

Investigator-Initiated Clinical Research Agreement (Draft)

(A typical interventional multicenter study with approved pharmaceuticals¹)

This Investigator-Initiated Specified Clinical Research Agreement (hereinafter “the Agreement”) is entered into by and between [Official Name of the Research Institution] (hereinafter “Representative Research Institution”) and XXXX (hereinafter “Company”), in view of the fact that the investigator-initiated clinical research (hereinafter “the Research”) set out in the following Research Implementation Particulars (hereinafter “the Particulars”) applies to the specified clinical research (hereinafter “Specified Clinical Research”) provided for in Article 2, paragraph (2) of Clinical Trials Act (hereinafter “the Act”), under Article 32 of the Act, Article 88 of the Ordinance for Enforcement of the Act (hereinafter “the Ordinance”) and other applicable laws and related notifications, concerning implementation of the Research.

[Research Implementation Particulars]

1. Name of the Research

Research name	
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2. Matters involving Representative Investigator and Institution to which the investigator belongs (the Representative Research Institution)²

Name of Representative Investigator	
Institution to which the investigator belongs (the Representative Research Institution)	

¹ This model agreement is assumed to be used when the clinical research proposed by the investigator is conducted in multiple Research Institutions.

² Corresponding to Article 88, items (iii) and (iv) of the Ordinance

In this model agreement, the matters to be set forth in the agreement under Article 88 of the Ordinance for Enforcement of the Clinical Trials Act (Article 88 of the Ordinance) are highlighted in yellow so that readers can see at a glance. For the whole article to be set forth under Article 88 of the Ordinance, only the title of the article is highlighted, while, for some provisions of an article to be set forth under Article 88 of the Ordinance, the whole provisions are highlighted.

The matters to be set forth under Article 88 of the Ordinance are as listed below:
(Matters to be set forth in the agreement)

Article 88 “Matters specified by an Ordinance of the Ministry of Health, Labour and Welfare” as provided in Article 32 of the Act are as listed below:

- 1 Date of execution of the agreement
- 2 Implementation period of “Specified Clinical Trial” (limited to the researches specified in Article 2, paragraph (2), item (i) of the Act; hereinafter the same applies in this article, the following article and Article 90).
- 3 Name and location of Marketing Approval Holder of Drugs which provides research funds and the name and location of the Research Institution.
- 4 Name of Investigator / Principal Investigator who conducts Specified Clinical Research
- 5 Timing of payment of research funds for Specified Clinical Research
- 6 Matters involving “publication of information, etc. on provision of research funds or other benefits” set forth in Article 33 of the Act
- 7 Matters involving the handling of deliverables of Specified Clinical Research
- 8 Matters involving the provision of information on side effects, efficacy and safety of pharmaceuticals
- 9 Matters involving the publication by recording in the database developed by the Ministry of Health, Labour and Welfare as specified in Article 24, paragraph (1) herein.
- 10 Matters involving the compensation and healthcare provision for any damage to health in a subject of Specified Clinical Research
- 11 Matters involving the creation of Standards for Conflicts of Interest Management specified in Article 21, paragraph (1) herein and the creation of Plan for Conflicts of Interest Management specified in Article 21, paragraph (3) herein
- 12 Matters involving the provision of information on the research funds provided to the Research Institutions by the groups which manage the research as specified in item (ii) of the following article herein (only to the extent that Marketing Approval Holders of Drugs and such groups enter into an agreement)
- 13 Other matters required for the provision of research funds

Institution)	
Location of Institution to which the investigator belongs (the Representative Research Institution)	
Department to which the investigator belongs	
Name of the manager of the Representative Research Institution	

3. Objective, etc. of and summary of medical devices for use in the Research

(1) Objective, description and period of the Research³

Objective	
Description	
Expected number of subjects	
Period	<p>From the scheduled start date to end date of the research as described below:</p> <ul style="list-style-type: none"> - Scheduled start date of the research (scheduled date of the publication under Article 24, paragraphs (1) and (7) of the Ordinance) XX/XX/20XX - Scheduled end date of the research (scheduled date of the publication under Article 24, paragraphs (4) and (7) of the Ordinance) XX/XX/20XX

(2) Summary of medical devices for use in the Research

Unapproved/off-label/approved under the Pharmaceutical and Medical Device Act	<input type="checkbox"/> Unapproved	<input type="checkbox"/> Off-label	<input type="checkbox"/> Approved
INN (Enter the development code if unapproved domestically and internationally)			
Trade name (Add country name for a foreign product.) ⁴			

4. Term of the Research Agreement•the Research Funds•Provided Goods•Loaned Goods

Term of the Research Agreement	From XX/XX/20XX to XX/XX/20XX
The Research Funds	<p>Total XXXXXXXXX yen (including consumption tax and local consumption tax) Breakdown (e.g.): XXXXXX yen for preparation stage XXXXXX yen for implementation stage</p>

³ Corresponding to Article 88, item (ii) of the Ordinance⁴ For the devices unapproved in Japan, please enter names of countries in which the trade name is used.

With/without Provided Goods and description	Without/With (See Annex 8)
With/without Loaned Goods and description	Without/With (See Annex 8)

Article 1 (Definitions)

In the Agreement, the definitions of the terms listed in the following items are as prescribed respectively in those items. In the event of any discrepancy in definition between Applicable Laws and Ordinances and the following items, the former shall prevail.

- (1) “Investigator-Initiated Clinical Research” means the clinical research for which the Representative Investigator assumes final responsibility, including proposing the clinical research, preparing the protocol, and conducting the clinical research appropriately.
- (2) “Investigator” means the person who conducts the clinical research specified in Article 1, item (ii) of the Ordinance, including a physician or a dentist who manages operations for the Research in the Research Institution.
- (3) “Multicenter study” means the clinical research conducted in multiple research institutions based on the protocol specified in Article 1, item (iii) of the Ordinance.
- (4) “Representative Investigator” means the person who is listed in paragraph (2) of the Particulars as an Investigator representing Investigators of multiple Research Institutions when a multicenter study is conducted.
- (5) “The Research Name” means the name listed in paragraph (1) of the Particulars.
- (6) “Sub-investigator” means the physician or dentist who shares operations for the Research under the Investigator’s direction in Research Institution, as specified in Article 1, item (v) of the Ordinance.
- (7) “The Researchers” mean all persons who engage in the Research, including Investigators (including Representative Investigator) and Sub-investigators.
- (8) “Representative Research Institution” means the institution listed in paragraph (2) of the Particulars, to which Representative Investigator belongs.
- (9) “Participating Research Institutions” mean the institutions listed in Annex 1 as Research Institutions other than Representative Research Institution.
- (10) “Research Institutions” mean Representative Research Institution and Participating Research Institutions.
- (11) “Manager of Representative Research Institution⁵” means the person who manages and supervises Representative Investigator in Representative Research Institution, as listed in paragraph (2) of the Particulars.
- (12) “Parties” collectively refer to Representative Research Institution, Participating Research Institutions, Representative Investigator, Investigators and Company.
- (13) “Contracting Parties” are main parties in agreement, to which rights or obligations under the Agreement are directly assigned, and mean Representative Research Institution and Company of “Parties”.
- (14) “The Research Objective” is listed in paragraph (3), item (i) of the Particulars.
- (15) “The Medical Device” means the medical device listed in paragraph (3), item (ii) of the Particulars.
- (16) “Certified Review Board” is the committee consisting of persons with special knowledge and experience in clinical research, which reviews and provides opinions for clinical research, as

⁵ According to Q46 of “Q&A ver. 1.0 for the Guidance for Conflicts of Interest Management under the Clinical Trials Act”: Manager of Research Institution refers to the director of the hospital, while the head of the institution to which investigators belong refers to the head of the university, company or organization to which investigators belong. They are described as “Manager of Research Institution or the head of the institution to which investigators belong” because the place where the department managing Conflicts of Interest is established varies among institutions and because the person who is responsible for statistical analysis or listed in the protocol and will clearly obtain benefits of conducting the clinical research does not necessarily belong to Research Institutions.

specified in Article 23 of the Act.

- (17) “The Research Funds” are the funds which the company listed in paragraph (4) of the Particulars provides to the Representative Research Institution.⁶
- (18) “Protocol” means the written plan of the Clinical Research (refer to Article 1, item (iii) of the Ordinance), which describes matters listed in Article 14 of the Ordinance.
- (19) “Trial Plan” shall be prepared in accordance with Form 1 (in relation to Article 39) of the Ordinance.
- (20) “j RCT” refers to “Japan Registry of Clinical Trials”, and “Trial Plan and research summary disclosure system”, the system to perform procedures for submission of Trial Plan to the Minister of Health, Labour and Welfare under provisions of the Act, for clinical researches to be conducted in Research Institutions.
- (21) “Applicable Laws and Ordinances” mean the ethical principles defined in the Declaration of Helsinki, the Act, the Ordinance, and other laws, regulations and notifications applicable to the Research.
- (22) “Primary Endpoint Report” means the summary of results of collected data for primary endpoint of Protocol, as specified in Article 24, paragraph (2) of the Ordinance.
- (23) “Clinical Study Report” means the document in which results of the Research are compiled, as specified in Article 24, paragraph (2) of the Ordinance.
- (24) “Source Documents” mean records and data on clinical findings, observations and other activities from clinical practices in subjects of the Research (including analysis data and compiled data thereof), as specified in Annex 7.
- (25) “Database for Statistical Analysis” means ●●●●.
- (26) “Procedures” mean the document in which procedures are specified so that each operation for the Research is performed constitutively and approximately.
- (27) “Samples” are defined as parts of the human body including blood, tissues, cells, body fluids and excreta, and DNA extracted from them, to be used in researches.
- (28) “Affiliate” means any corporation controlling, controlled by or under common control with oneself. In this item, “control” means the direct or indirect ownership of more than fifty percent (50%) of the stock or shares entitled to vote.
- (29) “The Confidential Information” means (1) any secret concerning subjects of the Research obtained in connection with implementation of the Research (refer to Article 11 of the Act), (2) any secret obtained in connection with implementation of the Research (refer to Article 61 of the Ordinance), and (3) technical or business information on the Research disclosed or provided by the other party during the term of validity of the Agreement.

Article 2 (The Research Objective)

1. The Agreement is intended to specify the relationship among Representative Investigator, Investigators, Representative Research Institution, Participating Research Institutions and Company for Investigators’ conducting the Research as Investigator-Initiated Clinical Research in Representative Research Institution and Participating Research Institutions and for Company’s reimbursing the expenses for the Research, and to specify descriptions required by Applicable Laws and Ordinances.

⁶ If direct payment from the Company to Participating Research Institutions and CRO occurs, Article 3 should be amended depending on the situation.

2. Contracting Parties shall confirm that the Research is duly conducted, respecting life, health and human right of subjects of the Research, in accordance with the basic philosophy of clinical research described in the Ordinance, under Investigator's responsibility, for the purpose of accumulation of information on the safety and efficacy for the Medical Device.
3. Contracting Parties shall confirm that Company does not provide the Research Funds as a means of unjustifiably inducing trade with Representative Research Institution, Participating Research Institutions, and the persons who engage in the Research.

Article 3 (Payment and handling of the Research Funds)

1. **Company shall pay the Research Funds listed in paragraph (4) of the Particulars as fair and reasonable expenses necessary for the Research to Representative Research Institution as described in Annex 2, in accordance with the terms of the Agreement.**⁷
2. Company shall pay the Research Funds by wire transfer to the following bank account held by the Representative Research Institution.⁸ The cost of the transfer shall be borne by Company.
XXXXXX Bank, XXXX Branch, Savings/Checking account [No.] [Name of account holder]
3. Representative Research Institution shall report in writing to Company that the milestone specified in Annex 2 has been achieved and send the invoice for the amount associated with the milestone.
4. Company shall confirm the content of the report and the invoice and notify the Representative Research Institution of the results within XX days of the date of receipt of the report and the invoice under the preceding paragraph.⁹
5. Upon the notification under the preceding paragraph, if Company makes an objection or requires additional fact-checking for the report or the invoice under paragraph (3) of this article, in response to the objection or request, the Representative Research Institution shall amend the report or the invoice as necessary, and shall re-send the amended report or invoice to Company, to which the preceding and this paragraphs shall apply mutatis mutandis.
6. Company shall pay the amount of the Research Funds described in the invoice by the end of the month following the month to which the day of notification of no objection to the content of the report and the invoice provided in paragraph (3) of this article belongs, under paragraph (4) of this article.
7. **If there is a surplus in respect of the Research Funds that have already been paid upon completion or discontinuation of the Research, the Representative Research Institution shall return this to the Company. Representative Research Institution shall destroy or return to Company the Goods (medical devices) with asset value purchased with the Research Funds according to the procedures designated by Company.**¹⁰
8. Representative Research Institution shall not, by itself or through Manager of Representative Research Institution and Representative Investigator, and Participating Research Institutions and Managers and Investigators thereof, use the Research Funds for any objective other than the Research Objective, in accordance with "Breakdown of the Research Funds" included in Annex 3.

⁷ Corresponding to Article 88, item (v) of the Ordinance

⁸ Direct payment from Company to CRO shall be specified to be in accordance with confirmation and direction by Representative Research Institution to avoid direct influence (management, supervision, etc.) over CRO.

⁹ Direct payment from Company to CRO shall be specified to be in accordance with confirmation and direction by Representative Research Institution to avoid direct influence (management, supervision, etc.) over CRO.

¹⁰ Corresponding to Article 88, item (xiii) of the Ordinance. This item would be added to ensure that the surplus in respect of the Research Funds is not considered as offering profits to the Research Institution. It also specifies that, in addition to money, the Goods with asset value purchased with the Research Funds shall be strictly destroyed or returned.

9. Representative Research Institution shall keep accounting records when providing Participating Research Institutions with part of the Research Funds and submit a list (of payment recipients and amounts) annually (no later than MM/DD for each information between MM/DD and MM/DD) to Company for reporting.
10. The Representative Research Institution shall submit an account report on the breakdown of the Research Funds to the Company within XX days after completion of the final payment, and the Company may audit the accounts of the Representative Research Institution relating to the Research Funds.
11. The Representative Research Institution shall retain documents related to the Research Funds between the first and last payment date and for X years after the last payment date for the Research Funds

Article 4 (Implementation of the Research)

1. Representative Research Institution shall have Manager of Representative Research Institution and Representative Investigator perform Representative Investigator's duties listed in Annex 4 as set forth in laws and ordinances and duly conduct the Research, in compliance with Applicable Laws and Ordinances, the Agreement and Protocol.
2. If Representative Research Institution shall entrust part of the Research operations to a third party (hereinafter "Contract Organization"), Representative Research Institution shall supervise and assume responsibility for the execution of operations entrusted to Contract Organization. In this case, Representative Research Institution shall have Contract Organization assume the obligations hereunder and, when becoming aware of Contract Organization's act in violation of Applicable Laws and Ordinances and the Agreement, shall immediately report to Company, rapidly execute corrective measures and also report the content of such corrective measures to Company.
3. Representative Research Institution shall enter into an agreement covering obligations to be borne by Participating Research Institutions (including "Duties of Investigators of Participating Research Institutions" in Annex 5) with Participating Research Institutions before the start of the Research.
4. Company may confirm the status of execution of the agreement between Representative Research Institution and Participating Research Institutions (including the original copy of the agreement) after obtaining prior consent of Representative Research Institution.
5. In the event of the breach of the agreement by a Participating Research Institution as specified in paragraph (3) hereof, Representative Research Institution shall have the Participating Research Institution immediately report the fact of the breach and, when receiving such report from the Participating Research Institution, shall immediately submit the content of such report to Company, promptly take measures to correct the breach, and report to Company.

Article 5 (Reporting the progress of the Research to Company)

Representative Research Institution shall report or submit the following matters set forth in each item (including information about Participating Research Institutions) to Company periodically or promptly at Company's request:

- (1) Trial Plan number of the Research
- (2) Certification number of Certified Review Board
- (3) A set of materials examined by Certified Review Board (including course and completion reports).
- (4) First Patient First Visit (first subject in)

- (5) Last Patient First Visit (last subject in)
- (6) First Patient Last Visit (first subject last visit)
- (7) Completion date for primary endpoint
- (8) Last Patient Last Visit (last subject last visit)
- (9) Database fixation date
- (10) Date of result publication to jRCT
- (11) Situation regarding patient enrollment and the discontinuation of the Research
- (12) Deviation from Trial Plan
- (13) ----- [Reportable matters shall be listed hereafter.]
- (14) Other information necessary to conduct the Research

Article 6 (Safety Information)¹¹

1. Company shall provide the Representative Research Institution with up-to-date information regarding safety and safe usage of the Medical Device.
2. The Representative Research Institution shall, by itself or through Representative Investigator, etc., report to Company timely the information regarding safety of the Medical Device in the Research, in accordance with Protocol (including, without limitation, serious adverse events; see Protocol for details).
3. The Representative Research Institution shall, by itself or through Manager of the Representative Research Institution and Investigator, cooperate as far as possible with Company in taking action related to the safety information on the Medical Device.

Article 7 (Provision of Medical Device or Goods)¹²

1. Company shall provide Medical Device or goods prescribed in Annex 8 (hereinafter collectively "Provided Goods") to the Representative Research Institution free of charge, to the extent necessary for the Research. Detailed conditions for the provision of Provided Goods shall be determined upon separate consultation between Company and Representative Research Institution.
2. The Representative Research Institution shall, by itself, assume responsibility for managing and storing the Provided Goods in accordance with applicable laws and regulations and information stated in accompanying documents, and shall use the Provided Goods solely for the purpose of executing the Research. The Representative Research Institution shall, by itself, take responsibility for use of the Provided Goods, and shall prepare and retain up-to-date records regarding the receipt and usage of the Provided Goods.
3. Representative Research Institution shall not provide the Researchers, Contract Organization or other third parties with the Provided Goods received from Company in connection with the Research for any purpose other than the Research and shall not have them use such goods.
4. If the Research is completed or discontinued, or if the Agreement is cancelled, Representative Research Institution shall return to Company without delay unused Provided Goods (including general-purpose goods that can be used for purposes other than the Research and the goods unused

¹¹ Corresponding to Article 88, item (viii) of the Ordinance. In this agreement draft, the premise is that the reporting scope and method for the information about safety is specified in Protocol as set forth in paragraph (2) of this article. If another method is used, including execution of a separate agreement for management of safety information, the article should be adjusted depending on actual conditions.

¹² This article assumes the case of medical devices or goods being provided. Please delete it if no medical devices or goods are provided. This article should be adjusted by each company based on how to provide Provided Goods to each Participating Research Institution (via Representative Research Institution or directly).

by Participating Research Institutions) received from Company in their present, existing condition as of completion, discontinuation or cancellation of the Research. If Company opts for the Provided Goods to be destroyed rather than returned, Representative Research Institution shall destroy the Provided Goods in accordance with Representative Research Institution's prescribed procedure and then record this, and if Company requests the issuance of a certificate of disposal, the Research Institution shall promptly comply with this request.¹³

5. Representative Research Institution shall impose on Participating Research Institutions, and Managers and Investigators thereof the obligations equivalent to its obligations in relation to handling of Provided Goods under paragraphs (2) to (4) of this Article and shall be responsible to have Participating Research Institutions perform such obligations.

Article 8 (Loan of Medical Device or Goods)¹⁴

1. During the term of the Agreement, the Company shall loan the Medical Device or Goods, etc. prescribed in Annex 8 (hereinafter the "Loaned Goods") to the Representative Research Institution free of charge for up to twelve (12) months for execution of the Research. Detailed conditions for the loan of Loaned Goods shall be determined upon separate consultation between Company and Representative Research Institution.
2. If the Loaned Goods are the Medical Device, the Company shall receive separately from the Medical Institution the "Letter of Confirmation Concerning Loan of Medical Device" prescribed by the Japan Fair Trade Council of the Medical Devices Industry.
3. The right of ownership and other rights pertaining to the Loaned Goods shall belong to the Company, and the Representative Research Institution shall manage the Loaned Goods with the duty of diligence of a good manager. The Representative Research Institution shall not invalidate the Loaned Goods by, for example, removing name plates or labels indicating the Company's right of ownership or their manufacturing or management number etc., and it shall not dismantle, repair, remodel or alter the Loaned Goods, transfer, loan or assign them to another Center, nor pledge them as security.
4. Representative Research Institution shall not use Loaned Goods for any purpose other than the Research nor allow the Researchers, Contract Organization or other third parties to use them for any purpose other than the Research.
5. If Loaned Goods are lost or damaged, Representative Research Institution shall compensate Company for such damage; provided, however, that this shall not apply if such loss or damage is not attributable to Representative Research Institution or Participating Research Institutions.
6. If the Research is completed or discontinued, if the Agreement is cancelled, or if the loan period for goods ends, the Representative Research Institution shall promptly return the Loaned Goods to the Company in their present and existing condition as of the time of completion or discontinuation of the Research, cancellation, or the end of the loan period.¹⁵
7. Representative Research Institution shall impose on Participating Research Institutions the obligations equivalent to its obligations in relation to handling of Loaned Goods under paragraphs

¹³ Each company should determine whether words indicating that provided medical devices shall not be reimbursed by insurance need to be added. Some companies appear to take measures such as labeling the devices as not being reimbursed by insurance.

¹⁴ This article assumes the case of medical devices or goods being loaned. Please delete it if no medical devices or goods are loaned. In the same manner as prescribed under the article for Provided Goods, this article should be adjusted by each company based on how to loan Loaned Goods to each Participating Research Institution (via Representative Research Institution or directly).

¹⁵ An article needs to be added accordingly for any provision of service besides provision or loan of medical devices or goods.

(2) to (6) of this Article and shall be responsible to have Participating Research Institutions perform such obligations.

Article 9 (Handling of Personal Information)

1. Contracting Parties shall comply with the Act or the Ordinance, or laws and ordinances for the protection of personal information, for implementation of the Research.
2. Contracting Parties shall take necessary measures for the prevention of the leaking, loss or damage and for the proper management of personal information (meaning “Personal Information” defined in Article 10 hereof; the same applies in this article) about subjects of the Research.
3. Contracting Parties shall not use and provide to any third party Personal Information beyond the scope of consent given by subjects of the Research; provided, however, that the foregoing restriction shall not apply if any requirement under the Act or the Ordinance, or laws and ordinances for the protection of personal information is met.
4. In the event of the breach or threatened breach of the Act or the Ordinance, or laws and ordinances for the protection of personal information regarding the handling of personal information about subjects of the Research, Contracting Parties shall immediately notify the other party thereof and promptly discuss the response thereto.

Article 10 (Handling of Samples)¹⁶

If Samples are handled in the Research, they shall be appropriately handled in compliance with Applicable Laws and Ordinances and the Act on the Protection of Personal Information (Law No. 57, May 30, 2003), etc.

Article 11 (Compensation and Other Measures)¹⁷

1. For implementation of the Research, Representative Research Institution shall beforehand establish the system to provide insurance and medical care and take other necessary measures in preparation for compensation and medical care for subjects of the Research in the event of injuries associated with the Research. The emergency medical center cooperating with each Participating Research Institution shall be as listed in Annex 1.
2. Representative Research Institution shall enter into an agreement with the Participating Research Institution concerning responsibilities and costs to be borne for the necessary measures provided for in the preceding paragraph.

Article 12 (Change to Protocol and Trial Plan)

1. The Representative Research Institution may have Representative Investigator change Protocol within the scope of the Research Objective. With a prior written consent of Company for the content of the change, the Representative Research Institution shall have Representative Investigator take necessary measures such as submitting Trial Plan in compliance with Applicable Laws and Ordinances. Company shall not reject the consent unless there is good reason.
2. Each contracting party may consult about and correct the amount and payment method of the Research Funds set forth in Article 3 herein in accordance with the content of revised Trial Plan.

¹⁶ If Samples are not specifically required, it may be specified that Samples shall “not be received” or “not be provided” by the Research Institution.

¹⁷ Corresponding to Article 88, item (x) of the Ordinance

Article 13 (Replacement of Representative Investigator, etc.)

1. If Representative Investigator turns out to become unable to continue his/her duties at the Representative Research Institution because of his/her resignation, dismissal, transfer, or any other reason, the Representative Research Institution shall immediately notify Company thereof in writing.
2. In the case of the preceding paragraph, Representative Research Institution shall take measures such as replacement of Representative Investigator to avoid the absence of Representative Investigator of the Research, and shall immediately notify Company thereof in writing, through consultation with Representative Investigator or Participating Research Institutions as necessary.
3. If Company makes an objection to the replacement of Representative Investigator under the preceding paragraph, Company may ask Representative Research Institution to consult with Representative Investigator, Representative Research Institution or Participating Research Institutions about whether or not the Research may be continued and procedures.
4. For measures such as the replacement of Representative Investigator, the Representative Research Institution shall have the Representative Investigator to be replaced notify Certified Review Board before replacement in compliance with Applicable Laws and Ordinances.
5. In the event of replacement of Investigators of Participating Research Institutions, Representative Research Institution shall have Representative Investigator submit a notification to Certified Review Board before replacement, in compliance with Applicable Laws and Ordinances.
6. In the case of the preceding paragraph, Representative Research Institution shall have Representative Investigator immediately notify Company thereof in writing.

Article 14 (Procedures at the end of the Research)

1. Representative Research Institution shall have Representative Investigator make the following responses including the publication under Article 24, paragraphs (1) and (7) of the Ordinances, in accordance with each of the following items. Publication under this article means recording in j RCT.
 - (1) Prepare within the following periods Primary Endpoint Report, and Clinical Study Report and its summary.¹⁸
 - A) Primary Endpoint Report
In principle, one (1) year after the end of the period for data collection for primary endpoints
 - B) Clinical Study Report and its summary
In principle, one (1) year after the end of the period for data collection for all endpoints
 - (2) When preparing documents under the preceding item, submit them to Company before doing so to Certified Review Board, for confirmation as follows:
 - A) Company shall examine Primary Endpoint Report, and Clinical Study Report and its summary from ethical viewpoint, and the viewpoints of appropriate use of the Medical Device pursuant to the Agreement, Handling of Personal Information (Article 7), Handling of Intellectual Property Rights (Article 15), and Confidentiality (Article 17), and shall respond to Representative Investigator within XX days thereafter. Provided, however, that Company should not be involved in the interpretation of results of the

¹⁸ Corresponding to Article 88, item (ix) of the Ordinance

Research.

- B) Representative Investigator shall be responsible for determining and submitting to Company the content of Primary Endpoint Report, and Clinical Study Report and its summary, taking the Company's response under the preceding A) into consideration in good faith.
- (3) Representative Investigator shall, after the confirmation under the preceding item, submit Primary Endpoint Report, Clinical Study Report and its summary to Manager of Representative Research Institution.
 - (4) Representative Investigator shall, for publication of the Research, seek the opinion of Certified Review Board in advance and publish it within one (1) month of the date the opinion is issued. Ensure no discrepancies between Primary Endpoint Report, Clinical Study Report and its summary, and published content.
 - (5) When submitting the summary of Clinical Study Report to Certified Review Board, promptly submit to the Minister of Health, Labour and Welfare the following documents additionally:
 - A) Protocol
 - B) Statistical Analysis Plan (only if prepared)
2. The Representative Research Institution shall have Representative Investigator submit Primary Endpoint Report, Clinical Study Report and its summary, and Statistical Analysis Plan (only if prepared) for the Research, to Company, within X months of publication.

Article 15 (Publication of the Research Results)^{19 20}

1. If Representative Investigator issues journal articles, presentations at academic conferences, press releases, etc. regarding the Research (hereinafter collectively "Publications"), each contracting party shall confirm that they are based on Protocol, Primary Endpoint Report, and Clinical Study Report.
2. Under the preceding item, if Representative Investigator issues Publications, the Representative Research Institution shall have Representative Investigator address each of the following items:
 - (1) If Representative Investigator prepares materials for Publications, Investigator shall follow Annex 6 "Materials for Publications and Schedule" and submit materials for Publications to Company.
 - (2) Company shall examine Materials for Publications under the preceding item from ethical viewpoint, and the viewpoints of appropriate use of the Medical Device pursuant to the Agreement, Handling of Personal Information (Article 9), Handling of Intellectual Property Rights (Article 17), and Confidentiality (Article 19), and shall respond to Representative Investigator by the deadline specified in Annex 6. Provided, however, that Company should not be involved in the interpretation of results of the Research
 - (3) Representative Investigator shall be responsible for determining the content of final Publications, taking the Company's response under the preceding item into consideration. Company shall not reject Publications unless there is good reason.
3. Representative Research Institution shall, concerning publication of results of the Research, have

¹⁹ Corresponding to Article 88, item (vii) of the Ordinance

²⁰ Setting conditions for publication of research results requires caution to keep Company from being deemed to interfere data analysis and published content.

Representative Investigator make adjustment to decide the content and timing thereof in accordance with Annex 6 “Materials for Publications and Schedule” upon consultation among Participating Research Institutions, Investigators and other Parties.

Article 16 (Ownership, Retention and Use of Source documents)²¹

1. Ownership of rights for Source Documents resulting from the Research shall be as specified in Annex 7 “Ownership and Use of Source Documents”.
2. Representative Research Institution shall, by itself or through Participating Research Institutions or Managers thereof, Representative Investigator or Investigators, retain Source Documents for five (5) years after the date of completion of the Research in compliance with Applicable Laws and Ordinances, and shall consign operations for retention of Source Documents to Contract Organization or have Contract Organization consign such operations if necessary.²²
3. Representative Research Institution shall, by itself or through Participating Research Institutions or Managers thereof, Representative Investigator or Investigators, manage and supervise to keep Source Documents from being used for any purpose other than the Research before Representative Investigator issues Publications under the preceding article; provided, however, that this shall not apply if Source Documents are used in clinical practice for subjects of the Research.
4. Representative Research Institution shall, for the dataset for statistical analysis or its replica, provide the dataset for statistical analysis to Company after licensing Company to use it as provided in Annex 7 within the scope of the objective under each of the following items, while Company may use the dataset for statistical analysis or its replica free of charge within the scope of the objective.
 - (1) To appropriately provide information about safety of the Medical Device;
 - (2) To ensure traceability in Company and its Affiliates; and
 - (3) For the subanalysis for the purpose of research and development for the Medical Device.
5. If Company performs or Representative Research Institution has Representative Investigator perform research (analysis) newly using the dataset for statistical analysis beyond the scope of the objective as prescribed in each item of the preceding paragraph, the party shall obtain the prior consent of the other party and appropriately perform it in compliance with Applicable Laws and Ordinances. Providing the dataset for statistical analysis to Company shall be after publication of the primary analysis article.
6. If Company provides or Representative Research Institution has Representative Investigator provide the dataset for statistical analysis to any third party, the party shall obtain the prior written consent of the other party.

Article 17 (Handling of Intellectual Property Rights)²³

If any patent right or other intellectual property right (however, except copyright; hereinafter the same applies in this article) appears to arise in connection with the Research, the Representative Research

²¹ Corresponding to Article 88, item (vii) of the Ordinance

²² To keep Investigator from bringing out data etc. when being transferred, it may be considered desirable to retain data etc. at a place other than the institution to which he/she belongs. Conditions should be adjusted depending on actual conditions, which are related to the burden of costs of retention.

²³ Regarding handling of intellectual property rights, we have created the draft of article indicating that intellectual property rights shall belong to Company. If the draft is not appropriate in practice, please consider to change the draft to the one containing “separately consulted” as specified below:
(Draft of article indicating that handling of intellectual property rights shall be “separately consulted”)

Institution shall notify Company promptly thereof. Any patent right or other intellectual property right arising in connection with the Research shall belong to Company.

Article 18 (Conflicts of Interest Management)

1. Representative Research Institution shall have Representative Investigator prepare the Conflicts of Interest Management Standards under Article 21, paragraphs (1) and (6) of the Ordinance.
2. Representative Research Institution shall have Manager of Representative Research Institution or the head of the institution to which investigators belong confirm the fact of involvement by companies (including third parties; the same applies in this article) in accordance with Conflicts of Interest Management Standards under the preceding paragraph and submit the report describing the results to Representative Investigator.
3. In the light of the content of the report under the preceding paragraph, Representative Research Institution shall have Representative Investigator prepare the Conflicts of Interest Management Plan specifying the method of appropriate handling for the involvement by companies. The Conflicts of Interest Management Plan should align with Applicable Laws and Ordinances.
4. Representative Research Institution shall have Representative Investigator hear opinions from Certified Review Board regarding Conflicts of Interest Management Standards and Conflicts of Interest Management Plan, under Article 21, paragraphs (4), (5) and (6) of the Ordinance, and manage conflicts of interest based on Conflicts of Interest Management Standards and Conflicts of Interest Management Plan.²⁴
5. Representative Research Institution shall, by itself and through Representative Investigator, properly release or publish information about the provision of the Research Funds by companies under the Agreement in accordance with “Guidelines on COI Management” developed by the Japanese Association of Medical Sciences or associated societies, including in the case of Publications of results of the Research, to ensure transparency of its relationship with companies.
6. Representative Research Institution shall impose, of the obligations set forth in each preceding paragraph, those to be performed by Managers of Participating Research Institutions, the head of the institution to which investigators belong or Investigators in Participating Research Institutions, on Participating Research Institutions.
7. Company shall also properly disclose the Research Funds based on “Guidelines for Transparency of the Relationship Between Corporate Activities and Medical Institutions” established by Company in accordance with Article 33 of the Act, Article 90 of the Ordinance and the Transparency Guidelines prescribed by the Japan Federation of Medical Devices Associations, and Representative Research Institution shall agree such publication. Representative Research Institution shall provide the information required for such publication by Company (including but not limited to the information on the institution to which Investigator belongs and his/her transfer, and identification numbers recorded in j RCT as specified in Article 24, paragraph (1) of the Ordinance; hereinafter “the Information for Publication”) promptly at Company’s request.²⁵
8. Representative Research Institution must state in an agreement with Participating Research Institutions that (1) Participating Research Institutions shall provide the Information for Publication at the request of Representative Research Institution and (2) Representative Research Institution shall agree to provide Company with the Information for Publication. Representative

²⁴ Paragraphs (1) to (4) of this article correspond to Article 88, item (xi) of the Ordinance.

²⁵ Please replace “Guidelines for Transparency ...” with the title of the guidelines of each company.

Research Institution shall, by itself and through Manager of Representative Research Institution and Representative Investigator, and Participating Research Institutions and Managers and Investigators thereof, agree to publish the Information for Publication under the preceding paragraph.

9. Representative Research Institution shall promptly provide the Information for Publication provided by Participating Research Institutions under the preceding paragraph at the request of Company.²⁶

Article 19 (Confidentiality)

1. Contracting Parties shall hold and maintain the Confidential Information in strictest confidence, shall not disclose, divulge or provide the information to a third party without prior written consent of the other party, shall not reproduce or duplicate the information beyond the scope of the Research Objective, and shall not use the information for any objective other than the Research Objective. However, Company may disclose and provide the Confidential Information to its Affiliates provided that Company shall impose on the Affiliates the obligations equivalent to Company's ones hereunder and shall be responsible to the Research Institution for performing such obligations.
2. Each contracting party may disclose and provide the Confidential Information only to its executives or employees who need the information for the performance of the Agreement (including those who engage in the Research); provided, that the party shall impose on these persons the obligations equivalent to the party's ones hereunder and shall be responsible to the other party for performing such obligations.
3. The party receiving such information shall not be under the obligations provided for in this following article if such information:
 - [1] is publicly known/used at the time of disclosure or provision by the other party;
 - [2] becomes publicly known after disclosure or provision by the other party without the responsibility of the receiving party;
 - [3] was in the receiving party's possession at the time of disclosure or provision by the other party;
 - [4] is obtained by the receiving party from a duly authorized third party without any secrecy obligation; or
 - [5] was independently developed by the receiving party without the use of the information disclosed or provided by the other party.
4. Notwithstanding provisions of paragraphs (1) and (2), if requested or ordered by a regulatory authority or court in compliance with laws and ordinances, each contracting party may disclose and provide the Confidential Information to the regulatory authority or court. However, in this case, each party receiving such request or order shall immediately notify the other party of being requested or ordered to the extent accepted by laws and ordinances, and consult with the other party about the scope of information to be disclosed or provided.
5. Unless otherwise provided for hereby, on completion of the Research or termination of the Agreement, whichever occurs sooner, the receiving party shall either return all the Confidential Information to the other party or destroy it, in accordance with the other party's instructions.
6. Notwithstanding each preceding paragraph, Contracting Parties shall hold and maintain in strictest

²⁶ Paragraphs (8) and (9) of this article corresponds to Article 88, item (vi) of the Ordinance.

confidence (1) any secret concerning subjects of the Research obtained in connection with implementation of the Research (refer to Article 11 of the Act) and (2) any secret obtained in connection with implementation of the Research (refer to Article 61 of the Ordinance) of the Confidential Information, and shall not disclose, divulge or provide such secret to a third party without due reason.

Article 20 (Exclusion of Anti Social Forces)

1. Each contracting party shall represent and warrant that it does not and will not fall under any of the following items or does not and will not perform the act coming under any of the following items:
 - (1) It falls under any of an organized crime group, an organized crime group member, a person for whom five years have not passed since the day on which the person ceased to be an organized crime group member, a quasi organized crime group member, an organized crime group-associated company, a corporate extortionist, rogue persons or groups proclaiming itself as a social activist or an organized special intellectual crime group, and any other person equivalent to the above (hereinafter collectively referred to as “Anti Social Forces”);
 - (2) Its officer, a person substantially involved in its management, or the Researcher who belongs to it falls under Anti Social Forces;
 - (3) A person who controls its financial and business policy decisions falls under Anti Social Forces;
 - (4) Unfair use of the Anti Social Forces for the purpose of gaining dishonest profits for itself or a third party or of damaging a third party;
 - (5) The act of providing funding or accommodation to Anti Social Forces with knowledge of the act encouraging the activities of Anti Social Forces; or
 - (6) Its officer, a person substantially involved in its management, or the Researcher who belongs to it is engaged in socially condemnable relationship with Anti Social Forces.
2. Each contracting party shall not make an unreasonable demand, by itself or through the use of a third party, by the use of violence, force, intimidating words or fraudulent means.
3. Where a fact falling under any of items of paragraph (1) or a fact of the act falling thereunder is found in any of the contractors, suppliers and other business associates used for performance of the Agreement by Representative Research Institution, Manager of Representative Research Institution or Representative Investigator, Company may request the completion of such trade and other necessary measures to Representative Research Institution. The Representative Research Institution which receives such request shall take necessary measures to a reasonable extent except when there are justifiable grounds.
4. Representative Research Institution shall apply the provisions equivalent to those of each preceding paragraph to the agreement with Participating Research Institutions.

Article 21 (Legal Compliance)²⁷

1. Each contracting party shall comply with Japanese laws, U.S. Foreign Corrupt Practices Act, and other laws related to corruption prevention (hereinafter “Corruption Prevention Laws”), and shall not provide or propose to provide government officials or other third parties involved in trade with money or facilities in a manner that violates Corruption Prevention Laws.

²⁷ As AMDD, the article pertaining to FCPA and insider trading regulation is added. Words in this article are assumed to be replaced with any words designated by each company as appropriate.

2. Representative Research Institution shall supervise itself, Manager of Representative Research Institution and Representative Investigator, and Participating Research Institutions and Managers and Investigators thereof to ensure that all of those comply with insider trading regulation under the Financial Instruments and Exchange Act (Act No. 25, April 13, 1948; including amendments).

Article 22 (Effective Period and Discontinuation and Cancellation of Agreement)

1. The term of validity hereof shall be the term of agreement listed in paragraph (4) of the Particulars.
2. If the Research is discontinued, Representative Research Institution shall inform Company in advance thereof and whether or not results of the Research are scheduled to be published at the time of the discontinuation, within XX days of decision on the discontinuation.
3. In any of the following cases, each contracting party may cancel all or part of the Agreement by notifying the other party in writing.
 - (1) If the Research is not started during a reasonable period after submission of Trial Plan to the Minister of Health, Labour and Welfare;
 - (2) If, based on adverse events during implementation of the Research or safety information notified by Company, the Ministry of Health, Labour and Welfare or any party hereto judges that it is impossible to ensure the safety of the Research Subjects;
 - (3) If the Research is significantly behind the schedule prescribed in Protocol;
 - (4) If the milestone specified in Annex 2 is not achieved;
 - (5) If the other party violates the Agreement and there is no sign of improvement after a reasonable period stipulated notwithstanding a demand for rectification;
 - (6) If continuation of the Agreement becomes difficult due to an ethical reason for discontinuing the Research or a legitimate reason which hinders the continuation of the Research;
 - (7) If the Research is discontinued pursuant to the preceding paragraph;
 - (8) If the other party violates Applicable Laws and Ordinances;
 - (9) If the other party breaches representations and warranties provided in paragraph (1) of Article 20, violates paragraph (2) of the same article, or does not respond to the request under paragraph (3) of the same article.
4. Paragraphs (7), (9), (10) and (11) of Article 3 (Payment and handling of the Research Funds), paragraphs (2), (4) and (5) of Article 4 (Implementation of the Research), paragraph (3) of Article 6 (Safety Information), Article 9 (Handling of Personal Information), Article 10 (Handling of Samples), Article 11 (Compensation and Other Measures), Article 15 (Publication of the Research Results), Article 16 (Ownership, Retention and Use of Source documents), Article 17 (Handling of Intellectual Property Rights), paragraphs (4), (5), (6) and (8) of Article 18 (Conflicts of Interest Management), Article 19 (Confidentiality), Article 21 (Legal Compliance), Article 23 (Damages), Article 24 (Assignment), Article 26 (Governing Law and Jurisdiction) and Article 27 (Consultation in Good Faith), and any other provisions which by their nature are expected to remain valid shall remain valid even after cancellation, discontinuation or expiration of the Agreement.²⁸

Article 23 (Damages)

²⁸ If any article for the provision or loan of medical devices and goods is added, No. of article which remains valid shall be changed. Please accordingly coordinate article No. as appropriate.

1. Representative Research Institution shall assume indemnity liability for the damage incurred by the intention or fault of Representative Research Institution or Representative Investigator, or a Participating Research Institution or Investigator to subjects of the Research. The agreement between Representative Research Institution and Participating Research Institutions shall indicate which party (Representative Research Institution or the Participating Research Institution) assumes indemnity liability for the damage incurred by the intention or fault of the Participating Research Institution or Investigator thereof to subjects of the Research. However, this shall not apply in cases where Company must directly assume product liability or tort liability towards third parties including the Research Subjects, such as when there is a defect in the Medical Device.
2. If the other party violates the Agreement, each contracting party shall be entitled to request compensation for the damage incurred thereby.
3. The exercise of the right of termination under the preceding paragraph shall not preclude the terminating party from seeking damages.

Article 24 (Assignment)

Neither contracting party hereto may assign rights or obligations arising from the Agreement to any third party, with the exception of Affiliates of the Company, without prior written consent of the other party.

Article 25 (Changes to Agreement)

The Agreement including annexes may only be revised, changed or extended based on a document that bears the signatures and seals of authorized representatives of each contracting party.

Article 26 (Governing Law and Jurisdiction)

The Agreement shall be governed and construed in accordance with the laws of Japan, and the ** District Court shall be the court of first instance with exclusive jurisdiction over any dispute arising in connection with the Agreement.

Article 27 (Consultation in Good Faith)

The contracting parties hereto shall consult with each other in good faith to determine any matters not provided for in the Agreement or other doubts arising in connection herewith.

In witness whereof, the contracting parties hereto have caused this Agreement to be executed by their representatives in duplicate, each party retaining one (1) copy thereof respectively.

XX/XX/20XX²⁹

Representative Research Institution
[Address]
[Organization]
[Title/Name]

Company³⁰
[Address]
[Organization]
[Title/Name]

I read, understood and will comply with all terms of the Agreement above.

XX/XX/20XX
Representative Investigator
(Signature)
[Organization]
[Title/Name]

²⁹ Corresponding to Article 88, item (i) of the Ordinance
³⁰ Corresponding to Article 88, item (iii) of the Ordinance

Annex 1. Participating Research Institutes

Participating Research Institution	Investigator	Organization, Title, etc.	Emergency medical center

Annex 2. Milestone³¹

Description/amount of payment	Milestone
First: Expenses necessary for the review by Certified Review Board XXXXX yen (Scheduled completion date: XX, 20XX)	In application to Certified Review Board [or] Within XX days after the execution of the Agreement
Second: Expenses necessary for implementation of the research XXXXX yen (Scheduled completion date: XX, 20XX)	When, after submission of Trial Plan to the Minister of Health, Labour and Welfare, the implementation of the Research is approved by Manager of the Research Institution (however, after registered in j RCT)
Third: Expenses for implementation stage XXXXX yen (Scheduled completion date: XX, 20XX)	Setting up payment depending on the progress of enrollment of subjects
Xth: Expenses for completion stage XXXXX yen (Scheduled completion date: XX, 20XX)	When completion of the Research is reported to Certified Review Board [or] When database for statistical analysis is fixed
Final: Expenses for completion stage XXXXX yen (Scheduled completion date: XX, 20XX)	When Primary Endpoint Report, and Clinical Study Report and its summary for the Research are received by Company and results of the Research are recorded in j RCT.

³¹ This should be adjusted depending on actual conditions. The Annex 2 corresponds to Article 3, paragraph (2) and Article 22, paragraph (3) in this template.

Annex 3. Breakdown of the Research Funds³²

Payee	Item	Detail		Total (Direct cost)	Remark
		Unit price	Person/day/unit		
	Expenses for consigned operations			yen	Registration, Office, DM service
	Insurance premiums			yen	
	Expenses to be reimbursed to subjects			yen	
	Expenses for storage of materials			yen	
	XX				
Total		----		yen	

³² Corresponding to Article 88, item (xiii) of the Ordinance

Annex 4. Duties of Representative Investigator (including duties as Investigator)

Matter	Applicable Law/Ordinance
Description	
1. Duties of Representative Investigator	Article 4, paragraph (2) of the Act; Articles 10 and 11 of the Ordinance
<p>(1) Have scientific knowledge and medical experience and knowledge, and receive adequate education and training.</p> <p>(2) Fully consider from an ethical and scientific perspective.</p> <p>(3) Conduct the clinical research in compliance with ordinances and Protocol.</p> <p>(4) Confirm from time to time that the research is appropriately conducted and take measures necessary to ensure appropriate research implementation.</p> <p>(5) When entrusting part of the operations of the research, perform necessary and appropriate supervision.</p> <p>(6) At the request of Manager of the Representative Research Institution, submit materials required by the manager and provide other necessary cooperation.</p>	
2. Responses at the onset of diseases	Article 4, paragraph (2) of the Act; Article 13 of the Ordinance
<p>(1) Prepare Procedures for responses at the onset of diseases suspected of being caused by implementation of the Research in compliance with Protocol, and respond according to the Procedures.</p> <p>(2) At the onset of diseases suspected of being caused by implementation of the Research, take necessary measures including discontinuation of the Research.</p>	
3. Preparation of Protocol	Article 4, paragraph (2) of the Act; Article 14 of the Ordinance
Prepare Protocol of the Research, which describes the matters listed in Article 14, items (1) to (18) of the Ordinance.	
4. Control of nonconformity	Article 3, paragraph (2), item (i) of the Act; Article 15 of the Ordinance
<p>(1) When becoming aware of the Research not complying with Applicable Laws and Ordinances or Protocol, promptly report that to Manager of Representative Research Institution and inform other Investigators thereof.</p> <p>(2) In the case of (1), if particularly significant incompliance is found, promptly seek the opinion of Certified Review Board.</p>	
5. Buildings and other facilities	Article 3, paragraph (2), item (ii) of the Act; Article 16 of the Ordinance
Depending on the content of the Research, confirm that the Representative Research Institution has facilities or equipment necessary for emergency medical service unless cooperation with other medical institutions ensures in advance the system necessary for emergency medical service in subjects of the Research.	
6. Monitoring	Article 3, paragraph (2), item (iii) of the Act; Article 17 of the Ordinance
<p>(1) Prepare Procedures for monitoring for implementation of monitoring as specified in the Procedures and Protocol.</p> <p>(2) Do not have the Researchers monitor the operations of which the parties are directly in charge.</p> <p>(3) Have those who engage in monitoring report results of the monitoring to Investigator.</p> <p>(4) When receiving notification of monitoring results under the above (3) from other Investigators,</p>	

inform other Investigators of the content of such notification.	
7. Audit	Article 3, paragraph (2), item (iii) of the Act; Article 18 of the Ordinance
<p>(1) As necessary, prepare Procedures for audit for each Protocol for implementation of audit as specified in the Procedures and Protocol.</p> <p>(2) Do not have the Researchers and those who engage in the monitoring conduct audit.</p> <p>(3) Have those who engage in audit report results of the audit to Investigator.</p> <p>(4) When receiving notification of audit results under the above (3) from other Investigators, inform other Investigators of the content of such notification.</p>	
8. Instructions for those who engage in monitoring and audit	Article 3, paragraph (2), item (iii) of the Act; Article 19 of the Ordinance
For monitoring and audit conducted by those who engage in monitoring and those who engage in audit, provide necessary instructions and management.	
9. Compensation to subjects of the research	Article 3, paragraph (2), item (iv) of the Act; Article 20 of the Ordinance
For implementation of the Research, beforehand establish the system to provide insurance and medical care and take other necessary measures in preparation for compensation (compensation, medical expenses, medical allowance) and medical care for subjects of the Research in the event of injuries associated with the Research.	
10. Preparation of Conflicts of Interest Management Plan	Article 3, paragraph (2), item (v) of the Act; Article 21 of the Ordinance
<p>(1) Develop standards for appropriate handling for the following involvements (hereinafter “Conflicts of Interest Management Standards” in this matter) and notify other Investigators:</p> <p>A) Provision of research funds and other involvement by Company (including special parties concerned) for the Research</p> <p>B) The provision of donations, and rewards for writing and speaking and other services, and other involvement by the company of medical devices for use in the Research, to 1) Representative Investigator, 2) other Investigators, 3) Sub-investigator, 4) persons responsible for statistical analysis and 5) persons listed in Protocol, who obviously benefit from implementation of the Research</p> <p>(2) Seek the opinion of Manager of the Representative Research Institution or the head of the institution about involvements under the preceding paragraph, and receive the report describing results of the confirmation.</p> <p>(3) In the light of the content of the report under (2), prepare the plan specifying the method of appropriate handling for the involvement by Company (hereinafter “Conflicts of Interest Management Plan” in this matter).</p> <p>(4) Seek the opinion of Certified Review Board about Conflicts of Interest Management Standards and Conflicts of Interest Management Plan.</p> <p>(5) For involvement by Company, in accordance with Conflicts of Interest Management Standards and Conflicts of Interest Management Plan, perform appropriate management.</p>	
11. Response to opinion of Certified Review Board	Article 3, paragraph (2), item (vi) of the Act; Article 22 of the Ordinance
<p>(1) When receiving any opinion from Certified Review Board, promptly report the content of the opinion to Manager of Representative Research Institution and inform other Investigators thereof.</p> <p>(2) In the case of (1), take necessary measures respecting the opinion of Certified Review Board.</p>	
12. Response to complaints and inquiries	Article 3, paragraph (2), item (vi) of the Act; Article 23 of the Ordinance
For appropriate and prompt response to complaints and inquiries about the Research, establish the contact	

for complaints and inquiries, prepare procedures for the response to complaints and inquiries, and develop other necessary systems.	
13. Publication of information	Article 3, paragraph (2), item (vi) of the Act; Article 24 of the Ordinance
<p>(1) Publish the matters set forth in Applicable Laws and Ordinances by recording in the database developed by the Ministry of Health, Labour and Welfare (Japan Registry of Clinical Trials: j RCT). The same is true when they are amended.</p> <p>(2) Prepare Primary Endpoint Report within one year in principle of the end of the period for collecting data for primary endpoints, and Clinical Study Report and its summary within one year in principle of the end of the period for collecting data for all endpoints.</p> <p>(3) Under the provision of (2), when preparing Primary Endpoint Report or Clinical Study Report and its summary, submit it to Manager of Representative Research Institution without delay, and, under the provision of (1), publish Primary Endpoint Report or the summary of Clinical Study Report and inform other Investigators thereof.</p> <p>(4) In submission under the provision of (3), seek the opinion of Certified Review Board in advance and publish as specified in (1) within one month of the date of the opinion. In this case, when submitting the summary of Clinical Study Report as specified in (1), promptly submit the following documents being attached to the summary of Clinical Study Report to the Minister of Health, Labour and Welfare.</p> <p>A) Protocol</p> <p>B) Statistical Analysis Plan (if prepared)</p> <p>(5) In the submission under the provision of (4), promptly report to Manager of Representative Research Institution and inform other Investigators thereof.</p>	
14. Ensuring the quality of medical devices	Article 3, paragraph (2), item (vi) of the Act; Article 25 of the Ordinance
<p>(1) Depending on the content of the clinical research, conduct the Research with the medical devices manufactured, taking necessary measures to ensure the quality of the Medical Device.</p> <p>(2) If a clinical research with an unapproved or off-label Medical Device is conducted or if determined to be necessary depending on the content of the clinical research, create or obtain the records on the Medical Device as listed below.</p> <p>A) Manufacturing date, number and code of the Medical Device, and other records on manufacturing of the Medical Device.</p> <p>B) If the Medical Device is obtained, records of quantity and date thereof.</p> <p>C) Records on disposal of the Medical Device</p>	
15. Considerations for environment	Article 3, paragraph (2), item (vi) of the Act; Article 26 of the Ordinance
Make necessary considerations not to have an adverse impact on environment.	
16. Handling of personal information	Article 10 of the Act; Articles 27 to 38 of the Ordinance
<p>(1) For handling personal information, identify the purpose of use as specifically as possible.</p> <p>(2) Do not obtain personal information through deception or by other wrongful means.</p> <p>(3) Do not handle the personal information obtained associated with implementation of the Research beyond the scope of consent given by subjects of the Research in advance.</p> <p>(4) Keep personal information accurate and updated within the scope necessary for achievement of the purpose of use.</p> <p>(5) Take necessary measures for the prevention of the leaking, loss or damage and for the proper management of personal information, and set implementation rules specifying the method.</p> <p>(6) When using personal information to conduct the Research, comply with Applicable Laws and Ordinances, and obtain consent from subjects of the Research.</p>	

<p>(7) If a subject of the Research requests the purpose of use of the personal information possessed by himself/herself and the Representative Research Institution (hereinafter “Possessed Personal Information” in this matter) to be notified, notify the requesting person thereof without delay (excluding exceptions provided in Applicable Laws and Ordinances).</p> <p>(8) If a subject of the Research requests the information identifying the subject of Possessed Personal Information to be disclosed, disclose such personal information to the requesting person without delay (excluding exceptions provided in Applicable Laws and Ordinances).</p> <p>(9) If it is determined not to disclose all or part of requested personal information because of falling within any exception under (8) or if there is not the personal information requested to be disclosed, notify the requesting subject of the Research thereof without delay.</p> <p>(10) If a subject of the Research requests the correction, addition or deletion (hereinafter “Corrections” in this matter) of the information identifying the subject of Possessed Personal Information for the reason that the content of the information is not true, perform necessary examinations and make Corrections to the content based on the results without delay.</p> <p>(11) If a subject of the Research requests the suspension of use or erasure (hereinafter “Suspension of Use” for the matter) of Possessed Personal Information for the reason that the information was inappropriately obtained or that the information is handled for any purpose other than the purpose of use, and such request is appropriate, suspend the use of the personal information to the extent necessary to correct the violation without delay (excluding exceptions provided in Applicable Laws and Ordinances).</p> <p>(12) As procedures to respond to the request for the disclosure of Possessed Personal Information, specify the matters listed in Applicable Laws and Ordinances.</p> <p>(13) If it is determined not to make notification of the purpose of use under (7), not to disclose Possessed Personal Information under (8), not to make Corrections under (10), or not to perform Suspension of Use under (11), notify the subject of the Research of such determination attempting to explain the reason.</p>	
17. Submission of Trial Plan	Article 5, paragraph (1) of the Act; Article 39 of the Ordinance
<p>(1) Before the start of Specified Clinical Research, submit Trial Plan in Form 1 under the Ordinance to the Minister of Health, Labour and Welfare.</p> <p>(2) In the submission under (1), promptly notify the Certified Review Board provided in the Trial Plan thereof, and report to Manager of Representative Research Institution and inform other Investigators thereof.</p>	
18. Procedures in submission of Trial Plan to the Minister of Health, Labour and Welfare	Article 5, paragraph (3) of the Act; Article 40 of the Ordinance
<p>(1) When attempting to seek the opinion of Certified Review Board, submit documents listed in Article 40, paragraph (1) of the Ordinance to the Certified Review Board.</p> <p>(2) After seeking the opinion of Certified Review Board, submit documents specified in the documents under (1) and other documents requested by Manager of the Representative Research Institution for the approval of implementation of the Specified Clinical Research at the Research Institution by the manager.</p>	
19. Submission of revised Trial Plan	Article 6, paragraphs (1) and (3) of the Act; Articles 41 to 43 of the Ordinance
<p>(1) For revision of Trial Plan, submit revised Trial Plan and a notification in Form 2 under the Ordinance by the following deadlines:</p> <p>A) Without delay after modification of the progress of Specified Clinical Research, for the matters involving the progress of those specified in Article 5, paragraph (1), item (v) of the Act; or</p> <p>B) Before modification, for the matters other than those listed under A).</p> <p>(2) For the change in the name of the person who engages in Specified Clinical Research, which is not associated with the change in the person who engages in Specified Clinical Research, or the change associated with that in the name of region or parcel number (minor change), notify Certified Review Board listed in the protocol of content thereof within ten days of the change date, and submit a</p>	

notification in Form 3 under the Ordinance to the Minister of Health, Labour and Welfare.	
20. Prohibition of the change in Certified Review Board	Article 44 of the Ordinance
After submission of Trial Plan to the Minister of Health, Labour and Welfare, except the case Certified Review Board is abolished or other unavoidable circumstances, do not change the Certified Review Board listed in Trial Plan.	
21. Notification of discontinuation of the Research	Article 8 of the Act; Article 45 of the Ordinance
In discontinuation of the Research, within ten days of the discontinuation, notify the Certified Review Board listed in the Trial Plan thereof and submit a notification in Form 4 under the Ordinance to the Minister of Health, Labour and Welfare.	
22. Explanation to subjects of the Research and obtaining their consent	Article 9 of the Act; Articles 46 to 52 of the Ordinance
Explain about the matters set forth in Applicable Laws and Ordinances to subjects of the Research in compliance with Applicable Laws and Ordinances, and obtain written consent from them. If all or part of the consent is withdrawn or rejected, take measures depending on the content of the withdrawal or rejection and explain thereon to subjects of the Research without delay (excluding exceptions provided in Applicable Laws and Ordinances).	
23. Retention of records of the Research	Article 12 of the Act; Article 53 of the Ordinance
<p>(1) For five years after the date of completion of the Research, create records on dates and locations with use of the Medical Device, matters identifying subjects of the Research, matters involving clinical practice and examinations in them, matters involving participation in the Research, and matters necessary for implementation of the Research, and retain such records along with Protocol, Trial Plan, documents for explanation to and obtaining consent from subjects of the Research, the document prepared by itself such as Clinical Study Report or its copy, the document on opinions by review received from Certified Review Board, documents concerning monitoring and audit, Source Documents, this agreement, document summarizing the Medical Device for use in the Research, and records created or obtained under 14. (2) and other documents necessary for implementation of the Research.</p> <p>(2) If records specified under (1) are modified, record the name of the person who modifies and the date of the modification, and retain them along with modified records.</p>	
24. Report of diseases to Certified Review Board	Article 13 of the Act; Article 54 of the Ordinance
Regarding implementation of the Research, when recognizing the onset of any disease set forth in Applicable Laws and Ordinances, report thereon during the period provided in Applicable Laws and Ordinances to Manager of Representative Research Institution and then to Certified Review Board, and promptly inform other Investigators thereof.	
25. Report of diseases to the Minister of Health, Labour and Welfare	Article 14 of the Act; Article 56 of the Ordinance
Regarding implementation of the Research, when recognizing the onset of any disease set forth in Applicable Laws and Ordinances, report it to the Minister of Health, Labour and Welfare as provided in Applicable Laws and Ordinances	
26. Periodic report to Certified Review Board	Article 17, paragraph (1) of the Act; Article 59 the Ordinance
<p>(1) Regarding the status of implementation of the Research, report the matters specified in the items of Article 59, paragraph (1) of the Ordinance to Manager of Representative Research Institution and then to Certified Review Board provided in the Trial Plan, and promptly inform other Investigators thereof.</p> <p>(2) In principle, the report under (1) shall be made within two months after expiration of the period, every one year starting from the date of submission of Trial Plan to the Minister of Health, Labour and Welfare.</p>	

27. Periodic report to the Minister of Health, Labour and Welfare	Article 18 of the Act; Article 60 of the Ordinance
<p>(1) Regarding the status of implementation of the Research, report the name of Certified Review Board provided in Trial Plan, appropriateness of the continuation of the Specified Clinical Research by the Certified Review Board, and the number of subjects who participate in the Research, to the Minister of Health, Labour and Welfare.</p> <p>(2) The report under (1) shall be made within one month after the date on which Certified Review Board offers any opinion.</p>	
28. Obligation of confidentiality	Articles 11 and 21 of the Act; Article 61 of the Ordinance
Do not disclose any secret concerning subjects of the Research obtained in connection with implementation of the Research.	
29. Creation and retention of records on those whose Samples existing are used for the Research	Articles 12 and 21 of the Act; Article 62 of the Ordinance
When creating and retaining records on those whose Samples existing are used for the Research, attempt to take necessary measures.	
30. Response to access and inspection by authorities	Articles 19, 20 and 35 of the Act
Following any access and inspection, collection of reports, emergency order, order for improvement or order for suspension (hereinafter collectively "Access and Inspections" in this matter) by authorities, report the fact, course and results of the Access and Inspections to Company without delay.	

If Applicable Laws and Ordinances are amended, make replacements as appropriate in accordance with amended Applicable Laws and Ordinances.

Annex 5. Duties of Investigators in Participating Research Institutions

Matter	Applicable Law/Ordinance
Applicable Law/Ordinance	
1. Duties of Investigators	Article 4, paragraph (2) of the Act; Articles 10, 11 and 12 of the Ordinance
<p>(1) Have scientific knowledge and medical experience and knowledge, and receive adequate education and training.</p> <p>(2) Fully consider from an ethical and scientific perspective.</p> <p>(3) Conduct clinical research in compliance with ordinances and Protocol.</p> <p>(4) Confirm from time to time that the research is appropriately conducted and take measures necessary to ensure appropriate research implementation.</p> <p>(5) When entrusting part of the operations of research, perform necessary and appropriate supervision.</p> <p>(6) At the request of Manager of Participating Research Institution, submit materials required by the manager and provide other necessary cooperation.</p> <p>(7) Share the necessary information related to the Research with Researchers of other Participating Research Institutions.</p>	
2. Responses at the onset of diseases	Article 4, paragraph (2) of the Act; Article 13 of the Ordinance
<p>(1) At the onset of diseases suspected of being caused by implementation of the Research in compliance with Protocol, respond according to the Procedures.</p> <p>(2) At the onset of diseases suspected of being caused by implementation of the Research, take necessary measures including discontinuation of the Research.</p>	
3. Preparation of Protocol	Article 4, paragraph (2) of the Act; Article 14 of the Ordinance
Prepare Protocol of the Research, which describes the matters listed in Article 14, items (1) to (18) of the Ordinance.	
4. Control of nonconformity	Article 3, paragraph (2), item (i) of the Act; Article 15 of the Ordinance
When becoming aware of the Research not complying with Applicable Laws and Ordinances or Protocol, promptly report to Managers of Participating Research Institutions and notify Representative Investigator thereof.	
5. Buildings and other facilities	Article 3, paragraph (2), item (ii) of the Act; Article 16 of the Ordinance
Depending on the content of the Research, confirm that Participating Research Institutions have facilities or equipment necessary for emergency medical service unless cooperation with other medical institutions ensures in advance the system necessary for emergency medical service in subjects of the Research.	
6. Monitoring	Article 3, paragraph (2), item (iii) of the Act; Article 17 of the Ordinance
<p>(1) Prepare Procedures for monitoring to ensure the implementation of monitoring as specified in the Procedures and Protocol.</p> <p>(2) Do not have the Researchers monitor the operations of which the parties are directly in charge.</p> <p>(3) Have those who engage in monitoring report results of the monitoring to Investigator.</p> <p>(4) As necessary, notify Representative Investigator of the content of the report under (3).</p>	
7. Audit	Article 3, paragraph (2), item (iii) of the Act; Article 18

	of the Ordinance
<p>(1) As necessary, prepare Procedures for audit for each Protocol to ensure the implementation of audit as specified in the Procedures and Protocol.</p> <p>(2) Do not have the Researchers and those who engage in the monitoring conduct audit.</p> <p>(3) Have those who engage in audit report results of the audit to Investigator.</p> <p>(4) As necessary, notify Representative Investigator of the content of the report under (3).</p>	
8. Instructions for those who engage in monitoring and audit	Article 3, paragraph (2), item (iii) of the Act; Article 19 of the Ordinance
For monitoring and audit by those who engage in monitoring and those who engage in audit, provide necessary instructions and management.	
9. Compensation to subjects of the research	Article 3, paragraph (2), item (iv) of the Act; Article 20 of the Ordinance
For implementation of the Research, beforehand establish the system and take other necessary measures in preparation for compensation and medical care for subjects of the Research in the event of injuries associated with the Research. If such injuries are covered, necessary information shall be provided at the request of Representative Investigator or Company.	
10. Preparation of Conflicts of Interest Management Plan	Article 3, paragraph (2), item (v) of the Act; Article 21 of the Ordinance
<p>(1) In accordance with Conflicts of Interest Management Standards prepared by Representative Investigator, seek opinions of Managers of Participating Research Institutions or the head of the institution to which investigators belong regarding the following involvements and receive the report describing results thereof.</p> <p>A) Provision of research funds and other involvement by Company (including special parties concerned) for the Research</p> <p>B) The provision of donations, and rewards for writing and speaking and other services, and other involvement by the company of medical devices for use in the Research, to 1) Investigator, 2) Sub-investigator, 3) persons responsible for statistical analysis and 4) persons listed in Protocol, who obviously benefit from implementation of the Research</p> <p>(2) In the light of the content of the report under (1), prepare the plan specifying the method of appropriate handling for the involvement by Company (hereinafter “Conflicts of Interest Management Plan” in this matter).</p> <p>(3) For involvement by Company, in accordance with Conflicts of Interest Management Standards and Conflicts of Interest Management Plan, perform appropriate management.</p>	
11. Response to opinion of Certified Review Board	Article 3, paragraph (2), item (vi) of the Act; Article 22 of the Ordinance
<p>(1) When being informed by Representative Investigator of the content of opinions of Certified Review Board, promptly report the content thereof to Managers of Participating Research Institutions.</p> <p>(2) In the case of (1), take necessary measures respecting the opinion of Certified Review Board.</p>	
12. Response to complaints and inquiries	Article 3, paragraph (2), item (vi) of the Act; Article 23 of the Ordinance
For appropriate and prompt response to complaints and inquiries about the Research, establish the contact for complaints and inquiries, prepare procedures for the response to complaints and inquiries, and develop other necessary systems.	
13. Publication of information	Article 3, paragraph (2), item (vi) of the Act; Article 24 of the Ordinance
(1) Prepare Primary Endpoint Report within one year in principle of the end of the period for collecting data for primary endpoints, and Clinical Study Report and its summary within one year	

<p>in principle of the end of the period for collecting data for all endpoints.</p> <p>(2) When being informed by Representative Investigator that the investigator has submitted the summary of Clinical Study Report to the Minister of Health, Labour and Welfare, promptly report the content thereof to Managers of Participating Research Institutions.</p>	
14. Ensuring the quality of medical devices	Article 3, paragraph (2), item (vi) of the Act; Article 25 of the Ordinance
<p>(1) Depending on the content of the clinical research, conduct the Research with the Medical Device manufactured, taking necessary measures to ensure the quality of medical devices.</p> <p>(2) If a clinical research with an unapproved or off-label Medical Device is conducted or if determined to be necessary depending on the content of the clinical research, create or obtain the records on the Medical Device as listed below.</p> <p>A) Manufacturing date, number or code of the Medical Device, and other records on manufacturing of the Medical Device.</p> <p>B) If the Medical Device is obtained, records of quantity and date thereof.</p> <p>C) Records on disposal of the Medical Device</p>	
15. Considerations for environment	Article 3, paragraph (2), item (vi) of the Act; Article 26 of the Ordinance
<p>Make necessary considerations not to have an adverse impact on environment.</p>	
16. Handling of personal information	Article 10 of the Act; Articles 27 to 38 of the Ordinance
<p>(1) For handling personal information, identify the purpose of use as specifically as possible.</p> <p>(2) Do not obtain personal information through deception or by other wrongful means.</p> <p>(3) Do not handle the personal information obtained associated with implementation of the Research beyond the scope of consent given by subjects of the Research in advance.</p> <p>(4) Keep personal information accurate and updated within the scope necessary for achievement of the purpose of use.</p> <p>(5) Take necessary measures for the prevention of the leaking, loss or damage and for the proper management of personal information, and set implementation rules specifying the method.</p> <p>(6) When using personal information to conduct the Research, comply with Applicable Laws and Ordinances, and obtain consent from subjects of the Research.</p> <p>(7) If a subject of the Research requests the purpose of use of the personal information possessed by himself/herself and the Research Institution (hereinafter “Possessed Personal Information” in this matter) to be notified, notify the requesting person thereof without delay (excluding exceptions provided in Applicable Laws and Ordinances).</p> <p>(8) If a subject of the Research requests the information identifying the subject of Possessed Personal Information to be disclosed, disclose such personal information to the requesting person without delay (excluding exceptions provided in Applicable Laws and Ordinances).</p> <p>(9) If it is determined not to disclose all or part of requested personal information because of falling within any exception under (8) or if there is not the personal information requested to be disclosed, notify the requesting subject of the Research thereof without delay.</p> <p>(10) If a subject of the Research requests the correction, addition or deletion (hereinafter “Corrections” in this matter) of the information identifying the subject of Possessed Personal Information for the reason that the content of the information is not true, perform necessary inspections and make Corrections to the content based on the results without delay.</p> <p>(11) If a subject of the Research requests the suspension of use or erasure (hereinafter “Suspension of Use” in this matter) of Possessed Personal Information for the reason that the information was inappropriately obtained or that the information is handled for any purpose other than the purpose of use, and such request is appropriate, suspend the use of the personal information to the extent necessary to correct the violation without delay (excluding exceptions provided in Applicable Laws and Ordinances).</p>	

<p>(12) As procedures to respond to the request for the disclosure of Possessed Personal Information, specify the matters listed in Applicable Laws and Ordinances.</p> <p>(13) If it is determined not to make notification of the purpose of use under (7), not to disclose Possessed Personal Information under (8), not to make Corrections under (10), or not to perform Suspension of Use under (11), notify the subject of the Research of such determination attempting to explain the reason.</p>	
17. Submission of Trial Plan	Article 5, paragraph (1) of the Act; Article 39 of the Ordinance
When being informed by Representative Investigator that the investigator has submitted the Trial Plan specified in Article 5, paragraph (1) of the Act to the Minister of Health, Labour and Welfare, promptly report the content thereof to Managers of Participating Research Institutions.	
18. Approval of Trial Plan by Research Institution	Article 5, paragraph (3) of the Act; Article 40 of the Ordinance
After seeking the opinion of Certified Review Board through Representative Investigator, submit the documents specified in Article 40, paragraph (1) of the Ordinance and other documents requested by Managers of Participating Research Institutions and receive approval from such managers for feasibility of the Specified Clinical Research in Participating Research Institutions.	
19. Explanation to subjects of the Research and obtaining their consent	Article 9 of the Act; Articles 46 to 52 of the Ordinance
Explain about the matters set forth in Applicable Laws and Ordinances to subjects of the Research in compliance with Applicable Laws and Ordinances, and obtain written consent from them. If all or part of the consent is withdrawn or rejected, take measures depending on the content of the withdrawal or rejection and explain thereon to subjects of the Research without delay (excluding exceptions provided in Applicable Laws and Ordinances).	
20. Retention of records of the Research	Article 12 of the Act; Article 53 of the Ordinance
<p>(1) For five years after the date of completion of the Research, create records on dates and locations with use of the Medical Device, matters identifying subjects of the Research, matters involving clinical practice and examinations in them, matters involving participation in the Research, and matters necessary for implementation of the Research, and retain such records along with documents for explanation to and obtaining consent from subjects of the Research, the document prepared by itself such as Clinical Study Report or the copy, the document on opinions by review received from Certified Review Board, documents concerning monitoring and audit, Source Documents, document summarizing medical devices for use in the Research, and records created or obtained under 14. (2) and other documents necessary for implementation of the Research.</p> <p>(2) If records specified under (1) are modified, record the name of the person who modifies and the date of the modification, and retain them along with modified records.</p>	
21. Report of diseases to Certified Review Board	Article 13 of the Act; Article 54 of the Ordinance
<p>(1) Regarding implementation of the Research, when recognizing the onset of any disease set forth in Applicable Laws and Ordinances, report thereon during the period provided in Applicable Laws and Ordinances to Managers of Participating Research Institutions, and then notify Representative Investigator thereof.</p> <p>(2) When being informed by Representative Investigator that the investigator has reported diseases to Certified Review Board, promptly report the content thereof to Managers of Participating Research Institutions.</p>	
22. Report of diseases to the Minister of Health, Labour and Welfare	Article 14 of the Act; Article 56 of the Ordinance
(1) Regarding implementation of the Research, when recognizing the onset of any disease set forth in Applicable Laws and Ordinances, report thereon to Managers of Participating Research Institutions within the period provided in Applicable Laws and Ordinances and then notify Representative	

Investigator thereof.	
(2) When being informed by Representative Investigator that the investigator has reported diseases to the Minister of Health, Labour and Welfare, promptly report the content thereof to Managers of Participating Research Institutions.	
23. Periodic report to Managers of Participating Research Institutions	Article 17, paragraph (1) of the Act; Article 59 the Ordinance
Regarding the status of implementation of the Research, report the matters specified in the items of Article 59, paragraph (1) of the Ordinance to Managers of Participating Research Institutions.	
24. Obligation of confidentiality	Articles 11 and 21 of the Act; Article 61 of the Ordinance
Do not disclose any secret concerning subjects of the Research obtained in connection with implementation of the Research.	
25. Creation and retention of records on those whose Samples existing are used for the Research	Articles 12 and 21 of the Act; Article 62 of the Ordinance
When creating and retaining records on those whose Samples existing are used for the Research, attempt to take necessary measures.	
26. Response to access and inspection by authorities	Articles 19, 20 and 35 of the Act
Following any access and inspection, collection of reports, emergency order, order for improvement or order for suspension (hereinafter collectively "Access and Inspections" in this matter) by authorities, report the fact, course and results of the Access and Inspections to Representative Investigator without delay.	

If Applicable Laws and Ordinances are amended, make replacements as appropriate in accordance with amended Applicable Laws and Ordinances.

Annex 6. Materials for Publications and Schedule (pertinent to Article 13, paragraph (2), item (i))

Materials for Publications	Deadline of Submission to Company by Representative Investigator	Deadline of response to Representative Investigator by Company
A manuscript, and figures and tables in accordance with ICMJE and the requirements for manuscript submission of the journal to which the manuscript is scheduled to be submitted (including Supplemental data)	By XX days before the scheduled date of the submission	Within XX days of the receipt from Representative Investigator
An abstract as specified by an academic conference for which a subject of speech is scheduled to be registered	By XX days before the deadline of subject registration for the academic conference	Within XX days of the receipt from Representative Investigator
Materials for Publications as specified by an academic conference at which they are scheduled to be presented (slide, poster manuscript, etc.)	By XX days before the first day of the academic conference	Within XX days of the receipt from Representative Investigator
Others (manuscripts, and figures and tables for press releases)	By XX days before the scheduled publication date	Within XX days of the receipt from Representative Investigator

Annex 7. Ownership and Use of Source Documents (pertinent to Article 14, paragraph (1))

Source Documents (Sample)	Representative Research Institution or Representative Investigator (including Participating Research Institution)	Company
Medical record data	○	--
EDC input data	○	△
Case report form (CRF)	○	--
Statistical Analysis Plan	○	△
Dataset for statistical analysis (fixed)	○	△
[Add more if necessary]		

○ means (Ownership).

△ means (Right to use)³³

³³ If the right to use is on the side of Company or the right itself belongs to Company, the consent thereto needs to be obtained from subjects of the clinical research in advance.

Annex 8. Provided Goods and Loaned Goods (pertinent to Article 7 and/or 8)

1. Provided Goods
2. Loaned Goods