Office of Non-clinical and Clinical Compliance, Pharmaceuticals and Medical Devices Agency

Ver. 3.2 (prepared on July 1, 2022)

**Checklist for GCP[[1]](#footnote-1) On-site Inspection/Document-based Compliance Assessment for New Drug (for Sponsor)**

|  |  |
| --- | --- |
| Name of sponsor (company) |  |
| Name of product subject to inspection<Nonproprietary name> | < > |
| On-site inspection | Name of document to be inspected(Date of clinical trial notification) |  |
| Date of inspection | MMM DD, YYYY |
| Name of inspector |  |
| Document-based inspection | Name of document to be inspected(Date of clinical trial notification) |  |
| Date of inspection | MMM DD, YYYY |
| Name of inspector |  |

**\* When electromagnetic methods are used to store, prepare, circulate, or provide documents, they shall be processed in accordance with related laws, regulations, notifications, etc.**

<<Reference>> Partial Revision of the New “Standard Forms for requesting clinical trials, etc.”
(HPB/RDD Notification No. 0710-4, PSEHB/PED Notification No. 0710-2, PSEHB/MDED Notification No. 0710-2 dated July 10, 2018)

• Use of the Standard Forms at the time of inspection

[ ]  Used

[ ]  Not used (Reason for not being used: )

# [I] Organization, Structure, etc. of Sponsor

\* Based on the presentation and the data submitted in advance

⚫ Overall work flow (decision-making procedure)

⚫ Role and responsibility of the development unit, the safety information unit, and the audit unit

Issues:

# [II] Standards for Preparing Clinical Trials

## 1. Arrangement of Professionals with Adequate Expertise

[Article 4, Paragraph 2][[2]](#footnote-2) From April 1997 [[3]](#footnote-3)

[ ]  Compliant

[ ]  Qualified individuals are engaged throughout the course of the clinical trial
 From May 29, 1997 (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Appointment is recorded From May 29, 1997 (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Other ( )

## 2. Preparation and Revision of Protocol and Other Documents

Preparation by the sponsor From April 1997

1) Preparation of written operating procedures for the preparation of a protocol **[Article 4, Paragraph 1]**

[ ]  Compliant

Name of document:

Effective date of the written operating procedures applicable to the clinical trial period:

 MMM DD, YYYY

[ ]  Other ( )

2) Preparation of protocol **[Article 7, Paragraph 1]**

[ ]  Compliant

[ ]  Protocol is prepared in accordance with the written operating procedures

The following information shall be included:

[ ]  Name and address of the person who intends to sponsor the clinical trial (or, in the case of a corporation, its name and the address of its main office. If the person resides outside Japan, then his or her name and name of the country where the person is located, and name and address of the clinical trial in-country representative pursuant to GCP Ministerial Ordinance Article 15)

[ ]  When all or any of the duties related to the clinical trial are outsourced to another person or organization, the name and address of the contractor and the scope of the duties outsourced

[ ]  Name(s) and address(es) of the medical institution(s)

[ ]  Name(s) and title(s) of prospective investigator(s) **Until August 31, 2020**

[ ]  Name(s) of prospective investigator(s) **From September 1, 2020**

[ ]  The objectives of the clinical trial

[ ]  Summary of the test drug **Until August 31, 2020**

[ ]  Summary of drug(s) used in the clinical trial **From September 1, 2020**

[ ]  Clinical trial design

[ ]  Description of subject selection

[ ]  Description of direct access to source documents **From April 1998**

[ ]  Description of record (and data) keeping

[ ]  Name(s) and title(s) of coordinating investigator(s) (to whom the responsibilities for coordination are assigned pursuant to the provisions of GCP Ministerial Ordinance Article 18, if applicable)
 Until August 31, 2020

[ ]  Name(s) of coordinating investigator(s) (to whom the responsibilities for coordination are assigned pursuant to the provisions of GCP Ministerial Ordinance Article 18, if applicable) **From September 1, 2020**

[ ]  Names and titles of physicians or dentists constituting a coordinating committee (to which the responsibilities for coordination are assigned pursuant to the provisions of GCP Ministerial Ordinance Article 18, if applicable) **Until August 31, 2020**

[ ]  Names of physicians or dentists constituting a coordinating committee (to which the responsibilities for coordination are assigned pursuant to the provisions of GCP Ministerial Ordinance Article 18, if applicable) **From September 1, 2020**

[ ]  Statement that an Efficacy and Safety Assessment Committee has been established for the clinical trial (if established pursuant to the provisions of GCP Ministerial Ordinance Article 19)

[ ]  Dates and version numbers of the protocol preparation and revisions Until September 2008
 (PAB Notification No. 430 dated March 27, 1997; PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Dates and version numbers of the protocol preparation and revisions, or date and version number of the latest protocol From October 2008 (PFSB/ELD Notification No. 1001001 dated October 1, 2008)

[ ]  Site-specific information may be provided on separate protocol page(s). (Names, titles, telephone numbers, etc. of monitors and auditors)
 From October 2008 until March 31, 2012 (PFSB/ELD Notification No. 1001001 dated October 1, 2008)

[ ]  Site-specific information may be provided on separate protocol page(s). (Name(s) and address(es) of medical institution(s); name(s) and title(s) of prospective investigator(s); name, title, telephone number, etc. of the monitor in charge of each medical institution (or representative if there are multiple monitors))
 From April 1, 2012 until August 31, 2020 (PFSB/ELD Notification No. 1024-1 dated October 24, 2011)

[ ]  Site-specific information may be provided on separate protocol page(s). (Name(s) and address(es) of medical institutions; name(s) of prospective investigator(s); name, telephone number, etc. of the monitor in charge of each medical institution (or representative if there are multiple monitors)) From September 1, 2020 (PSEHB/PED Notification No. 0831-15 dated August 31, 2020)

[ ]  Other ( )

3) If the clinical trial is a non-therapeutic clinical trial where some subjects are to be enrolled although it would be difficult to obtain their own consent, the protocol shall include the following information **[Article 7, Paragraph 2]**

\* See the GCP Ministerial Ordinance, related notifications, etc. if applicable.

[ ]  Not applicable

[ ]  Compliant

[ ]  Statement that the investigational product affords no intended clinical benefit to the subject, and that some subjects are to be enrolled in the clinical trial although it would be difficult to obtain their own consent under GCP Ministerial Ordinance Article 50, Paragraph 1

[ ]  Reasons why some subjects are to be enrolled in the clinical trial although it would be difficult to obtain their own consent under GCP Ministerial Ordinance Article 50, Paragraph 1

[ ]  Explanation that the potential disadvantages which the subject may incur in the clinical trial are minimized

[ ]  Other ( )

4) If some subjects are to be enrolled in the clinical trial although it would be difficult to obtain the consent of the subjects or their legally acceptable representatives (life-saving clinical trial in case of emergency), the protocol shall include the following information **[Article 7, Paragraph 3]**

\* See the GCP Ministerial Ordinance, related notifications, etc. if applicable.

[ ]  Not applicable

[ ]  Compliant

[ ]  Statement that some subjects are to be enrolled in the clinical trial although it would be difficult to obtain their own consent under GCP Ministerial Ordinance Article 50, Paragraphs 1 and 2

[ ]  Explanation that an application for marketing approval of the test drug is intended to be submitted so that the drug will be used for emergency treatment to save lives of patients in a life-threatening condition

[ ]  Explanation that currently available treatments are unlikely to achieve sufficient therapeutic effects in the prospective subject

[ ]  Explanation that there is a sufficient possibility of saving the life of the prospective subject by using the test drug

[ ]  Statement that an Efficacy and Safety Assessment Committee has been established for the clinical trial

[ ]  Other ( )

5) Agreement with the investigator on the content of the protocol and that the clinical trial be conducted in compliance with the protocol (for medical institutions subject to inspection) **[Article 7, Paragraph 4]**

[ ]  Compliant

[ ]  Information necessary for examining the protocol contents is provided for the investigator in advance (PAB Notification No. 430 dated March 27, 1997)

[ ]  Agreement is given with name and seal or signature, and date in writing
 From May 29, 1997 until July 31, 2021 (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Agreement is given with signature and date in writing From August 1, 2021 (PSEHB/PED Notification No. 0730-3 dated July 30, 2021)

[ ]  Other ( )

6) Revision of the protocol

a Revision of the protocol as necessary whenever important information necessary to conduct the clinical trial properly becomes available (information on the quality, efficacy, and safety of the test drug) **[Article 7, Paragraph 5]** From April 1997 until July 31, 2021Revision of the protocol as necessary whenever important information necessary to conduct the clinical trial properly becomes available (information on the quality, efficacy, and safety of drug(s) used in the clinical trial) From August 1, 2021

[ ]  Not applicable

[ ]  Compliant

Version number (or revision date) Revised content:

[ ]  Other ( )

b Agreement with the investigator on the content of the revision and that the clinical trial be conducted in compliance with the revised protocol (for medical institutions subject to inspection) **[Article 7, Paragraph 5 (mutatis mutandis application of Article 7, Paragraph 4)]**

[ ]  Not applicable

[ ]  Compliant

[ ]  Information necessary for examining the revised contents is provided to the investigator in advance

[ ]  Agreement is given with name and seal or signature, and date in writing
 From May 29, 1997 until July 31, 2021 (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Agreement is given with signature and date in writing From August 1, 2021 (PSEHB/PED Notification No. 0730-3 dated July 30, 2021)

[ ]  Other ( )

7) Preparation and revision of the sample case report form
 **[Article 7, Paragraphs 4 and 5]** From May 29, 1997 (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Not applicable

[ ]  If the information to be entered in the case report form can be provided sufficiently in the protocol, the protocol may be considered to include the information related to the sample case report form.
 **[Article 4, Paragraph 2]** **From April 1, 2012** (PFSB/ELD Notification No. 1024-1 dated on October 24, 2011)

[ ]  Compliant

[ ]  The sample case report form is prepared and revised in consultation with the prospective investigator

[ ]  The sample case report form is given with name and seal or signature, and date in writing
 From May 29, 1997 until July 31, 2021 (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  The sample case report form is given with signature and date in writing From August 1, 2021 (PSEHB/PED Notification No. 0730-3 dated July 30, 2021)

[ ]  Other ( )

## 3. Selection of Medical Institutions and Investigators **From April 1997**

### (1) Medical institution

1) Preparation of written operating procedures for the selection of medical institutions **[Article 4, Paragraph 1]**

[ ]  Compliant

Name of document:

Effective date of the written operating procedures applicable to the clinical trial period:

MMM DD, YYYY

[ ]  Other ( )

2) Selection of medical institutions (for medical institutions subject to inspection)
 **[Articles 6 and 35]**

[ ]  Compliant

Date of selection: MMM DD, YYYY (medical institution name: )

[ ]  Medical institutions are selected in accordance with the written operating procedures

The following requirements shall be met:

[ ]  Being well equipped with facilities and having sufficient personnel to conduct the necessary clinical observations and laboratory tests

[ ]  Being capable of taking necessary measures for the subject in the event of an emergency.

[ ]  Having an IRB (excluding cases applicable to the exceptional provisions) Until March 2008

[ ]  Having investigators etc., pharmacists, nurses and other adequate personnel for the proper and smooth conduct of the clinical trial

[ ]  Having an investigational product storage manager who can understand the nature of the investigational product and the protocol and appropriately store, control, and dispense the investigational product
 From May 29, 1997 until August 31, 2020 (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Having an investigational product storage manager who can understand the nature of the drug(s) used in the clinical trial and the protocol and appropriately store, control, and dispense the drug(s) used in the clinical trial From September 1, 2020 (PSEHB/PED Notification No. 0831-15 August 31, 2020)

[ ]  Capable of properly retaining records, etc.
 From May 29, 1997 (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Other ( )

### (2) Investigator

1) Preparation of written operating procedures for the selection of investigators
 **[Article 4, Paragraph 1]**

[ ]  Compliant

Name of document:

Effective date of the written operating procedures applicable to the clinical trial period:

MMM DD, YYYY

[ ]  Other ( )

2) Selection of investigators (for medical institutions subject to inspection) **[Articles 6 and 42]**

[ ]  Compliant

Date of selection: MMM DD, YYYY (Physician’s name: )

[ ]  Investigators are selected in accordance with the written operating procedures

The following requirements shall be met:

[ ]  Being fully qualified by education, training, and adequate clinical experience to assume responsibility for the proper conduct of the clinical trial

[ ]  Being well versed in the proper use of the protocol, Investigator’s Brochure, and investigational product(s) **Until August 31, 2020**

[ ]  Being well versed in the proper use of the protocol, Investigator’s Brochure, and drug(s) used in the clinical trial **From September 1, 2020**

[ ]  Having sufficient time to conduct the clinical trial

[ ]  Other ( )

## 4. Confirmation of Records that Assure Precision Control at Laboratories[Article 4, Paragraph 1] **From April 1, 2012** (PFSB/ELD Notification No. 1024-1 dated on October 24, 2011)

[ ]  Compliant

[ ]  Precision control at the laboratories is confirmed with relevant records to ensure that tests are appropriately performed and the clinical trial-related data are reliable at the laboratories for samples, etc. related to the clinical trial (including the laboratory, etc. at the medical institution)

-[ ]  The range of tests to be confirmed for precision control and how it is to be confirmed shall be decided between the sponsor and the medical institution in consideration of the positioning of each test data in the clinical trial From December 28, 2012 (PSEHB/PED Notification No. 1228-7 dated December 28, 2012)

[ ]  Other ( )

## 5. Preparation of Investigator’s Brochure **From April 1997**

1) Preparation of written operating procedures for the duties including the preparation of an Investigator’s Brochure **[Article 4, Paragraph 1]**

 From May 29, 1997 (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Compliant

Name of document:

Effective date of the written operating procedures applicable to the clinical trial period:

MMM DD, YYYY

[ ]  Other ( )

2) Preparation based on the data obtained in the studies specified in Article 5 of GCP Ministerial Ordinance and the information on the quality, efficacy, and safety of the test drug **[Article 8, Paragraph 1]**

\* If an Investigator’s Brochure cannot be prepared for reasons such as the test drug marketed by another company, it is acceptable to use a document describing the latest scientific knowledge of the test drug (package insert, interview form, academic papers, etc. It is desirable to attach both the package insert and the interview form.) only if its active ingredient has been approved in Japan and the safety of the test drug can be warranted. **[Article 8, Paragraph 1]**

 From September 1, 2020 (PSEHB/PED Notification No. 0831-15 dated August 31, 2020)

[ ]  Compliant

[ ]  Investigator’s Brochure is prepared in accordance with the written operating procedures

The Investigator’s Brochure includes the following information:

[ ]  Chemical name or identification code of the test drug

[ ]  Information on the test drug, such as its quality, toxicity, and pharmaceutical effects

[ ]  Results of clinical studies of the test drug, if any has been conducted

[ ]  Other ( )

3) Revision of the Investigator’s Brochure as necessary whenever important information necessary to conduct the clinical trial properly becomes available
 **[Article 8, Paragraph 2]
 [From April 1997 until March 2008: Article 20, Paragraph 3; From April 2008: Article 20, Paragraph 4]**

[ ]  Not applicable

[ ]  Compliant

[ ]  Investigator’s Brochure is revised in accordance with the written operating procedures

[ ]  Investigator’s Brochure is reviewed at least once a year **From May 29, 1997** (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Relevant information is reported to the investigator(s), the head(s) of medical institution(s), and the regulatory authorities prior to the revision of the Investigator’s Brochure

**From May 29, 1997** (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

Version number (or revision date) Revised content:

[ ]  Other ( )

## 6. Request to Investigator for Preparation of Written Information (i.e. Informed Consent Document) (for medical institutions subject to inspection) [Article 9] From April 1997

[ ]  Compliant

[ ]  Necessary data/information is provided (PAB Notification No. 430 dated March 27, 1997)

[ ]  Other ( )

## 7. Written Operating Procedures for Making Changes or Corrections to Case Report Forms (for medical institutions subject to inspection) [Article 4, Paragraph 1]

From May 29, 1997 (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

1) Provision of a manual for making changes or corrections to case report forms for the investigator

[ ]  Compliant

[ ]  Other ( )

2) Preparation of written operating procedures for making changes or corrections to case report forms by the person designated by the sponsor

[ ]  Not applicable

[ ]  Compliant

Name of document:

[ ]  Other ( )

## 8. Request to Medical Institution for Conduct of Clinical Trial (for medical institutions subject to inspection)

\* Submission of the latest versions of the following documents to the head(s) of the medical institution(s) prior to the request **[Article 10, Paragraph 1]** From April 1997

[ ]  Compliant

[ ]  Protocol
(The volume(s) related to the medical institution among those which have been prepared
**[Article 7, Paragraph 1; Article 10, Paragraph 1]** **From October 2008 until March 31, 2012** (PFSB/ELD Notification No. 1001001 dated October 1, 2008)
**[Article 7, Paragraph 1]** **From April 1, 2012** (PFSB/ELD Notification No. 1024-1 dated on October 24, 2011)

[ ]  Investigator’s Brochure Until August 31, 2020

[ ]  Investigator’s Brochure and documents describing the scientific knowledge of the drug(s) used in the clinical trial (excluding the test drug)\* From September 1, 2020

\* Package inserts, interview forms, academic papers, etc. of approved drugs From September 1, 2020 (PSEHB/PED Notification No. 0831-15 dated August 31, 2020)

[ ]  Sample of the case report form
(If the information to be entered in the case report form can be provided sufficiently in the protocol, the protocol may be considered to include the information related to the sample case report form. **From April 1, 2012** (PFSB/ELD Notification No. 1024-1 dated October 24, 2011)

[ ]  Written information (written information and informed consent form are an integrated document or a set of documents From May 29, 1997 (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997))

[ ]  List of prospective investigator and subinvestigators
(Curriculum vitae of each investigator and subinvestigator
 **From May 29, 1997 until September 2008** (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997))
(Curriculum vitae of the investigator. Curriculum vitae of the subinvestigator, if requested.
 **From October 2008** (PFSB/ELD Notification No. 1001001 dated October 1, 2008))

[ ]  Documents on the burden of expenses for the clinical trial
(including a document on payment to subjects (if any).) Until March 31, 2012

[ ]  Documents on the burden of expenses for the clinical trial (documents on payment to subjects (if any)) **From April 1, 2012** (PFSB/ELD Notification No. 1024-1 dated October 24, 2011)

[ ]  Document explaining the compensation available to subjects in the event of trial-related injury

\* The documents specified in each item are not necessarily prepared separately but may be put together as long as the contents are confirmed to be included.
 From December 28, 2012 (PSEHB/PED Notification No. 1228-7 dated December 28, 2012)

[ ]  Other ( )

## 9. Clinical Trial Contract

### (1) Contract with the medical institution(s) (for medical institutions subject to inspection) **[Article 13, Paragraph 1]** **From April 1997**

Contents of the contract

[ ]  Compliant

The contract includes the following information: (It is not necessary to include all information in one contract. From December 28, 2012 (PSEHB/PED Notification No. 1228-7 dated December 28, 2012))

[ ]  Date of concluding the contract

[ ]  Name and address of the sponsor

[ ]  When part of the duties is outsourced to a contractor, the name and address of the contractor and the scope of the duties outsourced Until December 27, 2012

-[ ]  If part of the duties is outsourced to a contract research organization, a contract shall be concluded among the three parties, i.e., the sponsor, the contract research organization, and the medical institution **From May 29, 1997** (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

-[ ]  It is acceptable to conclude appropriate written contracts between the sponsor and the medical institution and between the sponsor and the contract research organization as long as the duties at the sponsor and the medical institution can be performed smoothly.
 **From April 1, 2012** (PFSB/ELD Notification No. 1024-1 dated October 24, 2011)

[ ]  When all or any of the duties are outsourced to a contractor, the name and address of the contractor and the scope of the duties outsourced **From December 28, 2012**

-[ ]  If all or any of the duties are outsourced to a contract research organization, a contract shall be concluded among the three parties, i.e., the sponsor, the contract research organization, and the medical institution **From December 28, 2012** (PSEHB/PED Notification No. 1228-7 dated December 28, 2012)

-[ ]  It is acceptable to conclude appropriate written contracts between the person who intends to sponsor the clinical trial and the medical institution and between the person who intends to sponsor the clinical trial and the contract research organization as long as the duties related to the preparation and management of the clinical trial by the person who intends to sponsor the clinical trial and duties related to the conduct of the clinical trial at the medical institution can be performed smoothly. **From September 1, 2020** (PSEHB/PED Notification No. 0831-15 dated August 31, 2020)

-[ ]  As long as the duties at the sponsor and the medical institution can be performed smoothly, upon agreement among the three parties, i.e., the person who intends to sponsor the clinical trial, the contract research organization, and the medical institution, it is acceptable to conclude a contract between the two parties, i.e., the contract research organization and the medical institution. From December 28, 2012 (PSEHB/PED Notification No. 1228-7 dated December 28, 2012)

[ ]  Name(s) and address(es) of the medical institution(s)

[ ]  Name(s) and title(s) of the person(s) in charge of the contract from each party

-[ ]  It is acceptable that either of the head of the medical institution or a person appointed by the head of the medical institution serves as the contractor of the medical institution.
 From December 28, 2012 (PSEHB/PED Notification No. 1228-7 dated December 28, 2012)

[ ]  Name and title of the investigators, etc. **Until December 27, 2012**

[ ]  Name of the investigator **From December 28, 2012**

[ ]  Duration of the clinical trial

[ ]  Expected number of subjects **Until December 27, 2012**

[ ]  Description of the control/accountability of investigational products
 **From July 1997 until August 31, 2020** (PAB Notification No. 430 dated March 27, 1997)

[ ]  Description of the control/accountability of drug(s) used in the clinical trial
 **From September 1, 2020**

[ ]  Description of record (and data) keeping
 **From July 1997** (PAB Notification No. 430 dated March 27, 1997)

[ ]  Description of notifications given by the sponsor and the personnel of the medical institution
 **From July 1997** (PAB Notification No. 430 dated March 27, 1997)

[ ]  Description of maintenance of the confidentiality of the subjects From April 1998 (PAB Notification No. 430 dated March 27, 1997) (Prohibition of leakage of secrets related to subjects **(Article 80-2, Paragraph 10 of the Act[[4]](#footnote-4))**)

[ ]  Description of the expense for the clinical trial
 **From July 1997** (PAB Notification No. 430 dated March 27, 1997)

-[ ]  It is acceptable to describe the amount of expenses that can be calculated.
 From December 28, 2012 (PSEHB/PED Notification No. 1228-7 dated December 28, 2012)

[ ]  Statement that the medical institution conducts the clinical trial in compliance with GCP and the protocol

[ ]  Statement that the medical institution will provide the sponsor with direct access to records (source documents, contract, informed consent form and written information, other documents prepared by the medical institution staff members, protocol, documents obtained from the IRB, records of investigational product control/accountability and other clinical trial-related duties) upon request by the sponsor
 **From April 1998** (PAB Notification No. 430 dated March 27, 1997)

[ ]  Statement that the sponsor may cancel the contract if it is found that the medical institution has violated GCP, the protocol, or the relevant contract, resulting in interference with the proper conduct of the clinical trial (excluding cases stipulated in GCP Ministerial Ordinance Article 46)

[ ]  Description of compensation to the subject in the event of trial-related injuries

[ ]  Other matters necessary to ensure that the clinical trial is conducted properly and smoothly (clinical trial title, contents of the clinical trial, matters related to the procedures for recording and reporting of data, matters related to the confidentiality of information belonging to the sponsor
 **From May 29, 1997** (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997))

[ ]  The investigator shall also affix the name and seal or sign the contract or a copy of the contract to confirm the contents of the contract. **From May 29, 1997 until March 31, 2012** (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  The investigator shall confirm the contents of the contract, but does not necessarily have to sign it. **From April 1, 2012** (PFSB/ELD Notification No. 1024-1 dated October 24, 2011)

\* It is acceptable for persons other than the medical institution staff, such as the secretariat of the network of the core clinical trial hospital, to perform the duties supporting the contract between the medical institution and the person who intends to sponsor the clinical trial. From December 28, 2012 (PSEHB/PED Notification No. 1228-7 dated December 28, 2012)

[ ]  Other ( )

### (2) Outsourcing of part of the duties related to sponsoring and managing the clinical trial

**[Article 12]** **From April 1997 until December 27, 2012**

Outsourcing of all or any of the duties related to sponsoring and managing the clinical trial

**[Article 12]** **From December 28, 2012**

\* The duties related to notification of the clinical trial plan and reporting of adverse drug reactions to regulatory authorities cannot be outsourced to a contract research organization. From December 28, 2012 (PSEHB/PED Notification No. 1228-7 dated December 28, 2012)

1) Contract with the contractor **[Article 12, Paragraph 1]** From April 1997

[ ]  Not applicable

[ ]  Compliant

The following information shall be included:

[ ]  Scope of the duties outsourced

[ ]  Description of the operating procedures for the duties outsourced

[ ]  Statement that the person who intends to sponsor a clinical trial is entitled to ascertain whether the duties outsourced are conducted properly and smoothly in compliance with the operating procedures specified in the preceding item

[ ]  Description of the instructions to the contractor

[ ]  Statement that if the instructions specified in the preceding item are given, the person who intends to sponsor a clinical trial is entitled to ascertain whether appropriate measures are taken in response to the instructions

[ ]  Description of reports to be submitted by the contractor to the person who intends to sponsor a clinical trial

[ ]  Description of measures specified in GCP Ministerial Ordinance Article 14 relating to the duties outsourced (Procedures shall be established to take measures such as purchasing insurance. PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Other necessary matters related to the duties outsourced

[ ]  Documents or records (including data) to be retained by the contract research organization continuously after the completion of the operations and the period of retention
 **From April 1, 2012** (PFSB/ELD Notification No. 1024-1 dated October 24, 2011)

[ ]  Provision of direct access to all the documents and records (including data) to be retained by the contract research organization for regulatory inspection(s)
 **From April 1, 2012** (PFSB/ELD Notification No. 1024-1 dated October 24, 2011)

Name of the contractor:

Date of concluding the contract: MMM DD, YYYY

Duration of the outsourcing contract: MMM DD, YYYY to MMM DD, YYYY

Duties outsourced:

[ ]  Other ( )

2) Procedure for compensation for trial-related injuries attributable to the duties outsourced **From May 29, 1997** (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Not applicable

[ ]  Compliant

[ ]  The contract research organization, together with the sponsor, has established a procedure for compensation for trial-related injuries attributable to the duties outsourced. (In the case where the contractor performs the duties at the medical institution
 **From April 1, 2012** (PFSB/ELD Notification No. 1024-1 dated October 24, 2011))

[ ]  Compensation for trial-related injuries is processed in accordance with the written operating procedures (**From July 22, 2004** PFSB/ELD Notification No. 0722014 dated July 22, 2004)

[ ]  Other ( )

## 10. Compensation to Subjects [Article 14] From April 1997

1) Necessary measures such as purchasing insurance in preparation for compensation for trial-related injuries (including those attributable to the duties performed by the contractor)

[ ]  Compliant

[ ]  Procedures for compensation shall be established. From May 29, 1997 (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

Name of document:

Effective date of the written operating procedures applicable to the clinical trial period:

MMM DD, YYYY

[ ]  Insurance and other necessary measures

[ ]  Other ( )

2) Compensation for trial-related injuries

[ ]  Not applicable

[ ]  Compliant

[ ]  Other ( )

## 11. Clinical Trial In-Country Representative [Article 15] **From April 1997**

\* When the sponsor resides outside Japan (or when address of its main office is outside Japan in the case of a corporation)

[ ]  Not applicable

[ ]  Compliant

[ ]  The person who intends to sponsor the clinical trial and resides outside Japan has appointed a person eligible for sponsoring the clinical trial from among persons residing in Japan (including the head of a Japanese business office of a foreign company) to have him or her conduct the procedures for sponsoring the clinical trial.

[ ]  The clinical trial in-country representative provides the person who intends to sponsor the clinical trial and resides outside Japan with data or information necessary for the person who intends to sponsor the clinical trial to understand the relevant standards and the laws, regulations, administrative notifications, etc. related to the clinical trial when conducting the clinical trial in Japan. **From August 1, 2021** (PSEHB/PED Notification No. 0730-3 dated July 30, 2021)

[ ]  Other ( )

# [III] Standards for Clinical Trial Management

## 1. Control/Accountability of Investigational Products **From April 1997 until August 31, 2020**Control/Accountability of Drug(s) Used in the Clinical Trial **From September 1, 2020**

### (1) In-house control/accountability

1) Preparation of written operating procedures for the control/accountability of investigational products **[Article 4, Paragraph 1]** **From April 1997 until August 31, 2020**Preparation of written operating procedures for the control/accountability of drug(s) used in the clinical trial **[Article 4, Paragraph 1]** **From September 1, 2020**

\* For any drug used in the clinical trial, other than investigational products, which is not supplied by the sponsor and is stored in stock at the medical institution, the sponsor shall confirm the procedures for handling, storage, control, prescription, etc. specified at the medical institution. From September 1, 2020 (PSEHB/PED Notification No. 0831-15 dated August 31, 2020)

[ ]  Compliant

Name of document:

Effective date of the written operating procedures applicable to the clinical trial period:

MMM DD, YYYY

Storage facility for investigational products (or drug(s) used in the clinical trial):

Person responsible for the storage of investigational products (or drug(s) used in the clinical trial):
Title

Storage facility access control:

[ ]  Other ( )

2) Indication of the following information in the Japanese language on the container or package of the investigational products **[Article 16, Paragraph 1]**

[ ]  Not applicable

[ ]  Compliant

[ ]  Statement of “For clinical trial use only”

[ ]  Name and address of the sponsor
(if the sponsor resides outside Japan, name of the sponsor and name of the country where the sponsor is located, and name and address of the clinical trial in-country representative)

[ ]  Chemical name or identification code

[ ]  Manufacturing number or manufacturing code

[ ]  Storage method, expiration date (if necessary)

[ ]  Other ( )

3) In case of a global clinical trial for which the following information is indicated in the English language on the container or package of the investigational products
 **[Article 16, Paragraph 1]** **From April 2008 until December 27, 2012** (PFSB/ELD Notification No. 0326001 dated March 26, 2008)
In case of a global clinical trial or other applicable clinical trial for which the following information is indicated in the English language on the container or package of the investigational products **[Article 16, Paragraph 1]** **From December 28, 2012** (PSEHB/PED Notification No. 1228-7 dated December 28, 2012)

[ ]  Not applicable

[ ]  Compliant

a Information to be described

[ ]  Statement of “For clinical trial use only”

[ ]  Name and address of the sponsor

[ ]  Chemical name or identification code

[ ]  Manufacturing number or manufacturing code

[ ]  Storage method, expiration date (if necessary)

b Conditions for the description to be in the English language

[ ]  Protocol stipulates that a common investigational product(s) whose name is written in the English language is used Until December 27, 2012

[ ]  Protocol stipulates that a common investigational product(s) whose name is written in the English language or an unapproved drug(s) which is approved in the United States, Europe, etc. is used From December 28, 2012 (PSEHB/PED Notification No. 1228-7 dated December 28, 2012)

[ ]  Approval of the IRB

[ ]  For necessary measures to properly conduct the duties of control/accountability of investigational products,

-[ ]  documents explaining the reconstitution procedures and other handling procedures for the investigational products in the Japanese language shall be prepared and provided for the investigational product storage manager.

-[ ]  necessary measures shall be taken so that the medical institutions can properly conduct the duties of control/accountability of the investigational product(s) in the case of a global clinical trial or other applicable clinical trial using an unapproved drug(s) which is approved in the United States, Europe, etc., as an investigational product(s) and its brand name and other information is written in the English or other language
 From December 28, 2012 (PSEHB/PED Notification No. 1228-7 dated December 28, 2012)

[ ]  Other ( )

4) Information that must not be indicated in the documents attached to the investigational products, on the investigational products, or on their containers or packages (including the inner packages) **[Article 16, Paragraph 2]**

\* However, this does not apply to a clinical trial using investigational products which are not indistinguishable between the test drug and the comparator to the subject, investigators, etc., or clinical research coordinators. From August 1, 2021

[ ]  Compliant

[ ]  Proposed brand name

[ ]  Proposed indication(s)

[ ]  Proposed dosage and administration

\* When an investigational product whose proposed brand name, etc. is indicated on the product or its container or package (including an inner package) is used as an investigational product, appropriate measures shall be taken to prevent a mix-up between the investigational product and a marketed drug.
 From August 1, 2021 (PSEHB/PED Notification No. 0730-3 dated July 30, 2021)

[ ]  Other ( )

5) Measures to allow rapid identification in case of a medical emergency in a blinded study **[Article 16, Paragraph 3]** **From April 1997**
 (The implementation status of a blinded clinical trial is to be checked in III.8.2).)

[ ]  Not applicable

[ ]  Compliant

Identification method:

[ ]  When the blinding has been broken, it is detectable. **From May 29, 1997** (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Other ( )

6) Packaging to prevent contamination/deterioration during transport and storage
 **[Article 16, Paragraph 4]** **From April 1997**

[ ]  Compliant

Packaging form:

[ ]  Other ( )

7) Preparation of the following records concerning the investigational products
 **[Article 16, Paragraph 5]** **Until August 31, 2020**Preparation of the following records concerning the investigational products or drug(s) used in the clinical trial **[Article 16, Paragraph 5]** **From September 1, 2020**

[ ]  Compliant

[ ]  Records concerning the manufacture of the investigational products, such as the manufacturing date, manufacturing method, and manufactured quantity, and the results of the tests on the drug’s quality, such as its stability (including the records specified in the Good Manufacturing Practices (GMP) for Study Products)

-[ ]  (When necessary) A sufficient amount of lot samples to re-confirm that the specifications are met shall be secured to prepare and retain records of analysis of the lot samples over time.
As long as the stability is ensured, the lot samples shall be stored until the clinical trial data analysis is completed **From May 29, 1997** (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Records of the supply or retrieval of the investigational products, including the quantity and date, for each medical institution (for medical institutions subject to inspection)
 **Until August 31, 2020**

[ ]  Records of the supply or retrieval of the drug(s) used in the clinical trial, including the quantity and date, for each medical institution (for medical institutions subject to inspection)
 **From September 1, 2020**

\* Prohibition of the supply of investigational products before the clinical trial contract is concluded **[Article 11]**

Date of concluding the contract: MMM DD, YYYY Date of supply: MMM DD, YYYY

[ ]  Record of disposition

[ ]  Other ( )

8) Supply of the investigational products that have been manufactured at a manufacturing site which meets the requirements specified in the Good Manufacturing Practices (GMP) for Study Products to medical institutions **[Article 17]**

[ ]  Compliant

[ ]  (If applicable) It shall be ensured that the investigational products are coded and labeled in such a way that the blinding is maintained.
 **From May 29, 1997** (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Other ( )

9) Supply of the investigational products directly to medical institutions without involvement of a third party **[Article 17, Paragraph 2]** **Until March 2008**

[ ]  Not applicable

[ ]  Compliant

Method of supply:

Reason for the involvement of a third party:

[ ]  Other ( )

10) The sponsor shall establish procedures necessary to ensure the quality control, transport, and supply of the investigational products.
 **[Article 17]** From April 2008 (PFSB/ELD Notification No. 0326001 dated March 26, 2008)

[ ]  Not applicable

[ ]  Compliant

[ ]  Other ( )

11) When investigational products are supplied to medical institutions by using a transporting company, necessary measures, such as concluding a contract with the transporting company, shall be taken in advance to ensure the quality control, transport, and supply of the investigational products.
 **[Article 17]** **From April 2008** (PFSB/ELD Notification No. 0326001 dated March 26, 2008)

[ ]  Not applicable

[ ]  Compliant

Method of supply:

[ ]  Necessary measures are taken.

[ ]  Other ( )

### (2) Management of medical institutions (for medical institutions subject to inspection)

1)-1 Preparation of written operating procedures for the control/accountability of investigational products at the medical institution and providing the procedures for the head of the medical institution (or the investigational product storage manager with prior consent of the head of medical institution **From September 21, 2006 until December 27, 2012** (PFSB/ELD Notification No. 0921001 dated September 21, 2006)) **[Article 16, Paragraph 6]**

**From July 1997 until December 27, 2012** (PAB Notification No. 430 dated March 27, 1997)

Preparation of written operating procedures for the control/accountability of investigational products at the medical institution and providing the procedures for the medical institution **[Article 16, Paragraph 6]** **From December 28, 2012 until August 31, 2020**

[ ]  Compliant

Instructions necessary for the following matters to be performed properly and surely are included

[ ]  Receipt, handling, storage, control/accountability, and prescription of investigational products

[ ]  Retrieval of unused investigational products from subjects

[ ]  Return to the sponsor and other disposal

[ ]  Other ( )

1)-2 Preparation of written operating procedures for the control/accountability of drug(s) used in the clinical trial at the medical institution and providing the procedures for the medical institution **[Article 16, Paragraph 6]** **From September 1, 2020**

[ ]  Compliant

Instructions necessary for the following matters to be performed properly and surely are included

 **From September 1, 2020** (PSEHB/PED Notification No. 0831-15 dated August 31, 2020)

[ ]  Receipt, handling, storage, control/accountability, and prescription of drug(s) used in the clinical trial

[ ]  Retrieval of unused drug(s) used in the clinical trial from subjects

[ ]  Return to the sponsor and other disposal

[ ]  Other ( )

2) Preparation of documents explaining the reconstitution procedures and other handling procedures for the investigational products and providing the documents for the investigator/subinvestigators, clinical research coordinators, investigational product storage managers, etc., as necessary **[Article 16, Paragraph 7]** **From April 1997**

[ ]  Not applicable

[ ]  Compliant

[ ]  Other ( )

## 2. Multicenter Clinical Trial **From April 1997 until December 27, 2012**Preparing Document of Assignment **From December 28, 2012**

\* Establishment of a coordinating investigator or a coordinating committee
 **[From April 1997 until December 27, 2012: Article 18, Paragraph 1]
 [From December 28, 2012: Article 18]**

[ ]  Not applicable

[ ]  Compliant

[ ]  Preparation of documents describing the scope of the duties, the operating procedures, and other necessary information
 **[From April 1997 until December 27, 2012: Article 18, Paragraph 2]
 [From December 28, 2012: Article 18]**

[ ]  Other ( )

## 3. Establishment of Efficacy and Safety Assessment Committee [Article 19] From April 1997

\* Deliberation on the appropriateness of continuing the clinical trial or the revision of the protocol

[ ]  Not applicable

[ ]  Compliant

[ ]  The committee is independent from the sponsor, the investigator, and the coordinating investigator. Until April 3, 2013
 (PAB Notification No. 430 dated March 27, 1997, PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

\* For clinical studies intended to confirm efficacy, a committee established as a committee independent from the sponsor, the investigator, and the coordinating investigator is specifically called an “independent data monitoring committee.” From April 4, 2013 (PFSB/ELD Notification No. 0404-4 dated April 4, 2013)

[ ]  Written operating procedures for deliberation is prepared **[Article 19, Paragraph 2]**

Name of document:

Effective date of the written operating procedures applicable to the clinical trial period:

MMM DD, YYYY

[ ]  Deliberation is conducted in compliance with the procedures **[Article 19, Paragraph 2]**

[ ]  Records of deliberation are prepared and retained **[Article 19, Paragraph 3]**

-[ ]  Records are prepared with the approval of the Efficacy and Safety Evaluation Committee
 From May 29, 1997 (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Other ( )

## 4. Information on Adverse Drug Reactions

1) Preparation of written operating procedures for the collection of information on adverse drug reactions **[Article 4, Paragraph 1]** **From April 1997**

[ ]  Compliant

Name of document:

Effective date of the written operating procedures applicable to the clinical trial period:

MMM DD, YYYY

[ ]  Other ( )

2) Collection and evaluation of information on adverse reactions to the test drug
 **[Article 20, Paragraph 1]** **From April 1997 until August 31, 2020**Collection and evaluation of information on adverse reactions to the drug(s) used in the clinical trial **[Article 20, Paragraph 1]** **From September 1, 2020**

[ ]  Compliant

Method: In Japan
Outside Japan

[ ]  Other ( )

3) Provision of information on adverse reactions to the test drug to the head of the medical institution (for medical institutions subject to inspection)
 **[Article 20, Paragraph 1]** **From April 1997 until August 31, 2020**Provision of information on adverse reactions to the drug(s) used in the clinical trial to the head of the medical institution (for medical institutions subject to inspection)
 **[Article 20, Paragraph 1]** **From September 1, 2020**

[ ]  Not applicable

[ ]  Compliant

[ ]  Prompt notification to all the investigators and heads of medical institutions involved in the clinical trial are made **From May 29, 1997** (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

Date of provision Notified information

[ ]  Other ( )

4)-1 When receiving information on any unknown serious adverse drug reaction or known serious adverse drug reaction (death/life-threatening) concerning the test drug, the sponsor shall notify the investigators and the heads of the medical institutions of the information. (for medical institutions subject to inspection) **[Article 20, Paragraph 2]** **Until March 2009**

[ ]  Not applicable

[ ]  Compliant

[ ]  Information is notified immediately.

Date of receipt of information Date of notification Notified information

[ ]  Other ( )

4)-2 When becoming aware of any event concerning the test drug that is specified in Article 80-2, Paragraph 6 of the Act, the sponsor shall notify the investigators and the heads of the medical institutions of such events in a list for the test drug semi-annually after the date of submission of the first clinical trial notification within 2 months after the end of each period. (for medical institutions subject to inspection)
 **[Article 20, Paragraph 2]** **From April 2009 until June 30, 2014**
(The provisions then in force shall remain applicable until June 30, 2014 to clinical trials of which protocol was prepared before December 28, 2012. However, the revised provisions of Article 20, Paragraph 2 of the GCP Ministerial Ordinance may be applied at the discretion of the sponsor.)

[ ]  Not applicable

[ ]  Compliant

[ ]  Semi-annual notification is submitted (For the initial date of reckoning, see the PFSB/ELD Notification No. 1001005 dated October 1, 2008.)

Date of notification

<Information to be reported>

• Unknown, deaths/life-threatening events (Article 273, Paragraph 1, Item 1 of the Enforcement Regulations[[5]](#footnote-5))

• Unknown, other serious events (Article 273, Paragraph 1, Item 2 (a) of the Enforcement Regulations)

• Known, deaths/life-threatening events (Article 273, Paragraph 1, Item 2-b of the Enforcement Regulations)

• Known, other serious events (events listed in Article 273, Paragraph 1, Item 2 (1) to (5) of the Enforcement Regulations (excluding unknown events))

[ ]  Other ( )

4)-3 When becoming aware of any event concerning the test drug that is specified in Article 80-2, Paragraph 6 of the Act, the sponsor shall notify the investigators and the heads of the medical institutions of such events in a development safety update report and a Japanese serious adverse reaction list for each of the test drugs annually after the date of submission of the first clinical trial notification within 3 months after the end of each period. (for medical institutions subject to inspection)
 **[Article 20, Paragraph 2]** **From July 1, 2014 until August 31, 2020**
\* The same shall apply to cases in which no adverse drug reactions are reported during the period.
 From January 1, 2020 (PSEHB/PED Notification No. 0705-3 dated July 5, 2019)(The provisions of Article 20, Paragraph 2 of the GCP Ministerial Ordinance before the revision shall apply to clinical trials of which the protocol was prepared on or after December 28, 2012 and which was conducted before June 30, 2014. However, the revised provisions of Article 20, Paragraph 2 of the GCP Ministerial Ordinance may be applied at the discretion of the sponsor.)

[ ]  Not applicable

[ ]  Compliant

[ ]  Annual notification is submitted (For the initial date of reckoning, see the PFSB/ELD Notification No. 1228-11 dated December 28, 2012.)

Date of notification

<Information to be reported>

• Unknown, deaths/life-threatening events (Article 273, Paragraph 1, Item 1 of the Enforcement Regulations)

• Unknown, other serious events (Article 273, Paragraph 1, Item 2 (a) of the Enforcement Regulations)

• Known, deaths/life-threatening events (Article 273, Paragraph 1, Item 2-b of the Enforcement Regulations)

• Known, other serious events (events listed in Article 273, Paragraph 1, Item 2 (1) to (5) of the Enforcement Regulations (excluding unknown events))

[ ]  Other ( )

4)-4 When becoming aware of any event concerning the drug used in the clinical trial that is specified in Article 80-2, Paragraph 6 of the Act, the sponsor shall notify the investigators and the heads of the medical institutions of such events in a development safety update report and a Japanese serious adverse reaction list for each of the drugs used in the clinical trial annually after the date of submission of the first clinical trial notification within 3 months after the end of each period. (for medical institutions subject to inspection) **[Article 20, Paragraph 2]** **From September 1, 2020 until July 31, 2021**

\* The same shall apply to cases in which no adverse drug reactions are reported during the period.
 From January 1, 2020 (PSEHB/PED Notification No. 0705-3 dated July 5, 2019)

[ ]  Not applicable

[ ]  Compliant

[ ]  Annual notification is submitted (For the initial date of reckoning, see the PFSB/ELD Notification No. 1228-11 dated December 28, 2012.)

Date of notification

<Information to be reported>

• Unknown, deaths/life-threatening events (Article 273, Paragraph 1, Item 1 and Paragraph 2, Item 1 of the Enforcement Regulations)

• Unknown, other serious events (Article 273, Paragraph 1, Item 2 (a) and Paragraph 2, Item 2 (a) of the Enforcement Regulations)

• Known, deaths/life-threatening events (Article 273, Paragraph 1, Item 2 (b) and Paragraph 2, Item 2 (b) of the Enforcement Regulations)

• Known, other serious events (events listed in Article 273, Paragraph 1, Item 2 (a) (1) to (5) and Article 273, Paragraph 2, Item 2 (a) (1) to (5) of the Enforcement Regulations (excluding unknown events))

[ ]  Other ( )

4)-5 When becoming aware of any event concerning the drug used in the clinical trial that is specified in Article 80-2, Paragraph 6 of the Act, the sponsor shall notify the investigators and the heads of the medical institutions of such events in a development safety update report and a Japanese serious adverse reaction list for each of the test drugs annually after the date of submission of the first clinical trial notification within 3 months after the end of each period. (for medical institutions subject to inspection) **[Article 20, Paragraph 2]** **From August 1, 2021**

\* The same shall apply to cases in which no adverse drug reactions are reported during the period.
 From January 1, 2020 (PSEHB/PED Notification No. 0705-3 dated July 5, 2019)

[ ]  Not applicable

[ ]  Compliant

[ ]  Annual notification is submitted (For the initial date of reckoning, see the PFSB/ELD Notification No. 1228-11 dated December 28, 2012.)

Date of notification

<Information to be reported>

• Unknown, deaths/life-threatening events (Article 273, Paragraph 1, Item 1 and Paragraph 2, Item 1 of the Enforcement Regulations)

• Unknown, other serious events (Article 273, Paragraph 1, Item 2 (a) and Paragraph 2, Item 2 (a) of the Enforcement Regulations)

• Known, deaths/life-threatening events (Article 273, Paragraph 1, Item 2 (b) and Paragraph 2, Item 2 (b) of the Enforcement Regulations)

• Known, other serious events (events listed in Article 273, Paragraph 1, Item 2 (a) (1) to (5) and Article 273, Paragraph 2, Item 2 (a) (1) to (5) of the Enforcement Regulations (excluding unknown events))

[ ]  Other ( )

4)-6 When becoming aware of any event, which is unexpected based on the information in the Investigator’s Brochure for the test drug, among serious adverse drug reactions, the sponsor shall immediately notify the investigators and the heads of the medical institutions of the fact. (for medical institutions subject to inspection)
 **[Article 20, Paragraph 3]** **From April 2009 until August 31, 2020**

[ ]  Not applicable

[ ]  Compliant

[ ]  Information is notified immediately.

Date of receipt of information Date of notification Notified information

<Information to be reported>

• Unknown, deaths/life-threatening events (Article 273, Paragraph 1, Item 1 of the Enforcement Regulations)

• Unknown, other serious events (Article 273, Paragraph 1, Item 2 (a) of the Enforcement Regulations)

• Known, events requested to be reported by the regulatory authority (PFSB/ELD Notification No. 1024-1 dated October 24, 2011)

[ ]  Other ( )

4)-7 When becoming aware of any event, which is unexpected based on the information in the Investigator’s Brochure for the test drug or based on the scientific findings for the drug(s) used in the clinical trial (excluding the test drug), among serious adverse drug reactions, the sponsor shall immediately notify the investigators and the heads of the medical institutions of the fact. (for medical institutions subject to inspection)
 **[Article 20, Paragraph 3]** **From September 1, 2020**

[ ]  Not applicable

[ ]  Compliant

[ ]  Information is notified immediately.

Date of receipt of information Date of notification Notified information

<Information to be reported>

• Unknown, deaths/life-threatening events (Article 273, Paragraph 1, Item 1 and Paragraph 2, Item 1 of the Enforcement Regulations)

• Unknown, other serious events (Article 273, Paragraph 1, Item 2 (a) and Paragraph 2, Item 2 (a) of the Enforcement Regulations)

• Known, events requested to be reported by the regulatory authority (PFSB/ELD Notification No. 1024-1 dated October 24, 2011)

[ ]  Other ( )

5) Revision of the protocol and Investigator’s Brochure as necessary whenever important information necessary to conduct the clinical trial properly, including information on the quality, efficacy, and safety of the test drug, becomes available **[From April 1997 until March 2008: Article 20, Paragraph 3; From April 2008: Article 20, Paragraph 4]**

**From April 1997 until August 31, 2020**

Revision of the protocol and Investigator’s Brochure as necessary whenever important information necessary to conduct the clinical trial properly, including information on the quality, efficacy, and safety of the drug(s) used in the clinical trial, becomes available **[Article 20, Paragraph 4]** **From September 1, 2020**

[ ]  Not applicable

[ ]  Compliant

[ ]  Revision of the protocol is agreed by the investigator.

[ ]  Other ( )

**5. Monitoring From April 1998**

1) Preparation of written operating procedures for monitoring **[Article 21, Paragraph 1]**

[ ]  Compliant

Name of document:

Effective date of the written operating procedures applicable to the clinical trial period:

MMM DD, YYYY

[ ]  Requirements for monitors are described in the written operating procedures for monitoring (PAB Notification No. 430 dated March 27, 1997)

[ ]  Monitors with scientific and clinical knowledge necessary for monitoring activities are appointed **From May 29, 1997** (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Rationale for the selected monitoring strategy is documented (e.g., in the monitoring plan) **From January 1, 2020** (PSEHB/PED Notification No. 0705-3 dated July 5, 2019)

[ ]  Other ( )

 Preparation of the monitoring plan unique to the clinical trial
 **[Article 21, Paragraph 1]** From January 1, 2020 (PSEHB/PED Notification No. 0705-3 dated July 5, 2019)

Name:

Effective date of the plan applicable to the clinical trial period: MMM DD, YYYY

2) Implementation in accordance with the written operating procedures (for medical institutions/subjects subject to inspection) **[Article 21, Paragraph 1]**

[ ]  Compliant

[ ]  Other ( )

3) Monitoring shall be conducted by visiting the medical institutions, except when monitoring is adequately performed by other means. **[Article 21, Paragraph 2]**

[ ]  Compliant

[ ]  Monitoring is conducted before, during, and after the clinical trial
 **From May 29, 1997** (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Other ( )

4) When it is confirmed that the clinical trial is not being conducted in compliance with GCP or the protocol, the fact shall be immediately reported to the investigator of the medical institution. (for medical institutions/subjects subject to inspection) **[Article 22, Paragraph 1]**

[ ]  Not applicable

[ ]  Compliant

[ ]  It is reported to the investigator and, if necessary, to the head of the medical institution
 **From May 29, 1997** (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Appropriate measures to prevent the recurrence of deviations are taken
 **From May 29, 1997** (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

Date of report Reported information

[ ]  Other ( )

5) Submission of a monitoring report documenting the following information to the sponsor after each monitoring visit (for medical institutions/subjects subject to inspection)
 **[Article 22, Paragraph 2]**\* Central monitoring reporting can be made on a regular basis. From January 1, 2020 (PSEHB/PED Notification No. 0705-3 dated July 5, 2019)

[ ]  Compliant

The following information shall be included:

[ ]  Date and time of monitoring **Until July 31, 2021**

[ ]  Date of monitoring **From August 1, 2021**

[ ]  Medical institution monitored

[ ]  Name of the monitor

[ ]  Name of the investigators, etc. and clinical research coordinators interviewed

[ ]  Summary of the results

[ ]  Description of the facts of which the monitor notified the investigator such as GCP or protocol violations

[ ]  Actions to be taken concerning the matters above and the monitor’s comments on the actions

[ ]  Examination and follow-up of the monitoring report by a designated person
 **From May 29, 1997** (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Other ( )

## 6. Audit **From April 1998**

1) Preparation of written operating procedures for audit **[Article 23, Paragraph 1]**

[ ]  Compliant

Name of document:

Effective date of the written operating procedures applicable to the clinical trial period:

MMM DD, YYYY

[ ]  Requirements for auditors are described (PAB Notification No. 430 dated March 27, 1997)

[ ]  Target, method, and frequency of audit as well as the form and content of the audit report are described for the clinical trial system and the audit for individual clinical trials (PAB Notification No. 430 dated March 27, 1997, PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Other ( )

2) Preparation of an audit plan **[Article 23, Paragraph 1]**

[ ]  Compliant

Date of preparation: MMM DD, YYYY

[ ]  Other ( )

3) Auditors shall be independent of the development division/monitoring division. **[Article 23 Paragraph 2]**

[ ]  Compliant

Division responsible for audit:

[ ]  The person can conduct audit appropriately based on education, training, and experience
 **From May 29, 1997** (PAB/ELD Notification No. 445, PAB/SD Notification No. 68 dated May 29, 1997)

[ ]  Other ( )

4) Implementation of audits in accordance with the audit plan and the operation procedures **[Article 23, Paragraph 1]**

[ ]  Compliant

[ ]  Audit of the clinical trial system is performed (sponsor, medical institutions, and other facilities)

[ ]  Audit of individual clinical trials is performed (sponsor, medical institutions, and other facilities)

[ ]  Other ( )

5) Preparation of an audit report and submission of the report to the sponsor
 **[Article 23, Paragraph 3]**

\* Usually, the sponsor shall only “confirm the presence of the audit report.” If significant GCP non-compliance is observed, however, the sponsor may request access to the audit report.

[ ]  Compliant

[ ]  The audit report is present.

[ ]  Other ( )

6) Preparation of an audit certificate and submission of the certificate to the sponsor **[Article 23, Paragraph 3]**

[ ]  Compliant

[ ]  The audit certificate with the name and seal or the signature of the auditor shall be submitted to the sponsor.
 **From April 1, 2012 until August 31, 2020** (PFSB/ELD Notification No. 1024-1 dated October 24, 2011)

[ ]  The audit certificate specifying the date of certification and the certifier shall be submitted to the sponsor. **From September 1, 2020** (PSEHB/PED Notification No. 0831-15 dated August 31, 2020)

[ ]  Other ( )

## 7. Premature Termination of Clinical Trial (for medical institutions subject to inspection)

**From April 1997**

1) If a medical institution has violated GCP, the protocol, or the clinical trial contract, resulting in interference with the proper conduct of the clinical trial (excluding the cases specified in GCP Ministerial Ordinance Article 46), the clinical trial at the medical institution shall be prematurely terminated. **[Article 24, Paragraph 1]**

[ ]  Not applicable

[ ]  Compliant

[ ]  Other ( )

2) Notification to the head of the medical institution if the clinical trial is suspended or prematurely terminated **[Article 24, Paragraph 2]**

[ ]  Not applicable

[ ]  Compliant

[ ]  Suspension or premature termination of the clinical trial and the reason thereof are notified

Reason:

[ ]  Other ( )

## 8. Process for Preparation of Clinical Trial Report

1) Course until database lock

[ ]  Implementation of data management activities

[ ]  Process until database lock

Date of case review meeting (if applicable): MMM DD, YYYY

Date of database lock: MMM DD, YYYY

Release of database lock (if applicable): MMM DD, YYYY

Reason for the release of database lock:

Date of re-locking database (if applicable): MMM DD, YYYY

2) Implementation status of a blinded clinical trial

[ ]  Not applicable

[ ]  Compliant

[ ]  (If applicable) Indistinguishability of the test drug from the comparator has been confirmed.

[ ]  (If applicable) A randomization record has been prepared.

[ ]  Measures to distinguish the test drug from the comparator in an emergency have been taken. (See III.1.(1).5))

[ ]  (If applicable) Unblinding has been performed appropriately and documented.

Date of unblinding: MMM DD, YYYY

[ ]  Blinding was maintained.

[ ]  Other ( )

3) Analysis

[ ]  Process of the analysis

Date of finalization of the analysis plan: MMM DD, YYYY

Date of revision of the analysis plan (if applicable): MMM DD, YYYY

Date of approval of the analysis report (if applicable): MMM DD, YYYY

4) Preparation of written operating procedures for the preparation of a clinical trial report **[Article 4, Paragraph 1]** **From July 22, 2004** (PFSB/ELD Notification No. 0722014 dated July 22, 2004)

\* When preparing an interim report to be used for a marketing approval application for a drug, the sponsor shall also prepare written operating procedures to ensure that the investigator has examined the case report forms, confirmed that there is no problem, and approved them. **[Article 47, Paragraph 3 Note]** From September 1, 2020 (PSEHB/PED Notification No. 0831-15 dated August 31, 2020)

[ ]  Compliant

Name of document:

Effective date of the written operating procedures used to prepare the report: MMM DD, YYYY

[ ]  Other ( )

5) Preparation of a clinical trial report (document that summarizes the results of the clinical trial) when the clinical trial is completed or prematurely terminated **[Article 25]**

[ ]  Compliant

[ ]  Clinical trial report is prepared in accordance with the “Structure and Content of Clinical Study Reports” (ICH E3)
 **From April 1997** (PAB Notification No. 430 dated March 27, 1997)

[ ]  An audit certificate is attached
 From April 1997 (PAB Notification No. 430 dated March 27, 1997)

[ ]  Other ( )

6) Consistency of data

[ ]  Compliant

[ ]  The content of the case report forms, the results of the examination of data handling, etc. are appropriately reflected in the clinical trial report.

[ ]  Other ( )

7) Quality management system **[Article 4, Paragraph 1]** From January 1, 2020 (PSEHB/PED Notification No. 0705-3 dated July 5, 2019)

[ ]  Compliant

[ ]  The implemented quality management shall be described in the clinical trial report.

[ ]  Other ( )

## 9. Record Keeping From April 1997

1) Preparation of written operating procedures for record keeping **[Article 4, Paragraph 1]**

[ ]  Compliant

Name of document:

Effective date of the written operating procedures applicable to the clinical trial period:

MMM DD, YYYY

Document storage facility:

Document storage manager: Title

Storage facility access control:

[ ]  Other ( )

2) Record keeping (until the later date of either the date of marketing approval of the test drug or 3 years after the date of premature termination/completion of the clinical trial)

**[Article 26, Paragraph 1]**

[ ]  Compliant

[ ]  Protocol, contracts, clinical trial reports, and other documents prepared by the sponsor in accordance with the provisions of the GCP Ministerial Ordinance, or copies thereof are retained

[ ]  Case report forms, the written notification to the sponsor pursuant to GCP Ministerial Ordinance Article 32, and other records obtained from the heads of medical institutions or investigators in accordance with the GCP Ministerial Ordinance are retained

[ ]  Records of the duties related to sponsoring and managing the clinical trial, such as monitoring and audits, are retained

[ ]  Data generated in conducting the clinical trial are retained

[ ]  Records specified in GCP Ministerial Ordinance Article 16, Paragraph 5 are retained

• Records concerning the manufacture of the investigational products, such as the manufacturing date, manufacturing method, and manufactured quantity, and the results of the tests on the drug’s quality, such as its stability

• Records of the supply or retrieval of the investigational products, including the quantity and date, for each medical institution Until August 31, 2020

• Records of the supply or retrieval of the drug(s) used in the clinical trial, including the quantity and date, for each medical institution From September 1, 2020

• Records of disposal of the investigational products Until August 31, 2020

• Records of disposal of the drug(s) used in the clinical trial From September 1, 2020

[ ]  Other ( )

# [IV] Implementation Status of Clinical Trial at Medical Institutions Subject to Document-based Inspection(To be confirmed based on the records retained by the sponsor)

**Presence or absence of medical institutions suspected to be non-compliant with GCP**

[ ]  Absent

[ ]  Present

Necessity of additional inspection
[ ]  Absent
[ ]  Present

Description:

1. The terms “GCP” and “GCP Ministerial Ordinance” in this checklist refer to the “Ministerial Ordinance on Good Clinical Practice for Drugs” i.e., the Ordinance of the Ministry of Health and Welfare No. 28 of March 27, 1997 (As last amended by the Ordinance of Ministry of Health, Labour and Welfare No. 161 of December 28, 2012). [↑](#footnote-ref-1)
2. Text enclosed in square brackets indicates relevant article/paragraph number of the GCP Ministerial Ordinance. [↑](#footnote-ref-2)
3. Date enclosed in a box indicates since/until when the relevant check item is effective. [↑](#footnote-ref-3)
4. The terms “Act” in this checklist refer to the “Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices” i.e., Act No. 145 of August 10, 1960. [↑](#footnote-ref-4)
5. The term “Enforcement Regulations” in this checklist refers to the “Ministerial Ordinance for Enforcement of the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices” i.e., the Ordinance of the Ministry of Health and Welfare No. 1 dated February 1, 1961. [↑](#footnote-ref-5)