Kyushu University
Standard Operating Procedure for Medical and Biological Research Involving Human Subjects

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Chapter 1 General Provisions

No. 1 Purpose and Basic Policies

The purpose of this manual is to prescribe the research and operational procedures that must be followed, in accordance with the "Ethical Guidelines for Medical and Biological Research Involving Human Subjects" (2021 Ministry of Education, Culture, Sports, Science and Technology; Ministry of Health, Labour and Welfare; and Ministry of Economy, Trade and Industry Notification No. 1) (hereafter, "the Guidelines") and the "Kyushu University Regulations for Medical and Biological Research Involving Human Subjects" (2021 Kyushu University Regulations No. 48), in order to ensure the proper implementation of medical and biological research involving human subjects at the medical institutions stipulated by the "Kyushu University Medical Ethics Council Regulations" (hereafter, "the Medical Institutions"). All relevant parties must follow this manual to pursue research which adheres to the basic policies enumerated below.* Blue text indicates textual changes made by the university to the Guidelines. The same shall apply hereafter.

1) Undertake research which has social and academic significance.
2) Ensure the research is scientifically reasonable within the context of the given research field.
3) Weigh the relative benefits of the research against any drawbacks, including the burden placed on research subjects.
4) Submit to review by an independent and impartial ethical review board.
5) Provide research subjects with adequate information beforehand and obtain their free and informed consent.
6) Extend special consideration to socially vulnerable persons.
7) Perform appropriate management of personal information and other sensitive data used in research.
8) Ensure the quality and transparency of research.

No. 2 Definition of Terms

The following is the definition of terms used in this manual.

(1) Medical and biological research involving human subjects

This refers to research performed at the Medical Institutions which uses humans as subjects and is conducted for the purpose of a. or b. below (hereafter, "Research").

a. To obtain knowledge, via 1), 2), 3) or 4) below, which will contribute to citizens' health preservation and promotion, patient recovery from injury or illness, or quality of life improvement.
   1) Understand the etiology of injury or illness (including the frequency and distribution of various health-related phenomena and the factors affecting them)
   2) Understand pathology
   3) Verify improvement in, or effectiveness of, injury and illness prevention methods
   4) Verify improvement in, or effectiveness of, medical diagnostic and treatment methods

b. To obtain knowledge, via human-derived samples or information, about human genome and gene structure or function, or about genetic mutation or expression.

(2) Invasive procedure

This refers to any procedure which creates a physical or psychological injury or burden for the research subject as a result of punctures, incisions, drug administration, irradiation, psychologically traumatizing questioning, etc., conducted for research purposes or for purposes beyond those of normal diagnosis and treatment.

Invasive procedures which create minimal physical or psychological injury or burden for research subjects are referred to as “minimally invasive procedures.”

(3) Intervention

This refers to any activity performed for research purposes (including any medical activity which goes beyond the scope of normal diagnosis and treatment and which is conducted for research purposes) to control the presence or absence, or degree thereof, of factors (including health preservation or promotion-related activities and medical drug administration, examination, etc., performed to prevent, diagnose or treat injury or illness) which affect various human health-related phenomena.

(4) Human body-derived sample

This refers to anything taken from a human body (whether living or deceased), such as blood, fluid, tissue, cells and waste products, or the DNA taken from them, which is used for research purposes.

(5) Information used for research

This refers to any human health-related information or other information (including information related to the deceased) obtained from medical examination or treatment of research subjects, such as names of illnesses, content of drug administration, results of examinations or measurements, etc., which is used for research.

(6) Sample/information

This refers to human body-derived samples and information used for research.

(7) Existing sample/information

This refers to samples/information for which either of the following criteria apply.

1) Any sample/information which already exists prior to research plan creation
2) Any sample/information obtained after research plan creation but, at the time it is obtained, not for the purpose of the research in question

(8) Genetic information

This refers to information about personal genetic traits or makeup obtained in the course of research using samples/information or from heritable information associated with existing samples/information.

(9) Research subject

This refers to any person (living or deceased) for whom either of the following criteria apply.

1) A person upon whom research is performed (including anyone who has sought to have the research performed)
2) A person from whom existing samples, information, etc., have been obtained and which will be used for research

When referring not only to research subjects but to others associated with them, such as legal representatives, the expression “research subjects and related parties” is used.

(10) Research institution

This refers to any corporation or government institution which conducts research, or to any individual conducting research as a sole enterprise. However, this does not include those contracted to perform only some of the research-related tasks, such as sample/information storage and statistical processing.

When research is carried out by an individual not connected with a corporation or government institution (e.g., a physician who has his/her own clinic), this constitutes a case in which an individual is conducting research as a sole enterprise and is, therefore, treated as a “research institution.”

(11) Joint research institution

This refers to any institution with which research is carried out jointly and in accordance with a research plan (this includes institutions which obtain new samples/information from research subjects to provide to other research institutions for the purposes of the research in question).

(12) Research affiliate

This refers to an institution, other than one which conducts research in accordance with the research plan, which solely obtains and provides to research institutions new samples/information from research subjects (not including cases where invasive procedures (but not minimally invasive procedures) are used to obtain samples) for the purposes of the research in question.

(13) Multi-institutional joint research

This refers to research which is conducted by multiple research institutions based on a single research plan.

(14) Researchers and related parties

This refers to the principal investigator and others who are involved in conducting the research. However, this does not include anyone who does not belong to a research institution and for whom any of the following apply.

1) Someone whose sole involvement is obtaining new samples/information and providing these to research institutions
2) Someone whose sole involvement is providing existing samples/information
3) Someone who is contracted to perform only some of the research-related tasks

(15) Principal investigator

This refers to the individual who is involved in conducting the research as well as responsible for supervising all tasks connected with the research at Kyushu University. As a rule, the principal investigator must be a Kyushu University staff member.

In cases of multi-institutional joint research, the term “research representative” can be used as an equivalent term for “principal investigator” when necessary.

(16) Research representative

This refers to the principal investigator who is the representative for the principal investigators of multiple research institutions in the case of multi-institutional joint research.

(17) Research director

This refers to the head of the department at Kyushu University which is conducting the research.

(18) Ethical review boards

This refers to boards and committees which have been established to investigate, from an ethical and scientific standpoint, the appropriateness of conducting or continuing research, as well as to review any necessary research-related matters.

(19) Informed consent

This refers to the consent of the research subjects and related parties regarding implementation or continuation of the research (including handling of samples/information), and this consent is freely given to the researchers and related parties, or the parties providing existing samples/information, based on an understanding of the research objectives, significance and methods, as well as the burdens to be borne by

research subjects, the expected outcomes (including risks and benefits), etc., as sufficiently explained by the researchers and related parties or the parties providing existing samples/information.

(20) Legal representative

This refers to someone who is considered capable of representing the will and interests of a living research subject and, if the research subject is objectively judged to be incapable of giving informed consent, can give informed consent to the researchers and related parties or the parties providing existing samples/information in place of the research subject.

(21) Legal representative and related parties

This refers to not only a legal representative of a living research subject but to someone who can give informed consent in place of a deceased research subject.

(22) Informed assent

This refers to the assent given by a research subject to the implementation or continuation of research when said research subject is objectively judged to lack the capacity to give informed consent and when this assent is given according to an understanding of the research which is based on an explanation provided in easy-to-understand terms which he or she can comprehend.

(23) Personal information

This refers to information about a living individual for which either of the following criteria apply.

1) The information includes names, dates of birth or other statements or descriptions (i.e., any matters (excluding individual identification codes) described or recorded in a document, drawing or electromagnetic record (created via an electromagnetic method (i.e., an electronic or magnetic method or any other method not comprehensible using human perception)), or expressed through voice, movement or other means) by which a person can be identified (including statements or descriptions which can be easily checked or compared with other information to identify a person)
2) The information includes individual identification codes

(24) Personal information (including the deceased)

This refers to personally identifiable information about a person, whether that person is living or deceased.

(25) Individual identification code

This refers to any characters, letters, numbers, symbols or other codes, as provided for under the Order for Enforcement of the Act on the Protection of Personal Information (Cabinet Order No. 507 of 2003) and other laws and regulations, by which the identity of a specific individual can be identified and into which a bodily partial feature of the specific individual has been converted in order to be provided for use by computers.

(26) Special care-required personal information

This refers to any personal information which reveals the person in question's race, creed, social status, medical history, criminal record, whether he or she has suffered criminal harm or injury, or any other matters which must be handled with special care so as not to cause unfair discrimination, prejudice or other disadvantage to said subject of the personal information.

(27) Anonymization

This refers to the total or partial deletion of personal information (including the deceased) statements or descriptions (including individual identification codes) which can be used for identifying the specific living or deceased individual (total or partial replacement of these statements or descriptions with statements or descriptions unrelated to the living or deceased individual is also meant by this term).

(28) Correspondence table

This refers to a table, or something similar, which can be used when it is necessary to identify research subjects from anonymized information by collating research subjects with the replacement statements or descriptions used at the time of anonymization.

(29) Anonymously processed information

This refers to information relating to individuals which is obtained by processing the following categories of personal information (limited to what is stipulated in the Act on the Protection of Personal Information; the same applies to (29) below) according to the measures described for each, and reconstruction of personal information from this information is not possible (limited to that for which the stipulations of the Act on the Protection of Personal Information apply).

1) Personal information corresponding to (23) 1)
Deletion of some of the statements or descriptions contained in the personal information in question (includes replacement of said statements or descriptions with other statements or descriptions via a method which does not possess a regularity enabling reconstruction of the original statements or descriptions).

2) Personal information corresponding to (23) 2)
Deletion of all individual identification codes contained in the personal information in question (includes replacement of said individual identification codes with other statements or descriptions via a method which does not possess a regularity enabling reconstruction of the original individual identification codes).

(30) Anonymized personal information

This refers to information relating to individuals which is obtained by processing the following categories of personal information (limited to that personal information which is subject to anonymized personal information processing, as per the stipulations of the Act on the Protection of Personal Information Held by Administrative Organs and the Act on the Protection of Personal Information Held by Incorporated Administrative Agencies, etc.; the same applies to (30) below) according to the measures described for each, and reconstruction of personal information from this information is not possible (limited to that for which the stipulations of the Act on the Protection of Personal Information Held by Administrative Organs and the Act on the Protection of Personal Information Held by Incorporated Administrative Agencies, etc. apply).

1) Personal information corresponding to (23) 1)
Deletion of some of the statements or descriptions contained in the personal information in question (includes replacement of said statements or descriptions with other statements or descriptions via a method which does not possess a regularity enabling reconstruction of the original statements or descriptions).

2) Personal information corresponding to (23) 2)
Deletion of all individual identification codes contained in the personal information in question (includes replacement of said individual identification codes with other statements or descriptions via a method which does not possess a regularity enabling reconstruction of the original individual identification codes).

(31) Adverse event

This refers to any undesirable or unintentional injury or illness, or symptom thereof (including abnormal laboratory test values) arising in the research subject, regardless of whether the cause is connected with the research conducted.

(32) Severe adverse event

This refers to an adverse event for which any of the following criteria apply.

1) The adverse event is fatal
2) The adverse event is life-threatening
3) The adverse event requires hospitalization or extension of the hospitalization period to treat
4) The adverse event leads to lasting or pronounced disability or malfunction
5) The adverse event gives rise to heritable congenital abnormalities
6) The adverse event, while not producing the outcomes described in 1) - 5) above itself, exposes the research subject to serious danger or other factors which must be dealt with in order to avoid the outcomes described in 1) - 5) above.

(33) Unforeseeable severe adverse event

This refers to a severe adverse event which is not included in the research plan, informed consent explanatory documents or elsewhere, or which, even if it has been included, has properties or severity different from what was anticipated.

(34) Monitoring

This refers to an examination which is carried out by a person designated by the principal investigator in order to ensure that the research is being conducted properly in terms of research subject safety, research reliability, adherence to the Guidelines and research plans and research progress.

(35) Audit

This refers to an examination which is carried out by a person designated by the principal investigator in order to ensure the reliability of research results and which checks to see whether the research has been conducted in line with the Guidelines and the research plan.

(36) Genetic counseling

This refers to support or assistance provided to research subjects and related parties, or to blood relatives of research subjects, which utilizes knowledge of genetics and counseling techniques to engage in a process of dialog and information sharing aimed at eliminating or ameliorating medical or psychological issues arising in connection with hereditary disorders and intended to help said parties in making and enacting their own decisions for their future.

No. 3 Scope of Application

This manual applies to research conducted by Kyushu University. However, in the case of research for which other laws, regulations, etc., apply, these shall take precedence over this manual.

In addition, research for which any of the following apply is not subject to this manual.

a. Research conducted under the provision of law

b. Research which falls under the scope of application of standards established by law

c. Research which only uses the samples/information described below

1) Any sample/information of already established academic value which is widely used for research purposes and which is generally available

2) Any information which has already been anonymized (limited to information which cannot be used to identify specific individuals and for which a correspondence table does not exist)

3) Any anonymously processed information or anonymized personal information which has already been created

Chapter 2 Responsibilities of Researchers and Related Parties

No. 4 Basic Responsibilities of Researchers and Related Parties

1 Consideration for Research Subjects and Related Parties

(1) Researchers and related parties shall respect the life, health and human rights of research subjects when conducting research.

(2) Researchers and related parties shall ensure their research is conducted properly by complying with laws, regulations, the Guidelines, etc. and by following a research plan which has been reviewed by ethical review boards and approved by the research director.

(3) Researchers and related parties shall, as a rule, obtain informed consent prior to conducting research.

(4) Researchers and related parties shall promptly and appropriately handle all concerns, questions, complaints, etc. (hereafter, "concerns, questions, etc.") from research subjects and related parties, as well as from other relevant parties.

(5) Researchers and related parties shall, with regard to the handling and anonymization of personal information, comply with the Guidelines, as well as laws and regulations related to personal information protection, rules and regulations established by Kyushu University and its Medical Institutions, etc., and shall ensure any information learned in the course of conducting research is not revealed without proper justification. The same shall apply even after the researchers and related parties are no longer associated with the implementation of the research in question.

(6) Researchers and related parties shall, when conducting research that is focused on a community or other group which shares certain common characteristic and has the possibility of revealing attributes specific to that community or group, explain the content and significance of the research to the research subjects and related parties and the community or group in order to secure their understanding with regard to the research.

2 Education and Training

Researchers and related parties shall, prior to conducting research, receive education and training in research-related ethics and the knowledge and technology required to conduct the research in question. This education and training shall also continue to be carried out on an as-needed basis during the research period.

No. 5 Responsibilities of the Research Director

1 Overall Supervision of Research

(1) The research director shall be responsible for performing that supervision which is required to ensure the approved research is carried out properly.

(2) The research director shall check, as necessary, that the research is being carried out properly and in accordance with this manual and the research plan, and shall take all necessary measures to ensure that this propriety is maintained.

(3) The research director shall ensure that all parties involved with the implementation of the research thoroughly understand that it must be carried out in a way which respects the life, health and human rights of research subjects.

(4) The research director shall ensure that no information learned in the performance of his/her duties is revealed without proper justification. The same shall apply even after the research director has left his/her position.

2 Development of Structures and Rules for Conducting Research

(1) The research director shall develop structures, rules, manuals, etc. (hereafter, "rules, manuals, etc.") necessary for carrying out research properly, shall implement measures to ensure research is carried out in line with these rules, manuals, etc., and shall revise the rules, manuals, etc., as needed.

(2) The research director shall, in the event of health hazards which affect research subjects connected with research conducted at relevant research institutions, ensure that compensation is made and other appropriate measures taken, as necessary.

(3) The research director shall ensure that research results and other research-related information is appropriately disclosed to the public, after ensuring that all necessary measures have been taken to protect the human rights of research subjects and related parties, as well as other relevant parties, and to protect the rights and interests of researchers and related parties, as well as of other relevant parties.

(4) The research director shall, as needed, personally inspect and assess whether the research at the relevant research institutions conforms to the Guidelines and shall take appropriate action based on the results of these inspections and assessments.

(5) The research director shall cooperate with reviews conducted by ethical review boards.

(6) The research director shall take steps to ensure that the researchers and related parties of the relevant research institutions receive education and training in research-related ethics and the knowledge and technology required to conduct the research in question. The research director shall also receive this education and training himself/herself.

(7) The research director may, in line with the rules established by Kyushu University and its Medical Institutions, entrust the authority and duties stipulated in the Guidelines to an appropriate party within Kyushu University.

(8) If the research uses Kyushu University Hospital patients as subjects, the director of the hospital shall appoint the chief pharmacist as the test agent administrator who will oversee usage of test agents and other pharmaceuticals at the hospital. However, when the research involves quasi-drugs or medical instruments, the principal investigator shall be appointed as the test agent administrator to oversee usage of said quasi-drugs or medical instruments. The rules for handling, storing and managing test agents and other pharmaceuticals are established separately.

Chapter 3 Proper Implementation of Research

No. 6 Research Plan-related Procedures

1 Creation and Alteration of Research Plans

(1) The principal investigator shall create a research plan before any research is attempted. The principal investigator shall also alter the research plan accordingly before any research is attempted which differs from the original research plan. All matters to be included in the research plan shall be created in line with the Guidelines.

(2) When creating the research plan for (1), the principal investigator shall ensure that the research is ethically appropriate and scientifically reasonable. He/she shall also comprehensively assess the burdens and anticipated risks and benefits for research subjects and shall take steps to minimize burdens and risks.

(3) Principal investigators conducting multi-institutional joint research shall appoint a research representative from amongst themselves to act as their representative in implementing multi-institutional joint research-related duties.

(4) Before multi-institutional joint research is attempted, the roles and responsibilities of the principal investigators at each of the joint research institutions shall be clarified and the research representative shall create, or alter, a single, overall research plan.

(5) If a principal investigator wishes to outsource any research-related duties, he/she shall specify the content of the duties to be outsourced and shall create, or alter, the research plan accordingly.

(6) If a principal investigator outsources a portion of the research-related duties, he/she shall require the contracted party to conclude an agreement, either in writing or via an electromagnetic method (referring

to any method which utilizes an electronic data processing system or other method which utilizes information communications technology; the same shall apply hereafter), which stipulates all matters that said party must comply with, and the principal investigator shall perform necessary and appropriate supervision of the party.

(7) Before any research is attempted which involves invasive procedures (but excluding minimally invasive procedures) and which accompanies medical activity going beyond the scope of normal diagnosis and treatment, the principal investigator shall take out insurance and ensure all other necessary measures are appropriately implemented for providing compensation to research subjects in the event that they are affected by health hazards.

2 Discussion with Ethical Review Boards

(1) The principal investigator shall seek the opinion of ethical review boards regarding the propriety of conducting research.

(2) As a rule, the research representative shall seek comprehensive review by a single ethical review board of multi-institutional joint research planning.

(3) The principal investigator shall, after receiving the opinion of an ethical review board, submit these results, along with all documents submitted to the ethical review board and all documents requested by the research director, to the research director in order to seek permission to conduct the relevant research at the relevant research institution.

(4) Notwithstanding the stipulations of (1) to (3), if the research needs to be conducted urgently in order to prevent the outbreak or spread of a public health hazard, it is permitted to commence this research prior to receipt of the ethical review board's opinion if the head of the research institution agrees. In such cases where the head of the research institution has agreed to the research, the principal investigator shall waste no time in seeking the opinion of the ethical review board and, if the opinion of said board is that the research should be paused or discontinued, or that the research plan should be altered, the principal investigator shall respond appropriately by pausing or discontinuing the research, or by altering the research plan, in line with the board's opinion.

(5) Notwithstanding the stipulations of (2), regarding multi-institutional joint research, if the principal investigator seeks the opinion of an individual ethical review board, he/she shall provide said ethical review board with all necessary information for conducting a review, including with regard to permission for research at joint research institutions, the results of reviews by other ethical review boards, and the status of progress for the research.

3 Approval by the Research Director

(1) The research director shall, when permission to conduct research is sought by the principal investigator, decide whether or not to approve the research, and what, if any, other measures related to the research need to be taken, in line with the opinion of the ethical review boards. If the opinion of the ethical review boards is that the research is inappropriate, the research director shall not approve the research.

(2) If the research director knows some fact, or learns some information, which could conceivably impact the course of ongoing research at the relevant institution, he/she shall promptly take all appropriate steps to address it, as needed, including pausing the research and investigating the cause of concern.

(3) If the research director knows some fact, or learns some information, which will, or has a likelihood of, harming the propriety of the research or the reliability of research results, he/she shall promptly take all necessary action.

4 Research Outline Registration

(1) For research which involves interventions, the principal investigator shall register an outline of the research on a public database, such as the Japan Registry of Clinical Trials (jRCT) maintained by Ministry of Health, Labour and Welfare, prior to the start of the research, and he/she shall update this

outline as needed to reflect research plan alterations and research progress. For all other research, as well, prior to its start, the principal investigator shall register its outline and shall update this outline as needed to reflect research plan alterations and research progress.

(2) With regard to the registration stipulated in (1), if there is some content which must not be publicly disclosed, so as to protect the human rights of research subjects and related parties or the rights and interests of researchers and related parties, as well as of other relevant parties, or because public disclosure would significantly hinder the implementation of the research, and if it is the opinion of ethical review boards and is approved by the research director, the requirement for registration shall not apply.

5 Ensuring Proper Implementation of Research

(1) The principal investigator shall direct and manage the researchers and other relevant parties involved with implementation of the research to ensure that the research is conducted properly, according to the research plan, so that the research results are reliable.

(2) The principal investigator shall, upon learning of a severe adverse event occurring in the course of research which involves invasive procedures, take all necessary measures in accordance with the separately established "Kyushu University Manual for Handling Severe Adverse Events in Medical Research Involving Human Subjects" (hereafter, "Manual for Handling Severe Adverse Events") and shall promptly submit the prescribed report.

6 Procedures Following the Conclusion of Research

(1) The principal investigator shall, upon conclusion (or discontinuation; the same shall apply hereafter) of the research, submit a report about all required matters to the ethical review boards and the research director in writing or via an electromagnetic method.

(2) Upon conclusion of the research, the principal investigator shall, without delay, publicly disclose the results of the research, after having taken all necessary measures to protect the human rights of research subjects and related parties, as well as other relevant parties, and to protect the rights and interests of researchers and related parties, as well as of other relevant parties. In addition, with regard to research which involves invasive procedures (but excluding minimally invasive procedures) and which involves interventions, the principal investigator shall submit a report without delay to the research director once the final announcement of results is made.

(3) Upon completion of research which involves interventions, the principal investigator shall, without delay, register the results of the research in the public database in which the research outline was registered, as stipulated in 4(1). For all other research, as well, the principal investigator shall endeavor to register the results of said research.

(4) In the case of research which involves invasive procedures (but excluding minimally invasive procedures) and which accompanies medical activity going beyond the scope of normal diagnosis and treatment, the principal investigator shall endeavor to ensure that the research subjects, even after the conclusion of the research, receive the best prevention, diagnosis and treatment stemming from the results of the research.

No. 7 Matters for Inclusion in Research Plans

Matters to be included in research plans shall be determined in line with the stipulations of the Guidelines. Matters to be included in research plans submitted to ethical review boards established by the Medical Institutions are determined separately by the relevant ethical review boards.

Chapter 4 Informed Consent

No. 8 Procedures for Receiving Informed Consent

1 Procedures for Receiving Informed Consent

Before researchers and related parties carry out research, and before the parties providing existing samples/information provide any existing samples/information, the researchers and related parties shall, as a rule, receive informed consent according to the prescribed procedures, and refer to the attached table, as established by the research plan approved by the research director. However, this requirement shall not apply in cases where an existing sample/information is provided, or the receipt of the provided existing sample/information is done, in accordance with legal and regulatory provisions.

2 Receipt of Informed Consent via Electromagnetic Methods

Researchers and related parties, and parties whose sole involvement is providing existing samples/information, may receive informed consent via an electromagnetic method instead of in writing, as stipulated in 1, provided all of the following considerations are satisfied.

1) It is appropriately verified that the party giving informed consent is the actual research subject or related party from whom it is sought.
2) Opportunities for research subjects and related parties to ask questions about the content of explanations are provided, and sufficient answers to these questions are given.
3) Even after informed consent is received, the matters consented to, including the explanatory matters stipulated in 5, can be easily accessed and read and, when specifically requested by a research subject or related party, these matters are delivered to him/her in writing.

3 Records Related to Sample/Information Provision

(1) Provision of samples/information

A principal investigator or party whose sole involvement is providing samples/information shall create records of sample/information provision and shall preserve them for a period of three years from the date of sample/information provision. At a research affiliate, parties whose sole involvement is providing samples/information shall ensure that the head of the research affiliate can access information about the provision.

(2) Receipt of provided samples/information

When receiving samples/information provided by other research institutions for research, the researchers and related parties shall confirm that the party providing the samples/information follows appropriate procedures and shall create a record of the sample/information provision.

The principal investigator shall preserve the records created by researchers and related parties for a period of five years from the reported date of research conclusion.

4 Alteration of Research Plans

As a rule, before researchers and related parties carry out research based on an altered research plan, they shall again perform the informed consent process, stipulated in 1, with regard to the altered sections. However, this

requirement shall not apply for altered sections of the research plan which have been approved by the research director, based on the opinion of ethical review boards.

5 Explanatory Matters

Matters to be explained to research subjects and related parties when seeking their informed consent shall be determined in line with the stipulations of the Guidelines. Matters to be included in informed consent-related explanatory documents submitted to ethical review boards established by the Medical Institutions are determined separately by the relevant ethical review boards under the Medical Ethics Council.

6 Matters for Notification or Disclosure to Research Subjects and Related Parties

Matters for notification or disclosure to research subjects and related parties, as per the stipulations of 1, shall be determined in line with the stipulations of the Guidelines. Matters to be included in explanatory documents which are submitted to ethical review boards established by the Medical Institutions and which relate to notifications or disclosures made to research subjects and related parties are determined separately by the relevant ethical review boards under the Medical Ethics Council.

7 Procedures for Using Samples/Information for Research Not Specified at the Time Consent Was Received

In the event that researchers and related parties have, when seeking the consent of research subjects and related parties, explained to them, as best as possible, the expected intended use of samples/information and, subsequently, a new purpose of use is specified, the researchers and related parties shall create or alter the research plan, shall notify or disclose information about the newly specified intended use to the research subjects and related parties, and shall, as a rule, ensure the research subjects and related parties have the opportunity to rescind their consent to the implementation of the research.

8 Handling of Research when Research Subjects Experience Urgent and Clearly Life-threatening Situations

When all of the following requirements are judged to have been met under an already established research plan, researchers and related parties may carry out research without the consent of research subjects or related parties. However, if said research is carried out, the procedure for seeking informed consent using a written document, or an electromagnetic method, stating all explanatory matters, as stipulated in 5, must be performed promptly.

1) The research subject is experiencing an urgent and clearly life-threatening situation.
2) In the case of research involving an intervention, there is no expectation that normal medical care will be sufficiently effective, and there is a sufficient likelihood that the danger to the life of the research subject can be avoided if the research is carried out.
3) Only the minimum necessary burden and risk for the research subject accompanies research implementation.
4) Neither the legal representative nor anyone who can be considered a legal representative can be contacted immediately.

9 Simplification of Informed Consent Procedures

(1) Researchers and related parties, or the parties providing existing samples/information, may simplify some parts of the procedures stipulated in 1 and 4 when seeking to carry out research which satisfies all of the following requirements and which is carried out according to a research plan approved by the research

director.

1) No invasive procedure (excluding minimally invasive procedures) accompanies research implementation.
2) Simplification of the procedures stipulated in 1 and 4 will not be disadvantageous to the research subject.
3) If the procedures stipulated in 1 and 4 are not simplified, it will make the research difficult to carry out and/or will significantly compromise the value of the research.
4) The research is recognized as being highly important for society.

(2) When researchers and related parties simplify the procedures stipulated in 1 and 4 according to the stipulations in (1), they shall take the following measures which are appropriate.

1) Publicize the purpose and content (including methods) of sample and information collection and use among the group to which the research subjects and related parties belong.
2) Promptly provide an ex post facto explanation to the research subjects and related parties (including to the group to which they belong).
3) If samples/information will be collected and/or used on an ongoing basis over a long period of time, endeavor to publicize this fact among the general public, including the purpose and methods of sample/information collection and/or use.

10 Revocation of Consent

In the event that consent from a research subject or related party is revoked or refused in line with any of the following, researchers and related parties shall, without delay, take action in accordance with the content of revocation or refusal and shall explain this to the research subjects and related parties. An exception to this, however, shall be if it is difficult to take said action and the research director approves, in accordance with the opinion of ethical review boards, that said action need not be taken. In such a situation, the researchers and related parties shall notify the research subjects and related parties of the decision not to act in accordance with the content of the revocation or refusal, and shall endeavor to explain and to convince them of the reasons for this decision.

1) Total or partial revocation of consent given with regard to the implementation or continuation of research
2) Based on notification or disclosure of research-related information, total or partial refusal of research implementation or continuation
3) In the context of the informed consent procedures stipulated in 8, total or partial refusal of research implementation or continuation
4) In the context of the procedures for obtaining informed consent from research subjects for research which a legal representative has given consent, total or partial refusal of research implementation or continuation

No. 9 Procedures for Receiving Informed Consent from Legal Representatives and Related Parties

1 Requirements for Consent by Proxy

(1) All of the following requirements must be satisfied for researchers and related parties, or the parties providing existing samples/information, to receive informed consent from a legal representative or related party as per the stipulations of No. 8.

a. All of the following matters are stated in the research plan.

1) Legal representative and related party selection policies
2) Explanatory matters for legal representatives and related parties (including the reasons why a given person must be a research subject when b. (i) or (ii) apply to said person)

b. Any of the following apply to the research subject.

(i) The research subject is a minor. However, if the research subject is a minor who has completed junior high school or the equivalent, or who is at least sixteen years old, and if he/she is judged to be sufficiently capable of making decisions about research implementation, informed consent shall be sought from the research subject instead of the legal representative, provided all of the following are stated in the research plan and the head of the research institution has given his/her approval, which is based on the opinion of ethical review boards regarding the implementation of the research.

1) Statements to the effect that no invasive procedure accompanies research implementation

2) Statements to the effect that the purpose of research and information about research implementation, including the handling of samples/information, will be disclosed and that the parents or guardians of the research subject are guaranteed an opportunity to refuse implementation or continuation of the research

(ii) The research subject is someone of legal age who has been objectively determined to lack the capability to give informed consent.

(iii) The research subject is a deceased person. This excludes cases where the research subject, while still alive, explicitly expressed his/her intention with regard to research implementation.

(2) When researchers and related parties, or the parties providing existing samples/information, seek informed consent from a legal representative or related party according to the process stipulated in No. 8, they shall select a legal representative or related party according to the selection policies of (1) a. 1) and shall explain to him/her all matters for explanation stipulated in No. 8-5 as well as all matters for explanation stipulated in (1) a. 2).

(3) If informed consent has been received from the legal representative and the research subject is a minor who has completed junior high school or the equivalent, or who is at least sixteen years old, and if he/she is judged to be sufficiently capable of making decisions about research implementation, the researchers and related parties, or the parties providing existing samples/information, shall seek informed consent from the research subject as well.

2 Procedures for Obtaining Informed Assent

(1) If informed consent has been received from the legal representative and the research subject is judged to be capable of expressing his/her intention with regard to research implementation, the researchers and related parties, or the parties providing existing samples/information, shall endeavor to obtain informed assent from the research subject. However, this stipulation does not apply when informed consent is received from the research subject in accordance with the stipulations in 1.

(2) Before attempting research for which it is anticipated that the informed assent procedures stipulated in (1) will be performed, the principal investigator shall include all matters to be explained to the research subject, and the method by which they will be explained, in the research plan in advance.

(3) The researchers and related parties, and the parties providing existing samples/information, shall, in the context of the informed assent procedures stipulated in (1), do their utmost to respect the expressed intention of the research subject if he/she expresses an intention to reject implementation or continuation of some or all of the research. However, this shall not apply in cases where implementation or continuation of the research is expected to directly benefit the health of the research subject and the legal representative has consented to its implementation/continuation.

Chapter 5 Handling of Results Obtained from Research

No. 10 Explaining Results Obtained from Research

1 Procedure for Explaining Results Obtained from Research

(1) The principal investigator shall establish and include in the research plan a policy, based on the characteristics of the research to be performed and results to be obtained, for explaining to the research subject the results obtained from the research. The following matters must be taken into consideration when establishing this policy.

a. Are the results sufficiently precise and reliable as information which can be used in assessing the condition of the research subject, e.g., his/her health?

b. Do the results represent important facts about the research subject, e.g., his/her health?

c. Is explanation of the results likely to seriously hinder proper implementation of the research tasks?

(2) Researchers and related parties shall, when seeking informed consent from research subjects and related parties, explain the policy established in (1) for explaining results obtained from research and shall ensure the research subjects and related parties understand this policy. If the research subjects or related parties then express their desire not to have the results obtained from the research explained to them, this shall be respected. However, even in situations where a research subject or related party has expressed his/her desire not to have the results obtained from the research explained, if the researchers or related parties determine that the results will seriously impact the life of the research subject or another, such as his/her blood relative, and if an effective method for addressing these effects exists, the researchers or related parties shall report this to the principal investigator.

(3) Upon receiving a report made in line with the provisions of (2), the principal investigator shall consider the propriety, method and content of explanation to the research subject and related parties in light of the following and shall seek the opinion of ethical review boards.

1) The impact on the life of the research subject and others, e.g., his/her blood relatives

2) The existence/absence of an effective treatment; the health status of the research subject

3) The likelihood that others, e.g., blood relatives of the research subject, are affected by the same issue

4) The content expressed at the time of obtaining informed consent with regard to explaining research results and other matters

(4) The researchers and related parties shall, after providing a sufficient explanation to the research subject and related parties which is based on the results of ethical review conducted in the context of (3), confirm the intentions of the research subject and, if the research subject still does not wish to receive an explanation of the research results, shall not explain the results to him/her.

(5) As a rule, results obtained from research involving a given research subject shall not be explained to anyone other than the research subject or related parties without the consent of the research subject. However, this shall not apply in cases where relevant parties, such as the blood relatives of the research subject, express their desire to have the results obtained from the research explained to them and where the principal investigator deems such explanation to be necessary based on the opinion of an ethical review board that necessary and sufficient reason exists for providing the explanation.

2 Research-related Consultation System

The principal investigator shall maintain a suitable system for facilitating research-related consultation with research subjects and related parties about results obtained from research, making sure sufficient consideration is given to the characteristics of the results and their medical and psychological impact. The principal investigator shall ensure this system prioritizes staying in close contact with the doctor who is in charge of medical treatment, as well as maintaining contact with genetic counselors and genetic services experts when genetic information will be handled.

Chapter 6 Ensuring Research Reliability

No. 11 Appropriate Research Handling and Reporting

1 Ensuring the Ethical Appropriateness and Scientific Reasonableness of Research

(1) Researchers and related parties shall, upon learning facts or obtaining information (excluding that corresponding to (2) below) which reveal, or indicate the likelihood of, loss of ethical appropriateness or scientific reasonableness of the research, promptly report this to the principal investigator.

(2) Researchers and related parties shall, upon learning facts or obtaining information which reveal, or indicate the likelihood of, loss of research propriety or research result reliability, promptly report this to the principal investigator or research director.

(3) In the event of an unintentional and/or improper leak of research-related information or some other situation which raises serious concerns with regard to respect for the human rights of research subjects and related parties or to the implementation of the research, researchers and related parties shall promptly report this to the research director and the principal investigator.

2 Management and Supervision of Research Progress and Ascertainment and Reporting of Adverse Events

(1) The principal investigator shall endeavor to ensure proper implementation of the research and the reliability of research results, such as by collecting information essential to research implementation.

(2) Upon receiving a report in line with 1 (1) about factors which could conceivably impact the continuation of research (but excluding reports corresponding to (3) below), the principal investigator shall report this to the research director without delay and, if necessary, pause or discontinue the research and/or alter the research plan.

(3) Upon receiving a report in line with 1 (2) or (3), the principal investigator shall promptly report this to the research director and, if necessary, pause or discontinue the research and/or alter the research plan.

(4) The principal investigator shall discontinue the research if it is determined that the expected risks outweigh the benefits or that sufficient results have been, or cannot be, obtained from implementation of the research.

(5) The principal investigator shall make reports to the research director about the progress of the research according to the established research plan and about the status of adverse events arising in conjunction with research implementation.

(6) When conducting multi-institutional joint research, the principal investigator shall share all necessary research-related information with the principal investigators at the joint research institutions, in accordance with the Guidelines.

(7) After receiving a report in line with the stipulations of 1(2) or (3), or 2(2) or (3), the research director shall, when necessary, consult with ethical review boards and, based on their opinion, promptly take appropriate action, including pausing the research and performing an investigation into the cause. In such cases, prior to receiving the opinion of ethical review boards, the research director shall instruct the principal investigator to take action as needed, including discontinuing the research or implementing provisional

measures.

3 Reporting to Ministers

(1) In the event that the research director learns that the research being carried out, or which was carried out, at the research institution in question does not comply with the Guidelines (including reports in line with the stipulations of 1(2) or (3), or 2(2) or (3)), he/she shall promptly take necessary action based on the advice of ethical review boards and shall, if the noncompliance is significant, provide a report to the university president, as well as to the Minister of Education, Culture, Sports, Science and Technology and the Minister of Health, Labour and Welfare (hereafter, simply "the Ministers"), on the status and results of action to address the noncompliance, and the research director shall also make this report public.

(2) With regard to whether the research at the research institution in question is compliant with the Guidelines, the research director, under the direction of the university president, shall cooperate with the investigation performed by the Ministers, or the parties designated by them, and shall take appropriate action based on the results of this investigation.

No. 12 Managing Conflicts of Interest

(1) Researchers and related parties shall comply with the Guidelines and with laws and regulations related to conflict of interest, as well as the rules and regulations established by Kyushu University and its Medical Institutions.

(2) When conducting research, the researchers and related parties shall report to the principal investigator any conflicts of interest, such as personal profits received, with regard to the research and shall take appropriate action to ensure transparency.

(3) In the case of research, such as that related to the efficacy or safety of medicinal drugs or medical instruments which has potential connections with commercial activities, the principal investigator shall ascertain the status of conflicts of interest relating to the research and shall include these in the research plan.

(4) The principal investigator shall submit a "Conflict of Interest Update Form," as stipulated by No. 6-2(3), to the research director.

(5) The researchers and related parties shall explain to research subjects and related parties, in the context of seeking informed consent according to the stipulations in No. 8, the status of conflicts of interest described in the research plan, as stipulated in (3).

No. 13 Preservation of Research-related Samples and Information

(1) Researchers and related parties shall ensure the accuracy of the information used in research and the materials related to this information (including the records relating to the provision of samples/information which is used in research; hereafter, "information and materials").

(2) When preserving samples and information obtained from the human body, the principal investigator shall follow the separately established "Procedures for the Preservation of Samples and Information Obtained from the Human Body" (hereafter, "Samples and Information Preservation Procedures") to describe the preservation methods in the research plan and to instruct/manage researchers and related parties in ensuring the accuracy of information and materials and in performing the management necessary to ensure no samples obtained from human bodies, nor information or materials, are unintentionally or improperly leaked, mixed up, stolen, lost, etc.

(3) The research director shall perform all supervision necessary for ensuring that samples obtained from human bodies, as well as information and materials, connected with the research being implemented at the relevant research institution are appropriately preserved in accordance with the Samples and Information Preservation Procedures.

(4) The principal investigator shall, in accordance with the Samples and Information Preservation Procedures, report to the head of the research institution on the status of management being carried

out as stipulated in (2).

No. 14 Monitoring and Auditing

(1) The principal investigator must work to ensure the reliability of research and, in the case of research involving interventions and accompanied by invasive procedures (but excluding minimally invasive procedures), shall perform monitoring and, when necessary, auditing according to the established research plan which has been approved by the research director.

(2) The principal investigator shall provide essential instruction and management of the persons responsible for performing monitoring and auditing of the research being conducted so that both tasks are carried out appropriately, in accordance with the research plan approved by the research director.

(3) The principal investigator must not give the task of auditing the research to anyone connected with the implementation or monitoring of the research.

(4) Those responsible for monitoring shall report the results of monitoring to the principal investigator. When necessary, the principal investigator shall report the results of monitoring to the research director.

(5) Those responsible for auditing shall report the results of auditing to the principal investigator and research director.

(6) The research director shall, upon receipt of monitoring and auditing results reports, and following consultation with ethical review boards, make a decision about the propriety of continuing the research, and he/she shall notify the principal investigator of this decision.

(7) The persons performing monitoring and auditing shall not disclose, or allow to be disclosed, without justifiable reason any information they learn in the course of performing their duties. The same shall apply even after the completion of said duties.

(8) The research director shall cooperate in the performance of monitoring and auditing as stipulated in (1) and shall take all necessary steps to facilitate its implementation.

Chapter 7 Responding to Severe Adverse Events

No. 15 Responding to Severe Adverse Events

1 Response of Researchers and Related Parties

In the event that researchers and related parties learn of a severe adverse event occurring in the course of research which involves invasive procedures, they shall take all necessary steps, such as providing an explanation to research subjects and related parties, in accordance with the manual and actions prescribed in 2(1) and 3 below, and shall promptly report the occurrence to the principal investigator.

2 Response of the Principal Investigator

(1) Before attempting research involving invasive procedures, the principal investigator shall describe in the research plan the procedures which researchers and related parties should take in the event of a severe adverse event, and he/she shall take all necessary steps to ensure that the response is proper and executed smoothly in accordance with said procedures.

(2) In the event that the principal investigator asks a research affiliate to obtain research-related samples/information and a severe adverse event occurs for the research subject, the principal investigator shall promptly obtain a report of the matter.

(3) The principal investigator shall, upon learning of a severe adverse event occurring in the course of research which involves invasive procedures, take all necessary measures in accordance with the “Manual for Handling Severe Adverse Events” and shall promptly submit the prescribed report.

3 Response of the Research Director

Before attempting research involving invasive procedures, the research director shall take all necessary steps to ensure the response to a severe adverse event will be properly and smoothly executed in line with the Manual for Handling Severe Adverse Events.

Chapter 8 Ethical Review Boards

No. 16 Establishment of Ethical Review Boards

In line with the Guidelines, Article 10 of the "Kyushu University Regulations for Medical and Biological Research Involving Human Subjects," and Article 7 of the "Kyushu University Medical Ethics Council Regulations," the directors of the Medical Institutions jointly establish ethical review boards to review matters such as the propriety of research implementation.

No. 17 Roles and Responsibilities of Ethical Review Boards

The roles and responsibilities of the ethical review boards established according to the provisions of the preceding paragraph are separately established by the Kyushu University Medical Ethics Council.

Chapter 9 Personal Information and Anonymously Processed Information

No. 18 Basic Responsibilities Relating to Personal Information

1 Protection of Personal Information

(1) Researchers and related parties, as well as research directors, shall, with regard to the handling of personal information, anonymously processed information and anonymized personal information, comply with the Guidelines, as well as laws and regulations related to personal information protection, and the rules and regulations established by Kyushu University and its Medical Institutions.

(2) Researchers and related parties, as well as research directors, shall, out of respect for the deceased and the feelings of surviving family and others connected with them, take all necessary and appropriate measures to ensure all deceased persons' personally identifiable information is handled with the same level of appropriate care as is given to the personal information of the living and, if requests are received for disclosure, revision, etc., of personal information held by researchers or related parties, or by research directors, all necessary steps shall be taken to ensure these requests are appropriately handled in accordance with the Guidelines.

2 Proper Acquisition

(1) Researchers and related parties shall not use deception or other wrongful means to obtain personal information in conducting the research.

(2) As a rule, researchers and related parties shall not handle personal information that goes beyond the scope of what research subjects and related parties consented to prior to the start of research.

Supplementary Provisions

1. All revisions to this manual must be approved by the Kyushu University Medical Ethics Council.

2. This manual shall come into effect from June 30, 2021.

Attached Table (related to No. 8 of Chapter 4)

As a rule, when using samples/information obtained from people, it is necessary to seek the research subject's informed consent by means of a written document describing all explanatory matters.

However, if conditions exist which make this difficult, the procedures for obtaining informed consent can be simplified to the extent stipulated in 9 of No. 8 (page 12).

The table below is provided as a reference for more easily understanding the differences between various situations; researchers and related parties must ultimately defer to the opinion of ethical review boards which have reviewed the entire research plan.

	Invasive procedure yes/no	Intervention yes/no	Type	IC, etc.			Examples/Considerations
1	Yes	—	Prospective	A			・Use of unapproved drug or medical instruments ・Long-term constraint on behavior...etc.
2	Yes (minimally invasive)	No	Prospective	A			・Obtaining an excess sample when taking blood or performing a biopsy ・Could conceivably create a psychological burden...etc.
3	No	Yes	Prospective	A	(B)		・Research using food, lifestyle constraints, etc. (Note 1)
4	No	No	Prospective sample	A	(B)		・Research using saliva or urine...etc. (Note 2)
5	No	No	Prospective information		B	(C)	・Investigation using questionnaires or interviews...etc. (Note 3)
6	—	—	Retrospective sample Retrospective information			C	・Use of blood or surgical or pathological specimens; collection of medical information...etc. (Note 4) ・Secondary use of samples/information obtained from prior research...etc. (Note 5)

A: Receive informed consent based on written document which details all explanatory matters.

B: Receive informed consent based on oral explanation of explanatory matters and record the method and content of explanation and content of consent.

C: When both A and B are difficult to perform, provide notification or public disclosure of research implementation (such as on the homepage) and ensure research subjects have an opportunity to refuse.

Note 1 When there are reasons, such as having a broad range of research subjects, which make A difficult, these reasons can be explained to the ethical review board and an alternative method, such as oral consent (B), can be used.

Note 2 Same as Note 1. However, when IC is sought for such purposes as conducting analysis of the research subject's genetic information, A must be used.

Note 3 When obtaining special care-required personal information, it is essential to receive appropriate consent,

such as oral consent; however, when the research subject answers via a questionnaire or interview that is accompanied by an explanatory document, this is treated as B. When reasons exist that make B difficult, they can be explained to the ethical review board and, instead, public information disclosure on the homepage (C) can be used.

Note 4 After C has been set up, so long as no complicating factors exist, researchers and related parties shall endeavor to guarantee that research subjects and relevant parties have the opportunity to opt out, for example by 1) sending out a notification, via mail or another method, that the explanatory matters are publicly displayed on the homepage or 2) providing an oral explanation to them when they arrive at the hospital.

Note 5 It is not necessary to re-obtain consent if only using analysis results from prior research; however, if samples/information which have been preserved are to be newly analyzed for a different purpose, Note 4 shall apply.