[Research Protocol]

**\* Black text: Standard phrasing (Do not delete)**

**\* Red text: Important notes (Delete before submission)**

**\* Blue text: Sample sentences. Please add or remove as necessary and change to black text at time of application.**

Date of application: (YYYY/MM/DD)

|  |
| --- |
| [Research title]  |
|  |
| **[Principal investigator (legally authorized representative)]**  |
| Full name (*furigana*) Full name (*kanji*)  |  |
|  |
| Institution |  |
| Job title  |  |
| Postal code  | 〒 |
| Address |  |
| Phone number |  |
| Email |  　　　　　　　　　**@** |

Date received:

|  |
| --- |
| Version 1.0 When **amending** the protocol (making changes that significantly impact the endpoint), increase the version number by 1 and reset the sub-version number to 0. When **revising** the protocol (making changes that do not significantly impact the endpoint), keep the version number unchanged and only increase the sub-version number by 1.  |

Revision history

|  |  |  |  |
| --- | --- | --- | --- |
| Version #  | Date | Details of change | Reasons for change |
| 1.0 | 202X.0X.XX | Establishment | - |
|  |  |  |  |

* When initially approved by the Ethical Review Subcommittee, ensure the version number is 1.0.
From version 1.0 onwards, all protocol amendments and revisions must be reported to the Ethical Review Subcommittee.
* Revised sections in an application for change (minor changes) and revised sections made in response to comments made by a review committee member must be in black and underlined.

**[Summary]**

|  |  |
| --- | --- |
| Item | Description |
| Objectives  | Complete this section with reference to the “Research objectives and significance” section of the main body of the protocol. If there are multiple objectives, separate them into one primary objective and other objectives (secondary).  |
| Research subjects  |  |
| Selection criteria  |  |
| Exclusion criteria  |  |
| Consent of subjects  | Complete this section with reference to the “Ethical considerations” section of the main body of the protocol.  |
| Investigational drug (investigational device, tests, test values, methodology) |  |
| Research method/design(treatment schedule, etc.)  | Is the research design (research plan) appropriate for achieving the research objectives?  |
| Outline of observation/examination schedule  |  |
| Research framework | Is the framework suitable for carrying out the research? |
| Primary endpoints  | Are the primary endpoints aligned with the research objectives?  |
| Target number of cases  | Target number of enrolled subjects:  |
| Enrollment period  | Research implementation period: YYYY/MM/DD – YYYY/MM/DD  |
| Research period  | Approval date – YYYY/MM/DD  |
| Analysis period  | YYYY/MM/DD – YYYY/MM/DD (Or “XX years after the end of the enrollment period,” “XX years after the end of the follow-up period”)  |

1. Research title: Enter the research title.
2. Background and overview of research

Concisely summarize the background information supporting the justification (scientific merit, ethical considerations, safety) of the research. An illustrative diagram (flowchart) that provides an overview of the entire picture from the research background may also be included.

Specifically:

* Include a definition of the target disease and describe current standard treatment methods, clinical practice guidelines, etc.
* Describe the latest epidemiological information, etc.
* For the rationale of the proposed trial treatment, state the content and concept of the treatment, legally authorized representative basic research reports on mechanisms related to new treatment methods, etc., results of non-clinical trials, results of preceding clinical trials in Japan and overseas, and the rationale for why it is considered superior to standard treatment in terms of efficacy, safety, convenience, etc.
* Where possible, you should describe the latest research trends and allow for evaluation from an objective standpoint.
1. Objectives and significance
* Concisely state the research objectives.
* Include the properties to be evaluated (e.g. efficacy, safety, clinical effect), i.e., the endpoints.
* Describe what the research aims to clarify, and touch on its subsequent contribution and significance to medicine.
1. Scientific rationale and basis for the research
* Describe whether the research design (research plan) is appropriate for achieving the established research objectives, and whether the primary endpoints of the research align with the research objectives.
* Include data, cited literature, and sources of information that support the justification for conducting the research.
1. Research plan, study population, trial design, and research method

5-1) Study population

* Describe the clinical picture of the study population, explaining why this specific population was chosen.
* Clearly describe the study population based on diagnostic standards, names of codes and rules (version numbers), etc.

5-2) Trial design

* Classification of observational/interventional study
* Cross-sectional study: Observes factors of interest (exposure) and outcomes at a single point in time
* Longitudinal study: Involves a passage of time between the observation of factors of interest (exposure) and outcomes, and includes comparisons between groups
* Phases of trial: Diagnostic interventional study / therapeutic interventional study / exploratory study / confirmatory study (If the phase is clear, specify Phase I, II, III, or IV, and pay attention to the following)
* Method of comparison: Before-and-after comparison / parallel-group comparison / crossover / uncontrolled
* Type of control: Placebo-controlled / active-controlled / dose-escalation / no treatment
* Allocation method for intervention (diagnostic/ therapeutic): No allocation / randomization / open-label / blinding (If blinding, specify the method: single-blind / double-blind / triple-blind)

(Examples)

Prospective observational study (cohort study)

Retrospective observational study (case-control study)

Cross-sectional study using questionnaires, case-control study

Cross-sectional study using questionnaires (anonymous/named), case-control study
(Whether intervention is involved)

This research is a non-interventional, non-invasive retrospective observational study.

This research is a non-interventional, minimally invasive prospective observational study.

5-3) Research subjects

* If subjects have diseases or abnormal drug reactivity, etc., describe the methods, etc., including whether the disease name or corresponding condition, etc. has been declared.
* If the research targets healthy individuals, clearly state that healthy individuals are the target subjects.
* If the research subjects are diverse (e.g. when the research targets both “prospective” and “retrospective” subjects), describe them separately, such as “Subject Group 1,” and “Subject Group 2.”
* If control patients are included in addition to the patients enrolled in the research, clearly indicate the distinction between “Case Group” and “Control Group.”

(A) Eligibility criteria

* Describe the specific method that demonstrates that subjects are selected in a rational manner, along with the selection criteria, such as disease name, disease stage, disease type, age, and sex.

(Examples) (1) Patients diagnosed with XXX at XXX Hospital/Clinic between January 1, 2022 and December 31, 2023

 (2) Patients whose written consent to participate in the research can be obtained

 (3) Patients who are 20 years of age or older at the time consent is obtained

(B) Exclusion criteria

* Describe criteria that would make it impossible to conduct the research, or treatment history, medical history, complications, etc., that would make it impossible to evaluate the results even if the research were conducted.

(Examples) (1) Patients with XXX

 (2) Other patients who, in the opinion of a physician, are deemed unsuitable for inclusion

5-4) Target number and research implementation period

(A) Target number

* State the specific target number. When comparing multiple cases or comparing with past cases, include the breakdown for each case.
* If multiple institutions participate, describe both the overall target number and the target number for Kanazawa University.
* When using past specimens or information, state the relevant period.

Overall target number: XXX (Target number for XXX institution: YYY)

Rational for setting target number: Describe the statistical rationale for setting the target number. Clearly state the method of statistical analysis, and specify the handling of discontinued/withdrawn cases and missing values.

(Example) (Example when not set based on statistical rationale): This research is an observational study under routine clinical practice, and the number was set as the feasible number of cases within the research period.

(B) Research period

* Clearly describe the start and end dates from the commencement of the research to its completion.
* The research period refers not only to the period of research subject enrollment and observation but also includes the subsequent period for data tabulation and analysis.
* In the case of <prospective research>, also state the enrollment period (the period for enrolling subjects) and the observation period (the period from subject enrollment until the end of observation).
* In the case of <retrospective research>, also state the researched period (the period covered by the information/data used).
* If the research is to be continued beyond that period, an application for extension must be submitted each time.

(Example) Research period: Approval date – March 31, 2021
Enrollment period: Approval date – December 31, 2019
\* Delete if retrospective research
Observation period (follow-up period ): 1 year from end of enrollment
\* Delete if retrospective research
Researched period: January 1, 2015 – December 31, 2015
\* Delete if prospective research
Analysis period: Approval date – March 31, 2021

\* The research start date for collaborative research institutions will be the approved date of research implementation at each research institution.

\* Only include if multi-institutional joint research. Please delete if not multi-institutional joint research.

5-5) Research method

* Describe, to the extent possible, the research procedures, methods for obtaining specimens/information, and methods of data analysis.
* If providing specimens/information to a joint research institution for analysis, also describe the research method of the joint research institution.
* If research methods, etc. may be added as the research progresses, include a statement to that effect as well.
* Clearly describe whether residual samples collected during routine clinical practice will be used, or if additional samples will be collected for research purposes during routine clinical practice, or if samples will be separately collected solely for research purposes (whether there will be new invasiveness). Describe what will be conducted in this research, making clear the differences from what would be performed in routine clinical practice even without the devising of this research.

(Example) This is an observational study using specimens/information obtained during the course of routine clinical practice, and no additional specimens/information will be obtained for the purpose of this research.

(Example) Residual specimens obtained during the course of routine clinical practice will be used.

(Example) An additional XXX ml of blood will be collected once only for the purpose of this research during a blood test as part of routine clinical practice.

(Example) XXX will be collected for the purpose of this research.

■ In cases where measurements/tests are performed specifically for this research

* When conducting research in which genetic information is handled, or when conducting medical research, based on the characteristics of the research to be conducted and the results obtained from that research, etc., a policy for explaining the results obtained from that research, etc. to research subjects must be established and described in the research protocol, with due consideration to the following matters.

■ Describing the disclosure of test results from this research

(Example: Not disclosed)

This research aims to XXX (verb) XXX (particular disease aspect/factor) in relation to XXX (disease name/category). Regarding the disclosure of test results, the accuracy of the obtained results is not sufficient. Disclosing the results is therefore unlikely to be beneficial to the research subjects and their relatives, and there is a concern that it may instead cause misunderstanding or anxiety. For this reason, individual results will not be disclosed at this time.

(Example: Not disclosed)

This research is a cohort study and is not intended to be analyzed for the purpose of treating individual patients. Regarding the disclosure of test results, since further research would be necessary in the future in order to link the findings of this research to actual treatment, the test results are not immediately useful for the treatment of individual diseases, etc. For this reason, test results will not be disclosed to the research subjects.

(Example: Disclosed in some cases)

This research aims to XXX (verb) XXX (particular disease aspect/factor) in relation to XXX (disease name/category). Regarding the disclosure of test results, the accuracy of the obtained results is not sufficient. Disclosing the results is therefore unlikely to be beneficial to the research subjects and their relatives, and there is a concern that it may instead cause misunderstanding or anxiety. For this reason, individual results will not be disclosed at this time. However, if results are obtained that are deemed medically beneficial for disclosure, the research subjects may be contacted. At the time of obtaining consent, the wishes of each research subject regarding disclosure will be confirmed, and only those research subjects who expressed a desire for disclosure will be contacted. The results will not be disclosed, however, if the desire for disclosure is withdrawn during the research.

(Example: Disclosed)

This research aims to XXX (verb) XXX (particular disease aspect/factor) in relation to XXX (disease name/category). Regarding the disclosure of test results, the accuracy of the obtained results is sufficient, and it would be beneficial to the research subjects and their relatives. Therefore, the test results will be disclosed. At the time of obtaining consent, the wishes of each research subject regarding disclosure will be confirmed, and results will only be disclosed to those research subjects who expressed a desire for disclosure. The results will not be disclosed, however, if the desire for disclosure is withdrawn during the research.

■ In cases of research in which genetic information is handled

(Example)

This research is an analysis of changes in gene expression that occur in somatic cells in association with a disease. It is different from an analysis of heritable genomic changes. Therefore, since the necessity for genetic counseling is extremely low, genetic counseling will not be provided.

(Example)

This research is an analysis of changes in gene expression that occur in somatic cells in association with a disease. It is different from an analysis of heritable genomic changes. Therefore, the necessity for genetic counseling is extremely low. However, if the person providing the specimens/information feels anxious about the gene analysis or disease, etc. after receiving the test results, or if they request a consultation, genetic counseling will be provided.

■ In cases of multi-institutional joint research

* To understand the roles of each participating institution, the flow of specimens/information and the role of each institution should be described in an organizational chart.

■ In cases where interviews or self-developed questionnaires are used

* Submit an interview guide and questionnaire form.
* Regarding interviews, describe whether the audio or video of interviews will be recorded, along with the methods and considerations for the protection of personal information.
* If using a commercially available questionnaire, clearly indicate this by including the standard specifications, etc.

■ In cases where instruments or devices are used

* Include content that clearly indicates the size and safety, for instance, photos and standard specifications.
1. Observation/examination and reporting items (whether consent is obtained)
* Describe the observation, examination, and reporting items necessary for the research.
* If observations are to be conducted chronologically, include a timeline (schedule).
* If analyzing specimens/information, describe the items to be analyzed. If there are plans to add analysis items in the future, include a statement to that effect as well, and submit an application for change once the items have been confirmed.
* If analyzing data from medical records, etc. describe all items of those records. If a questionnaire form or a survey form listing the items is to be used instead, include a statement to that effect and attach the form.
* State whether the specimens/information to be used correspond to existing specimens/information.
* If using existing specimens/information, state whether consent was obtained from the research subjects in the past. If consent was obtained, attach the informed consent document from that time. If consent was not obtained, state whether there are plans to obtain new consent. If there are no plans to obtain consent, state the reason for this.

(Example for prospective research) Observation and examination schedule

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Schedule | 4 weeks | Day 0 | Day 1 | Day 7 | Day 30 |
| Obtaining consent  |  | ○ |  |  |  |
| Examination items  |  |  |  | ○ | ○ |
| Questionnaire collection period  |  | From Day ○  | At time of additional survey  |

1. Evaluating and reporting adverse events

(A) Defining adverse events, reporting method

□ Not applicable

□ Applicable

* If the research involves invasiveness, describe the adverse events that could occur due to the invasiveness as well as the methods of response should adverse events occur.

(Example 1) This research is a non-interventional, prospective observational study. In the event of an adverse event due to the minimal invasiveness of the research, however, necessary measures will be taken and a report will be made to the head of institution/principal investigator.

(Example 2) This research is a non-interventional, prospective observational study. It involves no new invasiveness, and there is no possibility of an adverse effect occurring as a result of it.

(B) Burdens imposed on research subjects, anticipated risks and benefits, overall assessment, and measures to minimize those burdens and risks

* Burdens: Undesirable events that are certain to be imposed on research subjects as a result of the research being conducted. This includes, for example: events related to “invasiveness,” such as physical or mental suffering, health disadvantages (including those not perceived by the research subjects), and unpleasant conditions, as well as inconvenience (effort and time) and economic expenditure incurred by research subjects for the research to be conducted.
* Risks: Refers to the possibility of harm that may or may not actually occur as a result of the research being conducted. Such harm includes physical and mental harm, as well as economic and social harm that may be suffered as a result of the research being conducted.
1. Anticipated benefits
* If participating in the research does not yield any special clinical benefit, include a statement to that effect.
* If there is remuneration or other compensation for research subjects, include a statement to that effect and provide details.

(Example 1) This research is an observational study conducted within the scope of routine clinical practice. For this reason, all medical expenses for research subjects during the research period will be covered by the insurance of the research subjects and their copayments. Therefore, there are no special clinical or economic benefits for research subjects gained by participating in the research compared to routine clinical practice.

(Example 2) There will be no direct personal benefits to research subjects from participating in the research. The results of the research may be beneficial for the development of new XXX.

1. Anticipated risks and discomforts
* Describe the anticipated discomforts and their risks (possibility/probability of harm) that may arise from participating in the research, as well as measures to minimize these risks and countermeasures for adverse events.
* If there are any burdens in addition to risks, these must also be described. If it is anticipated that these burdens will be equivalent to routine clinical practice, include a statement to that effect.

(Example 1) Drug treatment in this research is conducted as part of routine clinical practice. While there is a risk of adverse events/side effects occurring during treatment, participating in research does not increase these risks compared to routine clinical practice.

(Example 2) This research is an observational study using data obtained from routine clinical practice. For this reason, there are no burdens or risks associated with participating in this research.

(Example 3) This research is an observational study. An additional XXX ml of blood will be collected once only during a blood test as part of routine clinical practice. As a result, the amount of blood collected will increase, but it is not expected to affect the research subject’s symptoms or course of treatment. During blood collection, the research subject’s condition will be carefully monitored, and blood collection will be stopped if they feel unwell.

(Example 4) This research involves XXX which will extend the consultation time by approximately 5 minutes beyond routine clinical practice. During this time, the research subject’s condition will be carefully monitored, and XXX will be stopped if they feel unwell.

(Example 5) Regarding any health damage incurred in association with participation in this research, appropriate treatment will be provided as an insured medical service, similar to routine clinical care, according to the patient’s condition. In such cases, the patient will be responsible for their medical expenses copayment. No ex gratia payments, allowances or other financial compensation will be provided.

1. Measures to minimize burdens and risks
* Include an overall assessment of anticipated benefits, and describe countermeasures for anticipated side effects, operational malfunctions, radiation exposure, etc. Clearly state that consideration is given to minimize discomforts and risks.

(Example) No special measures will be taken because this research is an observational study based on routine clinical practice and the examination items and frequency are the same as those in routine clinical practice.

(Example) Sufficient explanations will be provided in advance. If symptoms such as discomfort are shown, the blood collection will be stopped, and the physician will respond appropriately.

1. Endpoints
* Designate the most appropriate outcomes for meeting the research objectives as primary endpoints, and all other outcomes as secondary endpoints.

(1) Primary endpoints:

* In accordance with the research objectives, state the outcomes that best express the objectives.
* If the objective of the research is to assess efficacy, indicate outcomes that can evaluate efficacy.

(2) Secondary endpoints:

* Describe secondary endpoints that could serve as supplementary data for the primary evaluation.
* Secondary endpoints are not mandatory.
1. Statistical considerations
* Specify the rationale for setting the target number, as well as the analysis items, analysis methods, etc.
1. Data management and case report form: Entry and reporting
* Describe how data will be entered into case report forms, as well as the timing and method of data collection.
1. Ethical considerations

(11-1) Compliance with ethical guidelines, laws, and regulations

(Example) All persons involved in the research will carefully read and understand the *WMA Declaration of Helsinki* and the *Ethical Guidelines for Medical and Biological Research Involving Human Subjects* (Ministry of Education, Culture, Sports, Science and Technology (MEXT), Ministry of Health, Labour and Welfare (MHLW), Ministry of Economy, Trade and Industry (METI))—which all medical research involving human subjects should adhere to—and will conduct research in compliance with these.

(11-2) Methods of protecting personal information

* Describe how personal information will be managed, the name of the data custodian, the method of anonymization, whether a linkage table will be created, how the linkage table will be managed, how results will be published, and how personal information will be protected when publishing results, etc.
* Types of personal information
* Types and methods of anonymization

1) Anonymized

Method: Remove descriptions, etc. from research subject data and specimens that could identify specific individuals (e.g. names) and assign a new code or number instead to anonymize the research subjects. Create a linkage table that connects these codes (numbers) with the anonymized research subjects, and have this managed strictly by the data custodian to prevent external leakage of information.

2) Anonymized (limited to cases where specific individuals cannot be identified)

Method: Remove descriptions, etc. from research subject data and specimens that could identify specific individuals (e.g. names) and assign a new code or number instead to anonymize the research subjects. The linkage table that connects these codes (numbers) with the anonymized research subjects is not held at Clinic XXX.

3) Anonymized (limited to cases where specific individuals cannot be identified and no linkage table has been created)

Method: Remove descriptions, etc. from research subject data and specimens that could identify specific individuals (e.g. names) and assign a new code or number instead to anonymize the research subjects. Do not create a linkage table that connects these codes (numbers) with the anonymized research subjects. (In this research, no linkage tables are created at any of the facilities.)

(Examples)

Individuals involved in research will comply with applicable laws and regulations concerning the protection of the personal information of research subjects. Furthermore, they will exert their utmost efforts to protect the personal information and privacy of research subjects, and will not, without justifiable reason, disclose any personal information acquired in the course of conducting this research. The same will apply even after they have left their position.

When handling materials related to the research conduct, subjects’ personal information, etc., will be managed by assigning unrelated numbers, ensuring sufficient consideration for the protection of subjects’ confidentiality.
When handling materials, etc. related to the conduct of research, the personal information, etc. of subjects will be managed by assigning unrelated numbers, and adequate consideration will be given to protecting the confidentiality of subjects. Personal information and linkage tables of any anonymized data will be stored separately, each in a locked desk, and managed strictly by the principal investigator or data custodian (XXXXXX) to prevent leakage, theft, loss, etc.

When publishing research results in academic societies or at research meetings, etc., care will be taken to ensure that individuals cannot be identified, and anonymity will be maintained. After the discontinuation or completion of the research, electronic data related to the research and experiment/observation notebooks will be retained for a period of 10 years, and other research data, etc., will be retained for a period of 5 years from the date of the conference presentation or journal publication, whichever is later.

When handling specimens, etc. related to the conduct of research, adequate consideration will be given to protecting the confidentiality of subjects. When sending specimens, etc. to the research administration office or other related institutions, numbers will be used, and adequate consideration will be given to prevent any personal information of subjects from leaking outside the institution. Personal information and linkage tables of any anonymized data will be stored separately, each in a locked desk, and managed strictly by the principal investigator or data custodian (XXXXXX) to prevent leakage, theft, loss, etc.

When publishing research results in academic societies or at research meetings, etc., care will be taken to ensure that individuals cannot be identified, and anonymity will be maintained. After the discontinuation or completion of the research, electronic data related to the research and experiment/observation notebooks will be retained for a period of 10 years, and other research data, etc., will be retained for a period of 5 years from the date of the conference presentation or journal publication, whichever is later.

1. Procedures for obtaining informed consent
* From the following, select and describe the informed consent procedures that are appropriate for the use of specimens/information and research methods.
* Written informed consent
* Verbal + recorded informed consent (documented in medical records, etc.)
* Opt-out via public disclosure of information

\* There are also descriptions about the guaranteed freedom to participate or not participate, and about the freedom to withdraw consent.

[Reference] Procedures for informed consent, etc.

Yes

Existing specimens/information （提供も含む）のみ

New specimens/information

Yes

Written IC

(1) Does the research involve invasiveness?

Written IC

Verbal IC + Record

In principle, IC

No

Written IC

Verbal IC + Record

Yes

(2) Does the research involve intervention?

No (IC is difficult)

No

If difficult, opt-out

Yes

(3) Are specimens collected from the human body used?

No

Written IC

Verbal IC + Record

Yes

In principle, consent

If obtaining consent is difficult, opt-out

(4) Is sensitive personal information acquired/provided?

No

Yes

Written IC

Verbal IC + Record

Opt-out

(5) Is only information other than (4) used?

[Reference] Procedures, etc. for obtaining informed consent from legally authorized representative, etc.



|  |  |  |  |
| --- | --- | --- | --- |
| Has the subject completed the junior or senior high school curricula, or is the subject 16 years of age or older? | Is the subject capable of making decisions? | Does the research involve invasiveness? | (1) Both legally authorized representative (LAR) and subject: IC  |
|  |  |  | (2) LAR: Notification + Right to refuseSubject: IC |
|  | Is the subject capable of expressing their own wishes? |  | (3) LAR: ICSubject: IC |
|  |  |  | (4) Only LAR IC |

* The term “minor” will be defined in accordance with the provisions of the Civil Code, referring to an unmarried person under 20 years of age prior to April 1, 2022, and an unmarried person under 18 years of age from April 1, 2022 onward.

■ If subjects include minors (under 18 years of age) [research with minimal invasiveness]

* In the case of a minor aged 16 years or older who has decision-making capacity, informed consent (IC) must be obtained from both the research subject themselves and their legally authorized representative (LAR). If the research subject does not have decision-making capacity, IC must be obtained from the LAR.
* In the case of a minor under 16 years of age, IC must be obtained from their guardian or other LAR.
* In the case of a young child, if they have decision-making capacity, endeavor to create an assent document wherever possible and strive to obtain informed assent from the research subject themselves.

■ If subjects include minors (under 18 years of age) [research with no invasiveness]

* In the case of a minor aged 16 years or older who has decision-making capacity, IC must be obtained from the research subject themselves and an opt-out opportunity by their guardian must be provided. If the research subject does not have decision-making capacity, IC must be obtained from the LAR.
* In the case of a minor under 16 years of age, IC must be obtained from their guardian or other LAR.
* In the case of a young child, although not mandatory, if they have decision-making capacity, endeavor to create an assent document wherever possible and strive to obtain informed assent from the research subject themselves.

■ Also describe the following when obtaining informed consent from an LAR.

1. Policy for LAR selection
(The basic policy for LAR selection will be to choose an individual considered capable of representing the wishes and interests of the research subject, such as the research subject’s guardian)
2. Matters to be explained to the LAR
The same content will be explained to the LAR as that described in the informed consent document.
3. Reason for the need to include persons requiring an LAR as research subjects
(For example: It is found that conduct of the research itself would be difficult unless minors are included as research subjects)

(Example) The principal investigator or co-investigator will provide the research subject with an informed consent document that has been approved by the Ethical Review Committee, provide an adequate explanation both in writing and verbally, and obtain the research subject’s written consent on whether they will participate in the research, based on their free will.

(Example: If the research subject is a minor aged 16 years or older; research with minimal invasiveness)

Since the research involves minimally invasive procedures and since minors aged 16 years or older are included as research subjects, if they are deemed to have sufficient decision-making capacity, informed consent will obtained from both the research subject themselves and their legally authorized representative (LAR).

(Example: When obtaining informed assent)

Since the research involves minors under 16 years of age as research subjects, an informed assent document will be created explaining the research objectives and methods according to their level of understanding, and informed assent will be obtained from the research subject themselves.

(Example: When using opt-out)

Since this research is an observational study based on medical records and since it is difficult to obtain individual consent in advance, information on the research, including its objectives, will be posted in the outpatient clinic, and research subjects will be guaranteed the opportunity to refuse.

(Example: Policy for selection of legally authorized representative)

The legally authorized representative (LAR) will be the research subject’s guardian.

The LAR will be selected in consultation with the research subject’s guardian, the minor’s court-appointed legal guardian, and first-degree blood relatives, as appropriate.

The LAR will be the research subject’s guardian, the minor’s court-appointed legal guardian, spouse, parent, sibling, child/grandchild, grandparent, cohabiting relative, or a person considered equivalent to such close relatives (excluding minors).

The LAR will be selected in consultation with the research subject’s spouse and the research subject’s first-degree blood relatives.

■ If conducting research targeting local residents, etc.

* Efforts must be made to explain the research content and significance and to gain understanding.
* This includes characteristics influenced by genetic traits, environmental factors, and social factors. In addition to regional cohort studies, it also includes characteristics revealed through research such as human genetics using excavated human remains, etc.

(Example) This research targets local residents, etc. We will engage in continuous dialogue such as by repeatedly holding information sessions for local residents and providing information about the research even during its conduct, thereby explaining the content and significance of the research and gaining understanding for the research.

1. Cost burden to research subjects
* Specifically describe the financial burden on research subjects and state whether there is remuneration.

(Example: Remuneration provided)

If travel expenses are incurred as a result of participating in this research, they will be borne by the investigators in accordance with the regulations of the relevant Ethical Review Committee. In addition, remuneration will be provided in accordance with the regulations.
(Example: No remuneration provided)

If travel expenses are incurred as a result of participating in this research, they will be borne by the research participants themselves. No remuneration will be provided.

(Example: No cost burden)

There is no cost burden to research participants associated with participation in this research.

1. Funding and conflicts of interest in relation to the research
* Describe the main sources of funding for the research and any related conflicts of interest. If any materials, etc. other than funds are received, include a statement to that effect as well. Furthermore, if honoraria are paid, also include a statement to that effect.
* If there is a significant financial relationship that should be disclosed between the investigators and the primary funding provider or clinical research drug provider, include a statement to that effect.

(Example: No conflict of interest, no receipt of research funding)

(Example) This research will be conducted using the university’s operating funds. In the planning, conduct, and reporting of this research, it is confirmed that there are no “potential conflicts of interest” that could affect the research results and interpretation, and that the conduct of the research will not harm the rights or interests of the research subjects.

Furthermore, the research staff for this research have no interest in the company (or related institution). The research staff for this research will self-declare any conflicts of interest based on the regulations of the Ethical Review Subcommittee, and obtain its review and approval.

(Example: No conflict of interest, receives public research funding)

(Example) This research will be conducted with research grant funding (research project ID: XXX, research title: XXX). In the planning, conduct, and reporting of this research, it is confirmed that there are no “potential conflicts of interest” that could affect the research results and interpretation, and that the conduct of the research will not harm the rights or interests of the research subjects.

Furthermore, the research staff for this research have no interest in the company (or related institution). The research staff for this research will self-declare any conflicts of interest based on the regulations of the Ethical Review Subcommittee, and obtain its review and approval.

(Example: Conflict of interest, funded by contributions)

(Example) This research will be conducted using contributions from XXXXXX. In the planning, conduct, and reporting of this research, it is confirmed that there are no “potential conflicts of interest” that could affect the research results and interpretation, and that the conduct of the research will not harm the rights or interests of the research subjects.

Furthermore, this research involves participants who have an interest in Company XXX (or related institution) that manufactures and sells reagent YYY (or medical device ZZZ) that is the subject of this research.

The research staff for this research will self-declare any conflicts of interest based on the regulations of the Ethical Review Subcommittee, and obtain its review and approval. Additionally, when presenting at academic conferences or publishing papers, the funding will be disclosed to ensure the transparency of the research.

(Example: Conflict of interest, pharmaceuticals and funding)

(Example) This research will be conducted with financial support from Pharmaceutical Company XXX. In the planning, conduct, and reporting of this research, it is confirmed that there are no “potential conflicts of interest” that could affect the research results and interpretation, and that the conduct of the research will not harm the rights or interests of the research subjects.

Furthermore, this research involves participants who have an interest in Pharmaceutical Company XXX (or related institution) that manufactures and sells reagent YYY (or medical device ZZZ) that is the subject of this research.

The research staff for this research will self-declare any conflicts of interest to the conflict of interest review body based on the regulations of Clinic XXX or each research institution, and obtain its review and approval.

When publishing research results, the guidelines of the academic societies and journals where the results are presented will be observed, and any relevant circumstances will be accurately disclosed through self-declaration.

1. Compensation for health damage and details thereof (for research involving invasiveness)
* For research involving invasiveness (excluding minimal invasiveness) that involves medical procedures beyond routine clinical practice, describe the details of insurance or other necessary measures as a response to any health damage incurred by research subjects.
* In the case of multi-institutional joint research, describe the response taken at XXX, not for the entire research project.

(Example) This research is an observational study that utilizes specimens/information from research subjects obtained through routine clinical practice. Furthermore, the collection of specimens/information involves no invasiveness. Accordingly, it is expected that research subjects will not incur health damage as a consequence of this research, and thus no compensation will be provided.

(Example) This research is an observational study that utilizes specimens/information from research subjects obtained through routine clinical practice. Since the collection of specimens/information involves invasiveness, it is possible that research subjects will incur health damage. In such cases, the principal investigator will respond in good faith and provide appropriate medical care. These costs will be covered through the research subject’s insurance, and no special compensation will be provided by this research. These points will be explained to research subjects in advance, and their consent will be obtained.

(Example) Clinical research insurance will be obtained in preparation for potential compensation liability in the event research subjects incur health damage as a result of this research being conducted. In the unlikely event that severe health damage is incurred as a result of participation in this research (death, Grade 1 or 2 residual disability), compensation may be received from the insurance policy held by the investigators.

1. Responses related to the provision of medical care to research subjects after the research (for research involving medical procedures beyond routine clinical practice)
* Endeavor to ensure that research subjects are able to receive the best possible prevention, diagnosis, and treatment based on the results of this research.

(Example) After the completion of this research, the principal investigator will provide research subjects with the medical care deemed most appropriate, including the outcomes obtained from this research.

(Example) After the research, routine insured medical services will be provided to research subjects.

1. Specimens/information

(17-1) Type, storage, recording, and disposal of specimens/information

* Regarding the storage of specimens/information, the handling of specimens/information after the completion of the research, and the person responsible for storage, select and describe the applicable items below.

A. Specimens obtained from the human body

□ Not applicable

□ Applicable

Type of specimens: (Example) XXX ml of blood, bone marrow fluid, XXX tissue

Provide specific details, such as tumor tissue of XXX, blood, stool, urine.

Storage and disposal:

(Example) The principal investigator will instruct co-investigators and others to properly store specimens in accordance with established storage methods, and will implement necessary management to prevent leakage, mix-ups, theft, or loss of specimens. Collected blood samples will be disposed of immediately after the research concludes. When disposing specimens, they will be anonymized with due care for personal information.

Secondary use of specimens and information:

(Example 1) Specimens/information obtained in the research from research subjects will not be used for purposes other than the research objectives.

(Example 2) Specimens/information obtained in the research from research subjects may be used for future research not specified at the time consent is obtained. In such cases, once the new research plan has been reviewed by the Ethical Review Subcommittee, it will be implemented after a separate explanation has been provided to the research subjects.

(Example 3) Specimens/information obtained in the research from research subjects may be used for research on XXX. In such cases, the research will be implemented after a separate explanation has been provided to the research subjects.

Person responsible for storage: (Example) Specimens will be stored by the principal investigator, XXX XXX.

B. Information

□ Not applicable

□ Applicable

Type of information: (Example) Medical information obtained during routine clinical practice

Provide specific details, such as medical information and images from electronic medical records.

Storage and disposal:

(Example) The principal investigator will instruct co-investigators and others to properly store information in accordance with established storage methods, and will implement necessary management to prevent leakage, theft, or loss of information. Electronic data and experiment/observation notebooks will be retained for a period of 10 years, and other research data, etc., will be retained for a period of 5 years from the discontinuation or completion of the research or the publication of papers, etc., whichever is later, after which they will be destroyed.

Secondary use of specimens and information:

(Example 1) Specimens/information obtained in the research from research subjects will not be used for purposes other than the research objectives.

(Example 2) Specimens/information obtained in the research from research subjects may be used for future research not specified at the time consent is obtained. In such cases, once the new research plan has been reviewed by the Ethical Review Subcommittee, it will be implemented after a separate explanation has been provided to the research subjects.

(Example 3) Specimens/information obtained in the research from research subjects may be used for research on XXX. In such cases, the research will be implemented after a separate explanation has been provided to the research subjects.

Person responsible for storage: (Example) Information will be stored by the principal investigator, XXX XXX.

(Example: For long-term storage)

Since XXX XXX XXX XXX XXX XXX XXX XXX, specimens and information cannot be collected in necessary numbers without long-term accumulation. Accordingly, specimens and information, including records related to this research at Clinic XXX, will be stored for an extended period after obtaining consent from the individuals concerned, with personal information protected.

(17-2) Recording exchanges of specimens/information with other institutions

[When providing specimens/information to other institutions (including provision via the partial outsourcing of services)]

□ Not applicable

□ Applicable

(1) Method for creating records of provision

\* Regarding provision, always check in consultation with the receiving institution.

(Always state the purpose of provision, etc. in the explanation document.)

(2) Method of storing/location for storing records of provision:

(3) Name of receiving institution:

(4) Name of responsible person at receiving institution:

(5) Items of specimens/information being provided:

* Provide specific details about what kind of specimens/information are being provided, such as pathological specimens, medical information, etc.

[When receiving specimens/information from other institutions]

□ Not applicable

□ Applicable

(1) Method for creating records of provision

\* Regarding provision, always check in consultation with the sending institution.

(Always state the purpose of provision, etc. in the explanation document.)

(2) Method of storing/location for storing records of provision:

(3) Name of sending institution:

(4) Name of responsible person at sending institution:

(5) Method of informed consent at the sending institution:

* Describe what method is used to obtain informed consent, and whether an opportunity to refuse, such as by opting out, is provided, etc.

(6) Disclosing information to research subjects at the sending institution:

(7) Items of specimens/information being received:

* Provide specific details about what kind of specimens/information are being received, such as pathological specimens, medical information, etc.
* Describe the details of obtaining specimens/information.

(Example) Blood (obtain during clinical practice at institution XXX; obtained during the conduct of research XXX, etc.)

(8) Method for managing the sending institution’s linkage table:

(Example) The principal investigator or data custodian of each institution will manage the linkage table appropriately and not provide it to external parties, etc.

1. Attribution of research outcomes and publication of results
* Describe the attribution of research outcomes and publication of results.

(Example) Intellectual property rights may arise as a result of this research. These rights will belong to the nation, research institutions, collaborative research institutions (including private companies), and research personnel, etc. These intellectual property rights will not belong to the research subjects.

(Example) In principle, the results obtained by XXX XXX (← diagnostic method) in this research will not be disclosed to research subjects as they have not yet been sufficiently verified for certainty. However, if the principal investigator determines that not reporting the results would be detrimental to the research subjects, disclosure may be considered after combining with other diagnostic methods as much as possible and fully explaining the limitations of the accuracy of the results to the research subjects.

(Example) Using consent forms, the principal investigator will confirm in advance with the research subjects whether they wish to be informed if incidental findings with significant implications for their health, etc., are discovered during the conduct of the research which were not initially anticipated. If they wish to be informed, the information will be disclosed to the research subjects themselves.

■ In cases of research involving intervention

* For research involving intervention, prior to its implementation, the principal investigator will register an overview of the research in a public database, such as the database maintained by the Ministry of Health, Labour and Welfare (MHLW) (Japan Registry of Clinical Trials (jRCT)). The overview must be updated according to changes in the research protocol and the progress of the research.
* From the perspective of enabling centralized information retrieval, etc., the research will be registered in either jRCT or the public database established by the National University Hospital Council of Japan (NUHC). These databases allow for centralized information retrieval on the website of the National Institute of Public Health. Furthermore, each research institution may decide whether or not to also register in overseas public databases.

○ Japan Registry of Clinical Trials (jRCT)
https://jrct.niph.go.jp/

○ UMIN Clinical Trials Registry (UMIN-CTR), University hospital Medical Information Network (UMIN) Center
https://www.umin.ac.jp/ctr/index-j.htm

○ National Institute of Public Health website
<https://rctportal.niph.go.jp/>

(Example) Since this clinical research involves intervention, it will be registered with UMIN-CTR.

1. Research organization

Representative investigator: ABC (name), XXX (job title), Department of XXX, Hospital XXX/Clinic XXX (affiliation)

(1) Research organization

Principal investigator: ABC (name), XXX (job title), Department of XXX, Hospital XXX/Clinic XXX (affiliation)

(Role in this research):

Co-investigator: 　 ABC (name), XXX (job title), Department of XXX, Hospital XXX/Clinic XXX (affiliation)

(Role in this research):

(2) Research institution, scope of work:

<Example> Research institution: Hospital XXX/Clinic XXX
Principal investigator: ABC (name), Head of Urology Department
Scope of work: Provision of specimens, specimen collection, specimen analysis, data collection, data analysis, etc.

(3) Institutions providing only existing specimens/information (Role: Provision of specimens/information only)

\* Referring to the attached document “List of Institutions Providing Only Existing Specimens/Information,” attaching it as an appendix is acceptable.

If not confirmed at the time of submitting the protocol, it is acceptable to indicate as “(Planned)” and add later added via an application for change once confirmed.
The sending institution submits a notification using MHLW Form 1 “Notification of Provision of Specimens/Information to Other Research Institutions” or similar, in accordance with each institution’s regulations.

Upon receipt, the receiving institution keeps a record, for example by obtaining MHLW Form 2 “Record of Provision of Specimens/Information to Other Research Institutions.”

1. References
* List the literature cited in the research protocol.
* In the case of research using already approved pharmaceuticals or medical devices, attach their package inserts.
1. Scope of work and method of supervision in cases where any part of research work is outsourced

□ Research work not outsourced

□ Research work outsourced

Name of company:

Name of company representative: Name of company contact:

Address: Phone number:

Scope of work: \*Content of any outsourcing contract

1. Monitoring

□ Not applicable

□ Applicable

Not applicable for non-invasive research and minimally invasive research.

(Reference: Applicable for research involving invasiveness (excluding minimal invasiveness) that includes intervention. Specifically, describe the objectives, implementation framework (including name of contact person) and responsibilities, the scope of work, and implementation procedures (including method for reporting results), etc.)

1. Audits

□ Not applicable

□ Applicable

Not applicable for non-invasive research and minimally invasive research.

(Reference: Applicable for research involving invasiveness (excluding minimal invasiveness) that includes intervention. Specifically, describe the objectives, implementation framework (including name of contact person) and responsibilities, the scope of work, and implementation procedures (including method for reporting results), etc.)

1. Research administration office and inquiry contact point
* State the contact point for responding to inquiries, etc. from research subjects and their related parties.
* The research protocol may be made public to research subjects and parties outside the research institution.
* Note that the inclusion of mobile phone numbers is at the discretion of the individuals concerned.

Address: XXX XXX XXX

Research administration office, name of inquiry contact person (affiliation):

　　　　　TEL: XXX-XXX-XXXX

Always include page numbers in the document.

If performing invasive measurements, etc., attach materials that explain the performance and safety of the measuring equipment.

Attach any other materials that may be considered useful for reference.