

Provisional Translation (as of April 2026).

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PSEHB Notification No. 0831-9

August 31, 2020

To: Prefectural Governors

Director-General of Pharmaceutical Safety and  
Environmental Health Bureau, Ministry of  
Health, Labour and Welfare  
(Official seal omitted)

Reports of Malfunctions, etc. in Clinical Trials Related to  
Equipment/Devices, etc. to Pharmaceuticals and Medical Devices Agency

A notification on the reports of malfunctions and adverse events of medical devices during clinical trials (hereinafter referred to as “reports of malfunctions, etc. in clinical trials”) was made in 23, “Clinical trials of medical devices,” of the Note of PFSB Notification No. 0709004 of the Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated July 9, 2004, “Enforcement of the Act for Partial Revision of the Pharmaceutical Affairs Act and Blood Collection and Donation Service Control Act” (hereinafter referred to as “Enforcement Notification”), and the handling of these reports has been shown in PFSB Notification No. 0329-14 of the Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated March 29, 2013, “Reports of Malfunctions, etc. in Clinical Trials Related to Equipment/Devices, etc. to Pharmaceuticals and Medical Devices Agency.”

With the enforcement of the Act Partially Amending the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Act No. 63 of 2019) and 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 (Ordinance No. 155 of Ministry of Health, Labour and Welfare in 2020), handling of reports of malfunctions, etc. in clinical trials on medical devices has been specified as follows. Please be aware of this and inform related businesses, medical institutions, etc. under your jurisdiction of this matter.

#### Note

1. The terms in Article 274-2 used with modifications in Article 279 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”) are defined as follows.
  - (1) “Devices considered to have the same structure and principle as those of the study device concerned” are devices with the same shape, structure, raw materials, performance, etc. as those of the study device concerned. It should be determined whether a case occurring

overseas is subject to reporting according to the provisions of Article 274-2 of the Regulation. However, the cases that need to be reported urgently to the government at least in the country where they occurred should be reported.

- (2) “Events suspected to be caused by the effect of use” are events other than those for which a causal relationship can be ruled out. The events for which the causal relationship is unknown are also included. For test devices such as drug-eluting stents in which drugs have already been combined with equipment/devices, etc., adverse events suspected to have been caused by the effect of drugs are also subject to reporting.
- (3) “Infections suspected to be caused by their use” refer to infections including those for which contamination of the study device concerned, etc. (the study device concerned or devices with the same shape, structure, raw materials, performance, etc. as those of the study device concerned, the same applies hereinafter) of biological origin with a pathogen is suspected (e.g., viral hepatitis, HIV infection, etc. suspected to be caused by raw materials, etc. of biological origin). Tests of markers for viruses such as HBV (hepatitis B virus), HCV (hepatitis C virus), and HIV turning positive are also subject to reporting.
- (4) “Events not expected from the Investigator’s Brochure of the test device concerned or existing scientific findings on the study devices, etc. concerned other than the test device” are events not described in the materials used for the latest judgment of expectedness at the time of evaluation of malfunctions, etc. (the Investigator’s Brochure or documents describing scientific findings on the study devices other than the test device such as instructions for use and academic papers [hereinafter referred to as “Investigator’s Brochure, etc.”]) or events that are described in these materials, but are not consistent with the description in nature, severity of symptoms, or occurrence tendency. For example, an unexpected serious case of an event should be reported even if the event is listed in the Investigator’s Brochure, etc.
- (5) “Disability” refers to the onset of incapacity that interferes with daily life.
- (6) “Malfunction” refers to a wide range of poor states of quality, safety, performance, etc. such as breakage and poor operation of a test device regardless of the stage (designing, delivery, storage, or use) where it occurs.
- (7) “Occurrence of malfunctions of the study device, etc. concerned that may result in cases, etc. in (a) or (b) of Item 1 or (a), (1) to (5) of the preceding item” refers to occurrence of malfunctions of the study device, etc. concerned that are considered to possibly result in death, disability, etc. although death, disability, etc. have not occurred in reality.
- (8) “Situations involving no risk of affecting safety judgment related to subject protection in the clinical trial concerned” refer to the situations including those where the obtained safety information does not include sufficient information that contributes to medical evaluation and it is difficult to obtain additional information that contributes to the evaluation in consideration of the information sources, occurrence status, etc., or where the contents of the obtained safety information are significantly different from the status of use in subjects of the clinical trial concerned and therefore there is no risk of affecting the safety judgment related to subject protection.

Specifically, the situations where it is difficult to judge whether the safety information is true or not as it has been derived from anonymous posting of adverse events on the internet or provision of information or inquiries from consumers or other non-healthcare professionals to the call center, which makes medical discussion or collection of additional information difficult, or the cases of malfunctions, etc. that occurred with the method of use different from those used in the clinical trial and are unique to the method of use concerned are applicable.

However, even in the case of such information, if the accumulation of such information indicates an increase in the number, frequency, etc. of diseases, etc. suspected to be caused by the effect of the use of the test device, etc. concerned or infections suspected to be caused by their use, the change in such tendency needs to be reported separately.

- (9) “Implementation of actions that prevent the occurrence or spread of public health hazards including discontinuation of manufacturing, import, or marketing, recall, and disposal of devices used overseas with the same structure and principle as those of the study device” includes discontinuation of manufacturing, etc. overseas in light of efficacy or safety, changes in indications, operation methods, directions for use, manufacturing methods, etc., and revision of important precautions with distribution of doctor letters.
- (10) “For study devices other than test devices, actions that prevent the occurrence or spread of public health hazards in combined use with the test devices” refer to measures to prevent the occurrence or spread of public health hazards related to study devices other than test devices that is likely in concomitant use with the test devices in the clinical trial concerned.
- (11) “There is a risk of cancer or other serious diseases, disabilities, or death” indicates the onset or possible onset of clinically significant diseases (e.g. cancer, deafness, blindness, etc.) attributable to the use of the test devices, etc. concerned or infections due to their use based on the epidemiological survey reports, results of studies in animals, etc., physical tests, chemical tests, or electrical tests, etc.
- (12) “Marked changes in the tendency of occurrence such as the number of cases, frequency, and conditions of occurrence of diseases, etc. suspected to be caused by the effect of their use or infections suspected to be caused by their use” are clear changes that are observed in the number of cases, frequency, conditions of occurrence (for example, the number of cases or frequency as a whole has not changed so greatly, but the number of cases or frequency is found to have particularly increased in light of specific ages, complications, operation methods, directions for use, etc. when stratified), symptoms, or severity, etc. of diseases suspected to be caused by the effect of the use of the test devices concerned, etc. or infections suspected to be caused by their use.
- (13) The phrase, a device “does not have the efficacy, effect, or performance on the disease investigated in the clinical trial,” refers to the absence of efficacy, effect, or performance on the disease targeted in the clinical trial in the test device, etc. concerned based on precise and objective clinical studies, other animal studies, etc.
- (14) “Research reports” refer to reports such as research reports published in academic journals, etc. in Japan or overseas or reports of in-house research or research conducted by related companies.
- (15) Regarding “research reports considered not to affect the evaluation of efficacy and safety for the diseases investigated in the clinical trial of the test devices concerned, etc.,” for example, research reports on malfunctions, etc. expected in the clinical trial for which safety measures for subjects have already been taken (exclusion of certain subjects in whom the malfunctions, etc. concerned may occur, appropriate examination plans developed in the trial, etc.) or diseases, etc. suspected to be caused by the effect of the use of the test devices concerned, etc. or infections suspected to be caused by their use, showing no increase in the number of cases, frequency, etc. are assumed.

2. Reporting deadline, etc.

- (1) Reports of malfunctions, etc. in clinical trials should be made within 7 days if they correspond to Article 274-2, Paragraph 1, Item 1 and Paragraph 2, Item 1, within 15 days if they correspond to the same article, Paragraph 1, Item 2 and Paragraph 2, Item 2, and within 30 days if they correspond to the same article, Paragraph 1, Item 3 and Paragraph 2, Item 3 of the Regulation.
- (2) The matters specified in Article 274-2, Paragraph 4 of the Regulation must be reported every year starting from the date of the first clinical trial notification for the test device concerned, within 2 months after the expiration of the period.

3. Report forms

For reports based on Article 274-2, Paragraph 1, Paragraph 2, Item 1 and Item 2, (a) and (b), and the same paragraph, Item 3 of the Regulation, use Attached Form 1. For reports based on Item 2, (c) and (d) of the same paragraph, use Attached Form 2. For reports based on Paragraph 4 of the same article, use Attached Forms 3 and 4.

4. Handling for reporting

(1) Reporting by the sponsor of the clinical trial

Regardless of the necessity of submitting a notification of the clinical trial plan the sponsor requested, if the sponsor obtains important findings from a public health perspective regarding the efficacy and safety of a study device, the sponsor shall report the contents pursuant to the provisions of Article 274-2 of the Regulation. Even if all clinical trials related to the test device have been completed and an application for marketing approval is pending or being prepared regarding a medical device related to the said test device, these cases are subject to reporting until the marketing approval is granted.

(2) Reporting by the sponsor-investigator

Regardless of the necessity of submitting a notification of the plan for the clinical trial conducted by a sponsor-investigator, if the sponsor-investigator obtains important findings from a public health perspective regarding the efficacy and safety of a study device, the sponsor-investigator shall report such contents pursuant to the provisions of Article 274-2 of the Regulation. Even if all clinical trials related to the test device have been completed and an application for marketing approval is pending or being prepared regarding a medical device related to the said test device, these cases are subject to reporting until the marketing approval is granted.

5. How to submit

The reports of malfunctions, etc. in clinical trials shall be submitted to the Review Planning Division, Office of Review Management, Pharmaceuticals and Medical Devices Agency.

6. Handling of extremely significant safety information obtained during clinical trials

If the sponsor obtains extremely significant safety information such as the information on unknown serious malfunctions, etc., which are reasonably considered attributable to the use of study devices with structure and principle different from those of the medical devices marketed by the sponsor (including test devices to be marketed) (hereinafter referred to as “other companies’ study devices”) that would be considered to be the reason for suspension/discontinuation of clinical trials, it is desirable to appropriately provide the

information to the marketing authorization holders, etc. of the study devices concerned in Japan from the perspective of subject protection and improvement of public health safety in Japan, in addition to making above reports of malfunctions, etc. based on the above laws and regulations.

7. Application timing

This notification shall apply from September 1, 2020. However, in cases where a clinical trial notification was submitted in accordance with previous rules, based on “Points to Consider for Reporting of Malfunctions, etc. in Clinical Trials Related to Equipment/Devices, etc. to Pharmaceuticals and Medical Devices Agency” (PSEHB/MDED Notification No. 0831-10 of the Medical Device Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare, dated August 31, 2020), reports of malfunctions, etc. in clinical trials should be made according to the previous rules.

8. Abolition of notification

With the application of this notification, PFSB Notification No. 0329-14 of the Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, dated March 29, 2013, “Reports of Malfunctions, etc. in Clinical Trials Related to Equipment/Devices, etc. to Pharmaceuticals and Medical Devices Agency,” shall be abolished as of August 31, 2022.

## Investigational Device Malfunction/Adverse Event Case Report Form

<b>1. Management information</b>											
1) Control number	Identification number		Number of reports to PMDA			Report category	[1] 7 days	[2] 15 days	[3] 30 days		
	Report type	[1] Malfunction	[2] Adverse event	Site of occurrence of malfunction, etc.		[1] Japan	[2] Overseas ( )				
2) Date on which the first report was received	Month DD, YYYY			3) Date of most recent information	Month DD, YYYY						
4) Scheduled date of next report	Month DD, YYYY										
5) Status of malfunction of investigational device	[1] Yes		[2] No		[3] Unknown						
6) Onset status of adverse events in subjects, etc.	[1] Yes		[2] No		[3] Unknown						
7) Contact information of the person in charge	Name of the person in charge					Name of corporation					
	Department										
	Address										
	Tel				Fax			E-mail			
<b>2. Information on the subject, etc.</b>											
1) Abbreviated name of subject, etc.		2) Age	years old	3) Sex	Male/ Female	4) Body weight	kg	5) Height	cm		
6) Status of subject, etc. at the time of occurrence of malfunction, etc.	Malfunction										
	Name of malfunction					Known or unknown		[1] Known	[2] Unknown		
	Date of occurrence		Month DD, YYYY								
	Adverse event										
	Name of adverse event					Known or unknown		[1] Known	[2] Unknown		
	Onset date		Month DD, YYYY			End date		Month DD, YYYY			
	Seriousness					Outcome					
	Causality assessment			Attending physician, etc.							
Reporter											
7) Course of occurrence status of malfunction, etc.											

<b>3. Information on investigational device</b>			
1) Clinical trial identification code		2) Category	
3) Generic name		4) Classification	
5) Date of clinical trial notification			
6) Outline of clinical trial			
7) Details of investigational device			
8) Investigational device classification	[1] Specially controlled medical device	[2] Controlled medical device	[3] General medical device
	[1] Biological medical device	[2] Specified biological medical device	[3] Other
	[1] Single-use medical device	[2] Repeated-use medical device	
9) Status of use of investigational device	[1] Not used	[2] First use	[3] Number of uses ( times) or ( months, days, or hours after the start of use)
	[4] Unknown		
10) Current status of investigational device	[1] Recall of actual product	[2] Actual product not recalled (disposed, remaining in the body, recall planned, recall impossible)	
11) Concomitant therapies			
12) Remarks			
<b>4. Investigation results and actions, etc.</b>			
1) Investigation results			
2) Comments from the attending physician, etc.			
3) Reporter's comments			
4) Previous actions			
5) Future actions			

I hereby report the case of the malfunction/adverse event related to the investigational device as described above.

Month DD, YYYY

Address

Name

To: Chief Executive, Pharmaceuticals and Medical Devices Agency

**Report on Investigation of Research Reports of Investigational Device  
Report on Investigation of Actions Overseas Including Discontinuation of  
Manufacturing, etc., Recall, and Disposal of Investigational Device**

1. Management information							
1) Control number	Identification number		Number of reports to PMDA		Report type	[1] Research reports	[2] Action reports
2) Date on which first report was received		Month DD, YYYY		3) Date of most recent information		Month DD, YYYY	
4) Scheduled date of next report		Month DD, YYYY					
5) Status of malfunction of investigational device			[1] Yes	[2] No	[3] Unknown		
6) Onset status of adverse events in subjects, etc.			[1] Yes	[2] No	[3] Unknown		
7) Contact information of the person in charge	Name of the person in charge				Name of corporation		
					Department		
	Address						
	Tel		Fax		E-mail		
2. Information on investigational device							
1) Clinical trial identification code				2) Category			
3) Generic name				4) Classification			
5) Date of clinical trial notification							
6) Outline of clinical trial							
7) Details of investigational device							
8) Investigational device classification	[1] Specially controlled medical device	[2] Controlled medical device	[3] General medical device				
	[1] Biological medical device	[2] Specified biological medical device	[3] Other				
	[1] Single-use medical device	[2] Repeated-use medical device					
9) Remarks							

<b>3. Report contents and actions, etc.</b>		
1) Details of research report or action	Source of research report	
	Country where action is taken	
	Action category	
2) Previous actions		
3) Future actions		

I hereby report the investigation results of the investigational device as described above.

Month DD, YYYY

Address

Name

To: Chief Executive, Pharmaceuticals and Medical Devices Agency

Attached Form 3

## Investigational Device Periodic Safety Report

1) Clinical trial identification code		2) Category	
3) Generic name		4) Classification	
5) Date of the first clinical trial notification		6) Base date for reporting	
7) Outline of clinical trial			
8) Details of investigational device			
9) Investigational device classification	[1] Specially controlled medical device	[2] Controlled medical device	[3] General medical device
	[1] Biological medical device	[2] Specified biological medical device	[3] Other
	[1] Single-use medical device	[2] Repeated-use medical device	
10) Reporting period		11) Number of reports to PMDA	
12) Information on changes in investigational device			
13) Approval status overseas			
14) Occurrence status of malfunction, etc.			
15) Comments and safety measures based on accumulation			
16) Remarks			

I hereby submit a periodic safety report for the investigational device as described above.

Month DD, YYYY

Address

Name

To: Chief Executive, Pharmaceuticals and Medical Devices Agency

## List of Occurrence Status of Cases of Investigational Device Malfunctions/Adverse Events

Category	Clinical trials in Japan		Overseas clinical studies		Overseas post-marketing spontaneous reports	
	Within reporting period	Total	Within reporting period	Total	Within reporting period	Total
Approximate number of subjects						
Type of adverse event	Number of adverse events by type					
Type of malfunction	Number of malfunctions by type					
Remarks						