AMDD (American Medical Devices and Diagnostics Manufacturers' Association)
Investigator-Initiated Clinical Research Agreement (Sample)

This document is a sample investigator-initiated clinical research agreement applicable to the situation where a company, etc. provides funds to a research institution, etc. pursuant to an agreement to conduct investigator-initiated clinical research in which its medical devices are assessed. It was prepared by AMDD with reference to the Ethical Guidelines for Medical and Health Research Involving Human Subjects (Ministry of Education, Culture,Sports, Science and Technology and Ministry of Health, Labor and Welfare, 2014), the Guideline Concerning Clinical Research Using Approved Medical Devices (the Japan Federation of Medical Devices Associations, April 1, 2015), Q&A Concerning Involvement of Business Operators in Clinical Research (the Japan Fair Trade Council of the Medical Device Industry Notification No. 2497, July 30, 2015), and the Investigator-Initiated Clinical Research Agreement (Sample) of the Japanese Association of Pharmaceutical Medicine (JAPhMed).

AMDD assumes no responsibility or liability whatsoever for any damage to users or third parties as a result of the use of this document. Users are required to exercise their own judgment and responsibility in using this sample agreement.

Investigator-Initiated Clinical Research Agreement [1]

This Investigator-Initiated Clinical Research Agreement (hereinafter "the Agreement") dated as of XXXXXXX is entered into by and between [Name of Medical Institution] (hereinafter "Research Institution") and [Name of Company] (hereinafter "Company")[2] concerning implementation of [Title of Research] (hereinafter "the Research") for [Name of Medical Device] (hereinafter "the Medical Device"), wherein [Name of Investigator] (hereinafter "Investigator") is the Investigator.

Article 1. Purpose of the Agreement

The purpose of the Agreement is to prescribe the relationship between the Research Institution and the Company with respect to research wherein the Company believes that the so-called investigator-initiated research (i.e. clinical research conducted by the Research Institution on the assumption that (i) the Investigator who belongs to the Research Institution proposes the clinical research, prepares an appropriate protocol[3], etc. prior to implementing the research, and implements the clinical research appropriately in accordance with the above protocol, etc., while ensuring the reliability of the research results, and (ii) the Investigator exercises necessary management and supervision to ensure that the above clinical research is implemented appropriately and adverse events are identified and reported, and also assumes final responsibility for the clinical research (including responsibility for funding)) will contribute to the development of the health and welfare of human beings, is meaningful for the accumulation of information about the safety, efficacy, etc. of the Medical Device, and is medically and scientifically important as clinical research.

Article 2. Content of the Research and Consideration

1. The Research Institution shall implement the Research pursuant to the provisions of the Agreement and then prepare a report on the Research (hereinafter "Research Report"), and the Company shall pay the research funding (hereinafter "the Research Funding") prescribed in the Agreement as consideration.
2. The parties hereto confirm that, when implementing the Research, the Research Institution shall assume responsibility for implementing the Research properly, ensuring the reliability

[1] The title "Agreement on Investigator-Initiated Clinical Research" could also be used.
[2] This sample assumes that two parties (the Research Institution and the Company) are parties to the agreement. However, other possible formats would be to include the Investigator as a party to the agreement and use an agreement between the three parties or to keep the two-party agreement as it is and the Investigator signs the agreement to indicate he/she has read and understood the information contained therein (remember to provide a section where the Investigator affixes signature and seal on the final page.) Please note that in this case, if the Investigator is replaced, the Agreement would have to be renewed to include the new Investigator as a party to the agreement and the new Investigator would have to sign the agreement to indicate he/she had read and understood the information contained therein again.
[3] The term "protocol" used in this context denotes the research plan as a general term not defined in this Agreement. We used the different word "protocol" to distinguish between the general name and the defined name.

of the Research Results, and identifying and reporting adverse events relating to the Research, as defined in each of the items below, and shall have the Investigator assume the same responsibility, etc., and that the Research Institution shall also assume liability for compensation and final responsibility, etc. for monitoring and audits.

(1) Implementing the Research properly

Conducting the research in compliance with the ethical principles defined in the Declaration of Helsinki, the Ethical Guidelines for Medical and Health Research Involving Human Subjects (Public Notice of the Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labor and Welfare No. 3 of 2014; hereinafter "the Ethical Guidelines"), ICH-GCP and other related laws, ordinances, regulations and guidelines, etc. and in accordance with the research plan defined in Article 3 and written procedures, etc. that have been reviewed by the Ethical Review Board and approved by the Research Institution.

(2) Ensuring the reliability of the Research Results

The source materials of the Research are accurate, complete and readable and are reported in a timely manner; analysis data and relevant aggregate data based on the source materials (hereinafter "Data") are prepared accurately, and the Research Report and paper, etc. (including presentation slides, etc.) are prepared accurately based on the source materials and the Data.

(3) Identifying and reporting adverse events

When the Investigator learns of the occurrence of a serious adverse event associated with implementation of the Research, the Investigator promptly takes necessary measures and reports the circumstances of the occurrence of the adverse event to the Research Institution. The Research Institution also reports to the Company, the Ethical Review Board and, where necessary, to the Minister of Health, Labor and Welfare, and ensures that compensation or other necessary measures are properly undertaken.

3. The parties hereto confirm that the party which assumes final responsibility for the Research is the Research Institution and not the Company, and that, accordingly, the Company is not under any obligation imposed by Ethical Guidelines or related guidelines or other regulations and except as provided for in Article 4 Paragraph1 Item11 does not play any

part in the planning, implementation or other aspect of the Research.

4. The parties hereto confirm that the Company's payment of the Research Funds is not intended as an inducement, recommendation or non-recommendation to the Research Institution, the Investigator, the research centers stated in Annex 1 that are participating in the Research (hereinafter "Participating Centers") or researchers participating in the Research other than the Investigator who belong to the Research Institution or Participating Centers (hereinafter "Participating Researchers") to buy or not to buy, use or not to use specific products.

Article 3. Particulars of the Research

The particulars of the Research are as prescribed below, and other details are prescribed in the Protocol shown in Annex 2 (hereinafter "Research Plan;" provided, however, that this shall denote the amended version in the event of amendment in accordance with Article 11.)

(1) Name of the Medical Device:

(2) Title of research：

(3) Aim of research ("Aim of the Research"): [Example: To evaluate the safety and utility of ** in *** patients with ***.]

(4) Classification of research (intervention/non-intervention):

(5) Research period:

(6) Name of Research Institution which is entity responsible for the Research[4]：

(7) Investigator (refers to Principal Investigator in case of multicenter study):

(8) Planned number of subjects:

Article 4. Implementation of the Research

1. Regarding implementation of the Research, the Research Institution shall fulfill or adhere to each of the following items and shall also have the Investigator fulfill or adhere to the same.

(1) Implement the Research in accordance with the Research Plan and the conditions of the Agreement[5], and do its best to proceed with and complete the Research according to the schedule prescribed in the Research Plan.

(2) Explain the content of the Research to the subjects of the Research (hereinafter

[4] Refers to the Sponsor under ICH-GCP, and refers to the party stated as the Sponsor in the public database.
[5] If only an outline of the Research Plan is complete at the time of the execution of this Agreement, the parties should have a written agreement regarding the schedule of the Research in some detail.

"Research Subjects") and obtain prior written consent from the Research Subjects for participating in the Research, and then obtain prior written consent from the Research Subjects for accessing their personal information for the purpose of implementing monitoring and audits.

(3) Prioritize the human rights and welfare, etc. of the Research Subjects when implementing the Research and refrain from activities that might adversely affect the safety of Research Subjects even if the consent of the Research Subjects has been obtained.

(4) Comply with the Act on the Protection of Personal Information (Law No. 57 of May 30, 2003; including amendments) and other related laws, ordinances and guidelines, etc. and establish an appropriate framework for the protection of personal information with respect to the handling of personal information of the Research Subjects, etc.

(5) Adhere to Article 2, Paragraph 2, Item 2, and also register information about implementation of the Research with at least one of the following: the International Clinical Trials Registry Platform (ICTRP), the Japan Medical Association Center for Clinical Trials (JMACCT), UMIN-CTR, ClinicalTrials.gov or another public database approved by the World Health Organization (WHO), prior to enrolment of the first Research Subject for the Research, and similarly register information outlining the Research Results after completion or discontinuation of the Research in accordance with Article 15, to ensure the reliability of the Research Results.

(6) Report the progress of the Research to the Company every X months. The Company may also ask for additional reports if deemed necessary.

(7) Record the Data in such a way that it can be accurately reported, interpreted and verified.

(8) Appropriately monitor the Research Institution and Participating Centers. Take factors such as the purpose, design, complexity, scale and endpoints of the Research and whether or not it is a blind study into consideration when determining the scope and method of monitoring.

(9) Appoint a neutral party independent from the Research as the party in charge of audits, and then conduct audits.

(10) Cooperate with audits by the Company when audits are reasonably necessary, for example, for reporting to the regulatory authorities.

(11) Do not allow the Company, its executives or employees or other parties related to the

Company to be involved in the process of preparing Data or the Research Report, and do not allow the Company to view the Data until submission of the Research Report unless there is good reason, for example, at the request of the regulatory authorities. However, if it is indispensable to allow the Company to view or analyze the Data in the interests of the smooth execution of the Research, the Research Institution may, upon clearly specifying in the Research Plan the role to be assigned to the Company and the relevant procedure, allow this in such a way that it is not detrimental to the reliability of the results of the Research or the neutrality of the Research. In this case, the Research Institution shall retain documentary evidence as to why such disclosure of Data to the Company or entrustment of analysis is not detrimental to the reliability of the results of the Research or the neutrality of the Research in accordance with Item (2) of the next paragraph.

2. The Research Institution shall fulfill or adhere to each of the following items in addition to the preceding paragraph.

   (1) Take appropriate measures to ensure the reliability of aggregate data before data locking, such as separating the data management function.

   (2) Retain source materials and documents and other records relating to the Data (Research Results, original copies of the Data, all versions of the Research Plan and written procedures, etc.) in an appropriate manner until the day on which X years have elapsed since the day on which completion or discontinuation of the relevant research was reported or the day on which X years have elapsed since the day on which the final publication of the results of the relevant research was reported, whichever is later. Exercise necessary supervision to ensure anonymity when the documents and other records are destroyed.

3. If the Investigator no longer belongs to the Research Institution or the Investigator is otherwise no longer able to continue performing his or her duties pertaining to the Research, the Research Institution shall immediately notify the Company in writing and shall then determine the Investigator's successor, without delay and with the approval of the Ethical Review Board and the Company. However, if the Investigator wishes to continue conducting the Research in the capacity of the Investigator, the Research Institution may allow the Investigator to maintain the role as Investigator and have his/her successor who

belongs to the Research Institution participate in the Research as a participating physician.[6]

4. If the Research Institution agrees to the participation of participating centers in the Research, the Research Institution shall have these participating centers assume the obligations under Paragraph 1 and Paragraph 2 of this Article and assume responsibility for the performance of obligations by these participating centers. If the Research Institution entrusts part of the Research operations to a third party (hereinafter "Contract Organization"), the Research Institution shall supervise and assume responsibility for the execution of operations entrusted to such parties. If the Research Institution confirmed that a participating center or Contract Organization acted in violation of the ICH-GCP or related laws, ordinances, regulations or guidelines, etc., the Research Institution shall be responsible for examining and executing corrective measures and shall also report to the Company.

Article 5. Ethical Review Board

The Research Institution shall establish internally or entrust to an external party an Ethical Review Board that satisfies the requirements under the Ethical Guidelines, and shall ask for and respect the Ethical Review Board's opinion on the research including the propriety of implementing research, its suspension or discontinuation, and any changes thereto.

Article 6. Payment of Research Funds [Optional: If providing funds】

1. The Company shall pay the Research Institution the Research Funds amounting to XXXXXXXXX yen in total (see Annex 3 for details) as expenses that are fair and reasonable for the Research. The parties hereto confirm that the Research Funds do not include the cost of procuring the Medical Device from the market.

2. The timing of payment of the Research Funds shall be as follows.

   (1) First payment

   XXXXXX yen (excluding consumption tax) Within XX days after a copy of the written opinion from the Ethical Review Board reaches the Company

   (2) Second payment

   XXXXXX yen (excluding consumption tax) On enrolment of XX subjects out of the planned

[6]Another possible approach is to have the research institution to which the Investigator transfers continue with the Research by succeeding to the Agreement through assignment. Please adapt accordingly.

number of subjects

(3) ・・・

(4) Xth payment

XXXXXX yen (excluding consumption tax) On receipt of the final Research Report stated in the Agreement

(5) Final payment

XXXXXX yen (excluding consumption tax) On publication of the paper, etc. concerning the results of the Research or on registration of an outline of the Research Results in accordance with Article 4, Paragraph 1, Item 5 if the paper, etc. was not published

3. The amount stated in the preceding paragraph shall be paid to the account in the name of the Research Institution shown below. Transfer charges shall be borne by the Company.

XXXXXX Bank XXXX Branch Savings/Current A/C XXXXXXX XXXXXXXXXXXX

4. The Research Institution shall send an invoice clearly specifying the title of the research and supporting documents to the Company no later than X days before each of the payments stated in Paragraph 2 of this Article.

5. The Company may, upon consultation with the Research Institution, refuse or defer part of the payment specified in this Article if progress on the Research is behind the schedule stated in the Research Plan.

6. The Research Institution shall use the Research Funds only for the purpose of execution of the Research in accordance with the itemization in Annex 3.

7. If the Research Institution uses the Research Funds to purchase general-purpose goods that can be used for purposes other than the Research, such as analysis software, the Research Institution shall use such general-purpose goods solely for the purpose of executing the Research and shall return them to the Company “as they are” promptly after completion or discontinuation of the Research.

8. If there is a surplus in respect of the Research Funds that have already been paid upon completion or discontinuation of the Research, the Research Institution shall return this to the Company.

9. The Research Institution shall submit an accounts report to the Company within XX days after completion of the final payment, and the Company may audit the accounts of the Research Institution relating to the Research.

10. The Research Institution agrees that, pursuant to the Company’s rules on transparency established in accordance with the Transparency Guidelines issued by the Japan

Federation of Medical Devices Association or the Japan Association of Clinical Reagents Industries, the Research Institution will disclose items to be disclosed in accordance with each of the categories of expense specified in said guidelines, with respect to the payment of the Research Funds by the Company pursuant to the Agreement.

11. The Research Institution shall retain documents relating to the Research Funds for seven (7) years after the final payment for the Research.

Article 7. Submission of Notifications and Research Reports

1. The Research Institution shall make reports to the Company at the times specified in each of the items below[7] respectively to share the progress of the Research with the Company.
   (1) ・・・・・
   (2) ・・・・・
   (3) ・・・・・
2. For the final report on the Research, the Research Institution shall submit a Research Report in the Company's indicated format to the Company within XX days after the date of the last hospital visit of the last Research Subject in the Research[8] or the date of discontinuation of the Research or cancellation of the Agreement, whichever comes first.
3. When submitting the Research Report to the Company in accordance with the preceding Paragraph, the Research Institution shall notify the method and timing of registration and publication of the Research Results provided for in Article 15.

Article 8. Measures, etc. Regarding Safety

1. The Company shall provide the Research Institution with up-to-date information regarding safety and safe usage of the Medical Device, which is necessary for implementation of the Research.
2. If a serious adverse event occurs, the Research Institution shall, by itself or through the Investigator, take necessary measures such as reporting to the Ethical Review Board and/or the Minister of Health, Labor and Welfare, and shall also be obligated to report side effects, etc. to the Minister of Health, Labor and Welfare pursuant to Article 68-10, Paragraph 1 of the Pharmaceutical and Medical Device Act.
3. The Research Institution shall, by itself or through the Investigator, report the matters prescribed in the each of the following items to the Company within twenty-four (24) hours

[7] Examples of possible report timings include (1) on enrolment of the first Research Subject, (2) on the last hospital visit of the last Research Patient, (3) on the date on which the database of aggregated data is locked, etc.

[8] It is also possible to set the database locking date as the first day of the calculation.

[within X business days] of first learning of such matters.

(1) ・・・・・

(2) ・・・・・

4. The Research Institution shall, by itself or through the Investigator, cooperate as far as possible with the Company in taking action related to safety.
5. The Research Institution shall revise the Research Plan, patient consent form, written procedures, etc. where necessary, based on safety information, etc.

Article 9. Provision of Medical Device or Goods [Optional: If providing Medical Device, etc.]

1. The Company shall provide the Medical Device or goods, etc. prescribed in Annex 4 (hereinafter the “Provided Goods”) to the Research Institution free of charge, to the extent necessary for the Research.
2. The Research Institution shall, by itself or through the Investigator, 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 Research Institution shall, by itself or through the Investigator, 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. The Research Institution shall not use the Provided Goods received from the Company in connection with the Research for any purpose other than the Research, and shall not provide the Provided Goods to the Investigator, Participating Researchers, Participating Centers, Contract Organizations or other third parties for any purpose other than the Research.
4. If the Research is completed or discontinued, or if the Agreement is cancelled, the Research Institution shall return to the Company any surplus of Provided Goods (including general-purpose goods that can be used for purposes other than the Research) received from the Company in their present, existing condition as of completion or discontinuation of the Research or cancellation. If the Company opts for the Provided Goods to be destroyed rather than returned, the Research Institution shall destroy the Provided Goods in accordance with the Research Institution’s prescribed procedure and then record this, and if the Company requests the issuance of a certificate of disposal, the Research Institution shall promptly comply with this request.

Article 10. Loan of Medical Device or Goods, Etc. [Optional: If Lending Medical Device, Etc.]

1. During the term of the Agreement, the Company shall loan the Medical Device or Goods, etc. prescribed in Annex 4 (hereinafter the “Loaned Goods”) to the Research

Institution free of charge for up to twelve (12) months for execution of the Research[9].

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 Research Institution shall manage the Loaned Goods with the duty of diligence of a good manager. The 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. The Research Institution shall not use the Loaned Goods for purposes other than the Research nor allow the Investigator, Participating Researchers, Participating Centers, Contract Organizations or other third parties to use them for purposes other than the Research.
5. If the Loaned Goods are lost or damaged, the Research Institution shall compensate the Company for such damage; provided, however, that this shall not apply if such loss or damage is not attributable to the Research Institution.
6. If the Research is completed or discontinued, or of the Agreement is cancelled, the 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 or cancellation.

Article 11. Change to the Research Plan

In accordance with the opinion of the Ethical Review Board pursuant to Article 5, the Research Institution may change the Research Plan to the extent that this does not harm the aim of the Research stated in Article 3, Item 3, and the Company may change the amount and method of payment of the Research Funds prescribed in Article 6 according to the content of the Research Plan after the change. If the Company judges that the change to the Research Plan defeats the purpose of the Research, the Company may cancel the Agreement upon notifying the Research Institution to this effect. The Research Institution shall, however, not be required to return any portion of the Research Funds which has been reasonably used prior to the date of notification of the request to change the Research Plan unless there are special circumstances surrounding the change to the Research Plan.

Article 12. Action in the Event of Investigation by the Regulatory Authorities

If a compliance investigation by the regulatory authorities or a third-party investigation pursuant to ethical guidelines is conducted, the Research Institution shall report the fact of the investigation, its

[9] Execute a Memorandum of Understanding Regarding the Extended Loan of Loaned Goods if the research period is longer than 12 months, and it is reasonable and necessary to loan the goods for more than 12 months.

progress and results to the Company without delay.

Article 13. Ownership and Use of Source Materials and Data

1. The source materials and Data obtained as a result of the Research shall belong to the Research Institution.
2. Notwithstanding the preceding paragraph, the Research Institution shall not, by itself nor through the Investigator, use the Data for research other than the Research until a report in the form of the Research Report prescribed in Article 7, Paragraph 2 is made, without first obtaining the Company's written permission.
3. The Research Institution shall manage and supervise the source materials and Data prepared by Participating Researchers to ensure that the Participating Researchers do not use them without the Research Institution's permission.[10]

Article 14. Intellectual Property Rights

The Research Institution shall notify the Company promptly of any patent rights or other intellectual property rights arising in connection with the Research, and the two parties shall consult with each other in good faith to determine the treatment thereof.

Article 15. Registration and Publication of the Research Results

1. On completion of the Research, the Research Institution shall, by itself or through the Investigator, take necessary measures to protect the human rights and personal information, etc. of the Research Subjects and to protect the intellectual property rights, etc. of researchers, etc. without delay, and shall then register and publish the results of the Research in the public database in which it registered the outline of the Research. The same shall also apply if, in the case of discontinuation of the Research based on the Research Plan, the Research Institution publishes the results of the Research as at the time of discontinuation.
2. The Research Institution shall, by itself or through the Investigator, endeavor to publish a paper, etc. about the Research in accordance with each of the items shown below.
   (1) The Research Institution shall send the Company the manuscript or abstract of the paper, etc. it plans to publish at least XX days before publication.
   (2) The Company shall review the manuscript or abstract of the paper, etc. and submit a response within XX days of receipt pursuant to the preceding item from the viewpoints of confidentiality, protection of personal information and appropriate use of the Medical Device pursuant to the Agreement as well as from ethical, medical and scientific viewpoints.
   (3) The Research Institution shall be responsible for determining the final content of the publication, taking the Company's response under the preceding item into

[10] Assumes multicenter study.

consideration.

3. If judged necessary to protect patent rights, etc. arising as a result of implementation of the Research, the Company may request that the Research Institution postpone publication until it files a patent application or completes preparations to file an application (provided, however, that such postponement shall not exceed six (6) months from the date on which the Research Institution initially intended to publish). The Research Institution shall cooperate over the timing and content of publication to enable the Company to take necessary measures to protect patent rights, etc., provided there are reasonable grounds for doing so.

Article 16. Compensation Liability and Indemnity Liability

1. The Research Institution shall assume compensation liability and indemnity liability for damage to the health of the Research Subjects and shall also assume liability with respect to all other legal action, losses and damages that might arise in connection with implementation of the Research and its results. If the Company suffers damage in connection with such legal action, losses, damage, etc., the Research Institution shall compensate the damage suffered by Company; provided, however, that this shall not apply in cases where the 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. The Research Institution shall purchase insurance and take other necessary and sufficient measures in advance in order to fulfill its obligations of compensation or indemnity which may arise in connection with the Research.
3. If damage to the health of Research Subjects occurs in connection with implementation of the Research, the Research Institution shall, by itself or through Participating Centers or the Investigator, promptly administer treatment or take other necessary measures.

Article 17. Confidentiality

1. For the duration of the Agreement and for ten (10) years after its expiration, the Research Institution shall treat in strict confidence information pertaining to the Medical Device or the Research disclosed by the Company (excluding information stated in the Research Report and information published through performance of the procedures under Article 15) (hereinafter the “Confidential Information”).
2. The Receiving Party shall use the Confidential Information solely for implementation of the Research and other limited purposes permitted under the Agreement, and shall not disclose the Confidential Information to third parties without first obtaining the written consent of the Disclosing Party; provided, however, that this shall not apply to the following information:
   (1) the Confidential Information which was published in accordance with conditions prescribed in the Agreement;

(2) information which was demonstrably already in the possession of or known to the Receiving Party at the time of disclosure;
(3) information which is or becomes generally available to the public other than as a result of the actions of the Receiving Party after receipt;
(4) information which is lawfully obtained by the Receiving Party from a third party without an obligation of confidentiality; or
(5) information which was demonstrably independently developed by the Receiving Party without the use of the Confidential Information.

3. Notwithstanding the preceding paragraph, the Company may disclose the Confidential Information to its affiliated companies where necessary upon imposing on them obligations of confidentiality equivalent to those contained herein.
4. If required to disclose the Confidential Information in order to comply with laws and regulations or if ordered by a court of law to disclose the Confidential Information, the Receiving Party may disclose the Confidential Information only to the extent necessary to meet these requirements; provided, however, that the Receiving Party shall notify the Disclosing Party in advance and shall, at the request of the Disclosing Party, cooperate with the Disclosing Party to enable the Disclosing Party to file an objection or take other appropriate measures.
5. On completion or discontinuation of the Research or termination or cancellation of the Agreement, whichever occurs sooner, the Receiving Party shall either return all the Confidential Information provided by the Disclosing Party to the Disclosing Party or destroy it, depending upon which option the Disclosing Party chooses.

Article 18.Conflicts of Interest

1. The Research Institution shall, by itself or through the Investigator, (i) state in the Research Plan and Patient Consent Explanation Document conditions that relate to conflicts of interests pertaining to research by researchers, etc., including sources of research funds, and conflicts of interest and personal interests pertaining to the Research Institution's research and shall then disclose this information to organizations, groups and associations, etc. to which it needs to be disclosed, in accordance with the Ethical Guidelines, and (ii) take necessary measures in accordance with the instructions of the Ethical Review Board and/or the Conflicts of Interest Management Committee, etc. to properly manage conflicts of interest in accordance with the guidelines on management of conflicts of interest established by relevant organizations, groups and associations, etc.
2. If a new conflict of interest arises in connection with the Agreement or activities pursuant to the Agreement, the Research Institution shall, by itself or through the Investigator, report everything to the Ethical Review Board and the Conflicts of Interest Management Committee, etc. without delay and consult them on measures to deal with the conflict of interest.
3. The Research Institution shall properly disclose information about the Company's

provision of research funds, etc. pursuant to the Agreement in accordance with the Guidelines on COI Management of the Japanese Association of Medical Sciences, etc., including in the case when the Research Institution makes the results of the research public by publishing a paper, etc., to ensure transparency about its relationship with the Company. The Company shall also properly disclose information about the provision of research funds in accordance with the Company's own rules on transparency established in accordance with the Transparency Guidelines prescribed by the Japan Federation of Medical Devices Associations and/or the Japan Association of Clinical Reagents Industries.

4. The Research Institution shall supervise the Investigator and Participating Centers to ensure that they comply with insider trading regulation under the Financial Instruments and Exchange Act (Act No. 25 of April 13, 2011) and that Participating Centers have Participating Researchers uphold such obligations.

Article 19. Effective Period and Cancellation of Agreement

1. The Agreement shall take effect from the date of execution hereof and be terminated as of the day on which the final payment is completed in accordance with Article 6.
2. If the Research Institution discontinues the Research based on the Research Plan, the Research Institution shall communicate this to the Company within XX days after making this decision, stating the timing of discontinuation and whether or not it plans to publish the results of the Research.
3. In any of the following cases, the parties hereto may cancel all or part of the Agreement by notifying the other party in writing.
   (1) If the Research is not started promptly pursuant to the provisions of Article 4, Paragraph
   (2) If the Company does not approve the Investigator's successor notified in accordance with Article 4, Paragraph 3 [or if such successor does not consent in writing to adhere to the conditions of this Agreement].
   (3) If, based on adverse events during implementation of the Research or safety information notified by the Company, the Research Institution, Investigator or the Company judge that it is impossible to ensure the safety of the Research Subjects.
   (4) If the Research is significantly behind the schedule prescribed in the Research Plan.
   (5) If the other party violates the Agreement and there is no sign of improvement 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 laws and regulations that apply to the Research are violated.
4. Article 8, Article 12, Article 16, Article 17, Article 18, Article 19, Article 20, Article 21,

Article 23, Article 24 and any other provisions which by their nature are expected to remain valid shall remain valid even after cancellation or expiration of the Agreement.

Article 20. Measures after Cancellation of the Agreement

If the Agreement is cancelled, the Research Institution shall prepare and submit to the Company a Research Report summarizing the results of the Research up to that point within XX days reckoned from the date on which the Research was cancelled.

Article 21. Assignment

Neither party to the Agreement may assign rights or obligations arising from the Agreement to any third party, with the exception of an affiliated company of the Company, without first obtaining the written consent of the other party.

Article 22. 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.

Article 23. 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 24. Consultation in Good Faith

The 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.
(Hereinafter blank)

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

Dated:

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

Dated:
Company [Name of Company]

[Address]
[Title/Name of Representative]

Annex 1 Participating Centers

Annex 2 Research Plan

Annex 3 Itemization of Research Funds

*Consideration for the labor of the researchers themselves is not included because the research is investigator-led research.[11]

Item	Expenses	Remarks
Outsourcing	yen	Registration, Secretariat, DM operations
Charges for tests not covered by NHI	yen	
Patient cooperation fee	yen	○○
○○	yen	○○
○○	yen	
Subtotal	yen	
Indirect expenses (←only institutions that require them)	yen	
Total	yen	

OR

Item	Direct expenses	Indirect expenses		Remarks
Secretariat expenses	yen	%	yen	
DM operations	yen	%	yen	
Outsourcing	yen	0 %	yen	
Charges for tests not covered by NHI	yen	%	yen	
Patient cooperation fee	yen	0 %	yen	○○
○○	yen	%	yen	○○
○○	yen	%	yen	
		%	yen	
Subtotal	yen	%	yen	
Total			yen	

[11] The general idea is that consideration for the labor of the Investigator prescribed in Article 3 (or Research Representative in the case of a multicenter study), Participating Researchers who are voluntarily involved in the Research, and Researchers under their control should not be paid out of the Research Funds.

Annex 4 Provided Goods and Loaned Goods

1. Provided Goods

2. Loaned Goods