification code shall be entered. In cases where a clinical trial is conducted for the approval of partial changes in approved product information such as addition of intended use and indications for an approved medical device, if a clinical trial notification related to the investigational device concerned has been submitted in the past, the same clinical trial identification code shall be used, in principle, and a serial number shall be entered (for example, if a total of two notifications have been previously submitted, enter "3").

(2) Name and address of the manufacturing site or sales office (investigational device provider) of the main test device

[1] Company-sponsored clinical trials

Enter the name and address of the manufacturing site in cases of production, or the sales office in cases of import.

[2] Clinical trials conducted by sponsor-investigators

Enter the name and address of the investigational device provider. If the investigational device provider is a foreign manufacturer, enter the name (for a corporation, its name and the name of its representative) and address (for a corporation, the address of its main office) of the foreign manufacturer in Japanese and English.

(3) Shape, structure, and principle of the main test device

Enter them in accordance with Section 2, 4 of the Note for the Counsellor Notification.

(4) Raw materials, etc. of the main test device

Enter them in accordance with Section 2, 5 of the Note for the Counsellor Notification.

(5) Manufacturing method of the main test device

Enter them in accordance with Section 2, 9 of the Note for the Counsellor Notification. It shall also be entered whether the device is manufactured or imported. If it is imported, enter the manufacturing method in the exporting country, name of the exporting country, name of the manufacturer, and the brand name in the exporting country.

(6) Proposed intended use and indications of the main test device

Enter them in accordance with Section 2, 3 of the Note for the Counsellor Notification.

(7) Proposed operation or usage method of the main test device

Enter it in accordance with Section 2, 7 of the Note for the Counsellor Notification.

(8) Outline of the clinical trial plan

[1] Objective

Specifically describe the details of the objective in order to be consistent with the objective described in the protocol. If there are multiple objectives with different characteristics, explain the reason for not developing separate plans.

[2] Planned number of subjects

Enter the planned number of subjects for whom the test device is to be used. In the case of a comparative study, enter the total number of subjects including the control group in parentheses. Different numbers of subjects depending on the numbers of lesions are acceptable.

[3] Target disease of the main test device

Enter the specific name of the disease. In cases of healthy subjects, state this.

[4] Operation or usage method of the main test device

Describe in detail the operation or usage method to be used.

[5] Study period

In the case of a clinical trial by the sponsor, the period from the earliest date of conclusion of a clinical trial contract with each medical institution to the latest date of scheduled completion of observation at each medical institution shall be entered as the day, month, and year. In the case of a clinical trial by the sponsor-investigator, the period from the date on which the investigational device is obtained from the investigational device provider to the latest date of scheduled completion of observation at each medical institution shall be entered as the day, month, and year.

[6] Reason for the fee

In principle, clinical trials are free of charge because of their intent, but if the study devices, study drug equivalents, and study product equivalents are transferred for a fee, the reason shall be described by type. Draw a diagonal line in the column if all are free of charge.

[7] Party that bears clinical trial expenses

In cases of investigator-initiated clinical trials, describe the party that bears the expenses and its adequacy. In cases of company-sponsored clinical trials, leave the column blank.

[8] Name and address of the medical institution

Enter the name, address, and main phone number of the medical institution.

[9] Name of the investigator

Enter his/her name.

[10] Name of the subinvestigator

Enter his/her name.

[11] Quantity of study devices to be delivered (received)

Enter the planned quantity of study devices, study drug equivalents, and study product equivalents to be delivered (received) at the medical institution by type. Appropriate quantity should be delivered (received) in consideration of the directions for use and the planned number of subjects.

[12] Planned number of subjects at each medical institution

Enter the planned number of subjects at each medical institution.

[13] Other

If a notification is made in joint names in the case of joint development and the company or person in charge is different for each medical institution, enter the company name or the name of the person.

For a multicenter clinical trial conducted by a sponsor-investigator, describe, etc. the names of other medical institutions. In this case, describe, etc. the name, affiliation, contact information, protocol identification code, etc. of all investigators as joint names. However, this shall not apply if the coordinating investigator has submitted a notification of the multicenter clinical trial concerned as a representative.

It is desirable to describe, etc. the items warranting special mention regarding each medical institution, if any. If the coordinating investigator makes reports of malfunctions, etc. as a representative for more than one investigator in a multicenter clinical trial conducted by a sponsor-investigator, describe in the remarks column that the coordinating investigator makes reports of malfunctions, etc. to the authorities after sharing information with all investigators.

[14] Names of coordinating investigators or member physicians of the coordinating committee

If a coordinating investigator or the coordinating committee is entrusted to coordinate details of a clinical trial, enter names, affiliated organizations, and affiliations of the coordinating investigator or members of the coordinating committee. If a coordinating investigator submits, as a representative, a notification of a multicenter clinical trial conducted by a sponsor-investigator in joint names of investigators at individual medical institutions, this coordinating investigator shall be listed as the representative notifier.

[15] Name and address of the party entrusted with the conduct (including requests and preparations) and management operations of the clinical trial and range of operations entrusted

When outsourcing all or a part of the operations related to the request, conduct (including requests and preparations), and management of the clinical trial, describe the name and address of the contractor and the scope of the outsourced operations.

[16] Name and address of the founder of the institutional review board (IRB)

Enter the name (the corporate name and name of the representative) and address of the founder of the IRB for each medical institution. If investigation and deliberation are to be conducted by the IRB established by the head of the medical institution concerned (excluding those jointly established by the head of the medical institution concerned and the head of another medical institution), enter "In-house lRB." It is not necessary to enter, etc. the name (the corporate name and name of the representative) and address of the founder of the IRB. If investigation and deliberation are to be conducted by the IRB jointly established by the heads of multiple medical institutions, enter, etc., the name of the jointly established IRB and the address of the office of the IRB concerned, instead of the name of the founder of the IRB.

If the IRB that conducts investigation and deliberation has not been determined at the time of the notification, it is acceptable to submit a notification of changes after the submission of the IRB notification.

(9) Remarks

- As the notification category, enter "Notification category: Subject to 30-day investigation," "Notification category: Subject to 14-day investigation," or "Notification category: Other."
- Enter the protocol identification code (protocol number).
- Describe the following matters, if applicable.

[1] Clinical trials on combination products

When conducting clinical trials using equipment/devices, etc. manufactured in an integrated manner with drugs or processed cells, etc., enter "Clinical trial on investigational combination product."

[2] Positioning of the clinical trial

Enter "Pivotal clinical trial" if a pivotal clinical trial is conducted, and enter "Expanded access program" if an expanded access program is conducted.

[3] When multiple test devices are used in a clinical trial with one notification, enter the matters listed in 1, (1), (4), and (5), 2, (2) to (7) and (8), [3] and [4] regarding test devices other than the main test device.

[4] If study devices (other than the test device), study drug equivalents, or study product equivalents are used, enter the following. If they cannot be entered in the remarks column, they may be entered in an appendix.

i) Whether they are drugs, medical devices, or regenerative medical products

Enter whether the study device (excluding the test device), study drug equivalent, or study product equivalent is a drug, medical device, in vitro diagnostic, or regenerative medical product.

ii) Names, etc. of study devices, study drug equivalents, or study product equivalents

Enter the generic names, etc. of study devices, study drug equivalents, or study product equivalents. If the study devices, study drug equivalents, or study product equivalents concerned have been approved in Japan, enter the brand names and approval dates of the study devices, study drug equivalents, or study product equivalents concerned.

iii) Information on categories of study devices, study drug equivalents, or study product equivalents

Enter whether they are comparators, concomitant drugs, etc.

iv) Approval status in Japan

Enter whether they are not approved, off-label, or approved.

v) Notification items for study devices (excluding the test device), study drug equivalents, or study product equivalents

Enter the structure and principle, ingredients and contents, component cells or transgene, and directions for use, etc. of the study devices (other than the test device), study drug equivalents, or study product equivalents according to the description method for test devices.

[5] If the coordinating investigator makes reports of malfunctions, etc. as a representative for more than one investigator in a multicenter investigator-initiated clinical trial, the coordinating investigator shall make reports of malfunctions, etc. to the authorities after sharing information with all investigators.

[6] Information necessary to identify the notification if a related clinical trial notification has been separately submitted (drug/medical device/regenerative medical product, investigational ingredient code or clinical trial identification code, number of notifications, date of clinical trial notification, etc.)

[7] If the clinical trial is a global clinical trial, that fact, participating countries, total number of subjects and proportion of subjects in Japan

- Enter the titles of materials attached to the notification.

3. Notifications of changes in clinical trial plans (related to Attached Forms 3 and 4 of the Director-General Notification)

(1) Number of notifications for the main test device

Enter the number of notifications entered in the clinical trial notification for which a notification of changes in clinical trials is to be submitted.

(2) Date of clinical trial notification for the main test device and number of changes

Enter the date of clinical trial notification for which a notification of changes in clinical trials is to be submitted. For the notification of changes in clinical trial plans, enter the number of changes to show that the present notification is the n-th notification of changes for each clinical trial notification.

(3) Reason for change

[1] Item

Enter the relevant matters (items) in the description in the clinical study notification.

[2] Before change

Describe the content before change.

[3] After change

Describe the content after change.

[4] Date of change

Enter the date on which a decision on the change was made or the scheduled date of change. For the operation or usage method and study period, enter the date on which a decision on the change was made. For addition of a medical institution, enter the scheduled date of conclusion of the contract at the medical institution concerned. For the names of investigators, etc., enter the (scheduled) date of change.

[5] Reason for change

Describe the reason for changes specifically for each item to be changed.

(4) Remarks

If any materials related to changes are attached to the notification, enter the titles of the materials.

4. Clinical trial discontinuation notifications (related to Attached Forms 5 and 6 of the Director-General Notification)

(1) Number of notifications for the main test device

Enter the number of notifications entered in the clinical trial notification for which a clinical trial discontinuation notification is to be submitted.

(2) Date of clinical trial notification for the main test device and number of notifications

Enter the date of the clinical trial notification for which a clinical trial discontinuation notification is to be submitted.

(3) Timing of discontinuation

Enter the date on which a decision on discontinuation was made.

(4) Reason for discontinuation

Describe the reason for discontinuation specifically.

(5) Status of subsequent actions

Describe specifically the status of actions taken after the decision of discontinuation.

(6) Status at each medical institution

[1] Name of medical institution

Enter the name of the medical institution.

[2] Quantity delivered (received)

Enter the quantity of study devices, study drug equivalents, and study product equivalents that have actually been delivered (received) at each medical institution by type. When an approved medical device already purchased at a medical institution is used as a study device such as that of a comparator, the transfer of the study device concerned to the investigational device storage manager at the medical institution shall be regarded as delivery (receipt).

[3] Quantity used

Enter the quantity of study devices, study drug equivalents, and study product equivalents that have actually been used at each medical institution by type.

[4] Quantity collected/disposed, etc.

Enter the quantity of study devices, study drug equivalents, and study product equivalents that have been collected/disposed of at each medical institution by type. For an installed large device, etc. that cannot be collected, describe the reason for not collecting it and measures taken for discontinuation of the clinical trial.

[5] Number of subjects

Enter the number of subjects at each medical institution.

(7) Remarks

If any materials related to the reason for discontinuation are attached to the notification, enter the titles of the materials.

5. Clinical trial completion notifications (related to Attached Forms 7 and 8 of the Director-General Notification)

(1) Number of notifications for the main test device

Enter the number of notifications entered in the clinical trial notification for which a clinical trial completion notification is to be submitted.

(2) Date of clinical trial notification for the main test device

Enter the date of the clinical trial notification for which a clinical trial completion notification is to be submitted.

(3) Status at each medical institution

[1] Name of medical institution

Enter the name of the medical institution.

[2] Quantity delivered (received)

Enter the quantity of study devices, study drug equivalents, and study product equivalents that have actually been delivered (received) at each medical institution by type. When an approved medical device already purchased at a medical institution is used as a study device such as that of a comparator, the transfer of the study device concerned to the investigational device storage manager at the medical institution shall be regarded as delivery (receipt).

[3] Quantity used

Enter the quantity of study devices, study drug equivalents, and study product equivalents that have actually been used at each medical institution by type.

[4] Quantity collected/disposed, etc.

Enter the quantity of study devices, study drug equivalents, and study product equivalents that have been collected/disposed of at each medical institution by type. For an installed large device, etc. that cannot be collected, enter the reason for not collecting it and measures taken for completion of the clinical trial.

[5] Number of subjects

Enter the number of subjects at each medical institution.

6. Development discontinuation notification

Enter the clinical trial identification code and the generic name of the test device for which discontinuation of development was decided, the date of the initial notification, the notification date, classification of notification, time of discontinuation (the decision date of discontinuation of development), and the reason for discontinuation (specific reason for discontinuation), and provide in the remarks column the submission data attached to the notification (if data are attached) and information on the notifier. In cases of implanted investigational devices that are continuously used in subjects after discontinuation of development, describe the handling of the devices in the remarks column.

If the test device for which discontinuation of development is decided is not the main test device, enter the “clinical trial identification code of the main test device” and “number of notifications” for the notification concerned in the “Remarks” column.

Attachment 2

Input Format, etc. for Electronic Media

1. Items to be recorded in electronic media attached to clinical trial notifications, etc.

(1) The electronic media to be submitted should be CD-R (format, ISO9660) or DVD-R (format, UDF), in principle. In principle, one notification shall be recorded in one electronic medium. Multiple notifications should not be recorded in one electronic medium, or one notification should not be divided into multiple electronic media.

(2) Record in electronic media using a format that does not allow for addition (disk at once).

(3) Notifications should be prepared using an electronic notification form. The electronic notification form and the "Entry Manual for Clinical Trial Notifications for Equipment/Devices, etc." are available on the PMDA website (in Japanese). (https://www.pmda.go.jp/review-services/trials/0003.html)

(4) The documents from [2] to [7] below shall be in PDF format. Do not use scanning, but prepare PDF files containing text information. For the files of [3] and [6], place bookmarks referring to the items described in PSEHB/MDED Notification No. 0831-12 of the Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated August 31, 2020, "Partial Revision of the 'Guidance on the Ministerial Ordinance on Good Clinical Practice (GCP) for Medical Devices,'" etc.

For notifications that do not require submission of submission data, only [1] should be recorded in electronic media.

In the case of replacing [2] to [7], record only the replacement files, and the comparison table of before and after the change shall be included in the same data file to prepare a PDF.

[1] Notification
[2] Document stating the reason why the conduct of the clinical trial concerned is scientifically justified
[3] Protocol
[4] Written information and informed consent form used for the informed consent
[5] Sample case report form (If the items to be entered in the case report form are clearly shown in the protocol, the submission is not required.)
[6] Latest Investigator's Brochure
[7] Documents describing the latest scientific findings related to the study devices other than the test device, study drug equivalents, and study product equivalents (package inserts/instructions for use, academic papers, etc.).
[8] Other

2. Items to be entered in electronic media or attached document

A label containing the following information should be attached on the electronic media, or the following information should be directly saved in the electronic media.

(1) Name of the notifier (for a corporation, its name) and the name, affiliation, phone number, and fax number of the person in charge of notification
(2) Clinical trial identification code, generic name, and classification of the main test device
(3) The classification of notification and number of clinical trial notifications concerned

(4) Date of notification (enter the date of the notification to be submitted)

3. How to name a file

(1) File name

The names of the files to be recorded in electronic media shall be created with half-width alphanumeric characters in the following format. See the "Entry Manual for Clinical Trial Notifications for Equipment/Devices, etc." for details of the file names of appendices, etc. of notifications.

[1] Notifications other than notifications of changes in clinical trial plans

Clinical trial identification code	_	Number of notifications	_	Classification of notification	_	Data information	.pdf

Example: "PMDA-123_01_S_D.pdf"

[2] Submission data for notifications other than notifications of changes in clinical trial plans

Clinical trial identification code	_	Number of notifications	_	Classification of notification	_	Data information	.pdf

Example: "PMDA-123_03_K_P.pdf"

[3] Notifications of changes in clinical trial plans

Clinical trial identification code	_	Number of notifications	_	Classification of notification	_	Number of changes	_	Data information	.pdf

Example: "PMDA-123_03_H_3_D.pdf"

[4] Submission data for notifications of changes in clinical trial plans

Clinical trial identification code	_	Number of notifications	_	Classification of notification	_	Number of changes	_	Data information	.pdf

Example: "PMDA-123_03_H_14_P.pdf"

[5] If there are multiple files of the same data information and they cannot be combined into one file, add "_" and an alphabet starting from A to identify the data, following the data information. For the file names of a notification for changes, use the same letters of the alphabet as those used for the file names at the time of the notification of the plan.

Examples: "PMDA-123_01_K_IB_A.pdf" "PMDA-123_01_K_IB_B.pdf"

[6] For replacement, provide the version number after the data information. Add "1" for the first replacement and increase the number by one each time the replacement is made. In the case of replacement, it is acceptable to record only the replacement file.

Example: "PMDA-123_01_K_P1.pdf"

[7] In the case of a development discontinuation notification, the number of notifications should be "00."

Example: "PMDA-123_00_END.pdf"

(2) General considerations

Use half-width alphanumeric characters and symbols for all characters. Enter the clinical trial identification code accurately including hyphens and spaces. Use lowercase letters for extensions. Use an underscore (half-width) for "_."

(3) Type of notification

Clinical trial notification	K
Notification of changes in clinical trial plans	H
Clinical trial completion notification	S
Clinical trial discontinuation notification	C
Development discontinuation notification	END

(4) Data information

[1]	Notification	D
[2]	Document stating the reason why the conduct of the clinical trial concerned is scientifically justified	R
[3]	Protocol	P
[4]	Written information and informed consent form used for the informed consent	IC
[5]	Sample case report form	CRF
[6]	Latest Investigator's Brochure	IB
[7]	Documents describing the latest scientific findings related to the study devices other than the test device, study drug equivalents, and study product equivalents (package inserts/instructions for use, interview forms [in cases of study drug equivalents], academic papers, etc.)	SF
[8]	Other	etc

Attachment 3

The data sets required by WHO are available at http://www.who.int/ictrp/network/trds/en/. Data sets as of August 2020 are as follows.

1. Primary Registry and Trial Identifying Number
2. Date of Registration in Primary Registry
3. Secondary Identifying Numbers
4. Source(s) of Monetary or Material Support
5. Primary Sponsor
6. Secondary Sponsor(s)
7. Contact for Public Queries
8. Contact for Scientific Queries
9. Public Title
10. Scientific Title
11. Countries of Recruitment
12. Health Condition(s) or Problem(s) Studied
13. Intervention(s)
14. Key Inclusion and Exclusion Criteria
15. Study Type
16. Date of First Enrollment
17. Sample Size
18. Recruitment Status
19. Primary Outcome(s)
20. Key Secondary Outcomes
21. Ethics Review
22. Completion date
23. Summary Results
24. IPD sharing statement

Attached Form 1

Development Discontinuation Notification

Clinical trial identification code	
Generic name	
Date of first clinical trial notification	
Timing of discontinuation	
Reason for discontinuation	
Remarks	

I hereby notify discontinuation of the development as described above.

Month DD, YYYY

Address: (for a corporation, location of its main office)
Name: (for a corporation, its name and the name of the representative)

To: Director of the Medical Device Evaluation Division, Pharmaceutical Safety Bureau, Ministry of Health, Labour and Welfare

(Note)

1. The paper size should be Japan Industrial Standard A4.
2. When not all the required information can be entered in the specified column, enter “as per appendix ( )” in the column and attach the appendix.
3. Enter the name of the person in charge of the notification and the contact telephone number/fax number in the remarks column. In the case of a foreign manufacturer, enter the contact telephone number/fax number of the in-country representative in the remarks column.