Ethical Guidelines for Medical and Biological Research Involving Human Subjects

March 23, 2021

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(Partially amended on March 27, 2023)

Ministry of Education, Culture, Sports, Science and Technology

Ministry of Health, Labour and Welfare

Ministry of Economy, Trade and Industry

Notice

- Only the original Japanese text of these Guidelines has legal effect, and the translation is to be used solely as reference material to aid in the understanding of these Guidelines.

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Preamble

Through the development of medical and biological science and medical technology, medical and biological research involving human subjects is contributing significantly to society in terms of maintaining and promoting people's good health, advancing the recuperation of patients from injury and disease, and improving the quality of life. As a result, it plays an important role in the development of human health and welfare and the fostering of new industries. The research bases and research itself are required to be developed continuously in the future.

On the other hand, medical and biological research involving human subjects can have major impacts on these research subjects both physically and mentally and, indeed, on society itself, as well as raise a variety of ethical, legal, and social issues by bringing about changes in medical practice and medical services. The welfare of those research subjects shall be given priority over the scientific and social results of research, and human dignity and rights shall be protected. In addition, such research will be more beneficial if it gains the understanding and trust of society. Therefore, while respecting academic freedom, Japan has established an institutional framework, taking into consideration corresponding systems in other countries, to ensure that medical and biological research involving human subjects is conducted properly and smoothly with respect for human dignity and human rights.

In Japan, related guidelines have been established successively by the relevant ministries and agencies since 2001, on the basis of the ethical norms and standards set forth in the Constitution of Japan, the Act on the Protection of Personal Information (Act No. 57 of 2003, hereinafter referred to as the "Personal Information Protection Act"), the related ordinances of Japan, the Declaration of Helsinki by the World Medical Association, and the Fundamental Principles of Research on the Human Genome by the Council for Science and Technology, Bioethics Committee (decided by the Council for Science and Technology, Bioethics Committee on June 14, 2000). In addition, the scope and methods of research have been continuously reviewed in accordance with the diversification of research subjects and methods, as well as with advances in medical and biological science, and medical technology.

In recent years, much research has been conducted that falls under both the Ethical Guidelines for Medical and Health Research Involving Human Subjects and the Ethical Guidelines for Human Genome/Gene Analysis Research. Since there are many similarities in the procedures stipulated in both guidelines, a new set of ethical guidelines was established in 2021, integrating the Ethical Guidelines for Medical and Health Research Involving Human Subjects with the Ethical Guidelines for Human Genome/Gene Analysis Research.

In consideration of the fact that research takes various forms, the basic principles are presented in these Guidelines. Under the Guidelines, the investigator, etc. are required to formulate a research plan, the appropriateness of which is reviewed by an ethical review committee. In conducting research, all of the parties involved are required to make appropriate judgments based on these basic principles and in accordance with the contents of individual research plans, etc.

Note:

- Ethical Guidelines for Human Genome/Gene Analysis Research (Public Notice of the Ministry of

Education, Culture, Sports, Science and Technology, the Ministry of Health, Labour and Welfare, and the Ministry of Economy, Trade and Industry No. 1 of 2001, repealed on June 30, 2021)

- Ethical Guidelines for Epidemiological Research (Public Notice of the Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labour and Welfare No. 2 of 2002, repealed on March 31, 2015)
- Ethical Guidelines for Clinical Research (Public Notice of the Ministry of Health, Labour and Welfare No. 255 of 2003, repealed on March 31, 2015)
- Ethical Guidelines for Medical and Health Research Involving Human Subjects (Public Notice of the Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labour and Welfare No. 3 of 2014, repealed on June 30, 2021)

Chapter 1 General Provisions

Part 1 Purposes and Basic Principles

The purposes of these Guidelines are to ensure that human dignity and rights are protected and that medical and biological research involving human subjects are promoted properly, by prescribing the rules and procedures with which those who are concerned in such research should comply. Any of those concerned in this type of research shall conduct their research in accordance with these Guidelines as basic principles for the matters as defined below:

(i) Conducting research with social and academic values;

(ii) Ensuring scientific validity that is suitable for the characteristics in a particular field of research;

(iii) Weighing the benefits to be derived from the research against the burdens and other disadvantages placed on research subjects;

(iv) Review by an independent and fair ethical review committee;

(v) Giving adequate prior explanations to and obtaining voluntary consent from research subjects;

(vi) Paying special consideration to vulnerable subjects;

(vii) Appropriately managing personal information, etc. used in research; and,

(viii) Ensuring integrity and transparency of research.

Part 2 Glossary

The terms used in these Guidelines shall be defined as follows:

(1) Medical and Biological Research Involving Human Subjects

Activities involving human subjects that are conducted for the purposes of A or B below:

A. To obtain knowledge that contributes to maintaining and promoting public health or to the recovery of patients from injury or illness, or to improving quality of life through the following (i), (ii), (iii), or (iv) below:

(i) Understanding the causes of injury and disease (including the frequency and distribution of various health-related events and the factors that affect them);

(ii) Understanding pathology;

(iii) Improving or verifying the effectiveness of injury and disease prevention methods; or,

(iv) Improving or verifying the effectiveness of diagnostic and therapeutic methods in medical care.

B. To obtain knowledge about the structures or functions of the human genome and genes and gene mutation or expression, using specimens and/or information of human origin.

(2) Invasiveness

To cause injuries or distress to the body and/or mind of a research subject by conducting a procedure for investigational purposes, such as puncture, incision, administration of drugs, irradiation, and questions related to a subject's mental trauma, etc.

Of various types of invasiveness, one causing minor injury and/or distress to the body and/or

mind of a research subject is called “minor invasiveness.”

(3) Intervention

A practice for investigational purposes to control the presence or absence of factors that can affect a variety of events occurring in relation to human health (including activities to maintain and promote good health and medical practices, such as medication and examinations for prevention, diagnosis, and treatment of patients), or the degree of such factors. The above-defined intervention also includes medical technique beyond usual medical practice that are conducted for investigative purposes.

(4) Specimens

A part of the human body (including that of deceased individuals) to be used (or which has been used) in research, such as blood, body fluids, tissues, cells, excrement, and DNA extracted from them, etc.

(5) Information Used in Research

Information on human health, such as name of disease, details of medication, and results of examinations and measurements obtained through diagnosis and treatment of research subjects, and other information (including that concerning deceased individuals) to be used (or which have been used) in research.

(6) Specimens and/or Information

Specimens and/or information used in research.

(7) Existing Specimens and/or Information

Of the above-defined specimens and/or information, specimens and/or information that correspond to any of the following:

(i) Specimens and/or information already existing prior to preparation of the research protocol; or,

(ii) Specimens and/or information acquired after preparation of the research protocol, but not intended to be used in the research defined in the said research protocol at the time the said specimens and/or information were acquired.

(8) Genetic Information

Information indicating the genetic characteristics and constitution of an individual that is obtained through the course of research conducted using specimens and/or information or passed on to offspring already associated with specimens and/or information.

(9) Research Subject

A person (including a deceased individual) who corresponds to any of the following:

(i) An individual on whom research is conducted (including an individual asked to be enrolled in the research); or,

(ii) An individual from whom existing specimens and/or information are used in research.

(10) Research Subjects, etc.

In addition to research subjects, this term includes representative, etc., as defined later.

(11) Research Implementing Entity

A legal entity, administrative organ, or individual business owner who conducts research, excluding contractors for a part of research work such as storage of specimens and/or information and statistical processing.

(12) Collaborative Research Implementing Entity

A research implementing entity collaboratively conducting research based on a research protocol (including any entities that acquire new specimens and/or information from research subjects for the said research and provide them to other research implementing entity(s)).

(13) Cooperating Research Institution

An organization, other than the research implementing entity where research is conducted based on a research protocol, that acquires new specimens and/or information from research subjects for the said research (excluding acquisition of specimens involving invasiveness (excluding minor invasiveness)), and only provides them to research implementing entities.

(14) Institution Collecting and Providing Specimens and/or Information

Of the above-defined research implementing entities, an institution that conducts research work to acquire specimens and/or information from research subjects or from other entity(s), to store and to provide the said specimens and/or information to other research implementing entity(s) repeatedly and on an ongoing basis (hereafter referred to as “collection and provision”).

(15) Academic Research Institution or the Equivalent

Academic research institution or the equivalent as defined in Article 16, paragraph (8) of the Personal Information Protection Act.

(16) Multi-institutional Joint Research

Research conducted at multiple research implementing entities based on a single research protocol.

(17) Investigator, etc.

Principal investigator(s) and others who are engaged in conducting research (including the execution of operations at the above-defined "institution collecting and providing specimens and/or information"), excluding persons who do not belong to the research implementing entity and

(i) only acquire new specimens and/or information, and provide them to research implementing entities;

(ii) only provide existing specimens and/or information; or,

(iii) only engage in a part of the work related to the research under entrustment.

(18) Principal Investigator

An individual who is engaged in conducting research and directing overall research work at the research implementing entity to which he/she belongs.

In the following, the principal investigator shall be read as representative investigator, as necessary, in the case of multi-institutional joint research.

(19) Representative Investigator

In the case of multi-institutional joint research, the principal investigator who represents the principal investigators of multiple research implementing entities.

(20) Chief Executive of Research Implementing Entity

The representative of a legal entity, the head of an administrative organ or an individual business owner who conduct research.

(21) Ethical Review Committee

An institution, utilizing a consensual decision-making system, which is organized to undertake examinations and reviews concerning the ethical justification and scientific validity to conduct or continue research and other relevant matters.

(22) Informed Consent

Consent given by research subjects, etc. based on their own free will concerning conduct or continuation of research (including the handling of specimens and/or information) after they receive sufficient explanation from the investigator, etc. or persons who only provide existing specimens and/or information concerning the purpose, the significance, and method of the said research, the burden on the research subjects, the predicted results (including risks and benefits), etc., and then understand them.

(23) Appropriate Consent

Consent given by research subjects, etc. concerning the acquisition and use (including provision) of specimens and/or information after the matters necessary for the research subjects,

etc. to determine consent have been clearly indicated in a reasonable and appropriate manner (and for personal or other related information, that shall meet the Personal Information Protection Act).

(24) Representative

An individual who is expected to speak for the will and benefit of a living research subject, and if the research subject is considered to be objectively unable to give informed consent or appropriate consent, is competent to give informed consent or appropriate consent to the investigator, etc. or persons who only provide existing specimens and/or information on behalf of the said research subject.

(25) Representative, etc.

An individual including the above-defined representative, as well as an individual who is competent to give informed consent or appropriate consent on behalf of the deceased research subject.

(26) Informed Assent

Expression of understanding and agreeing, with respect to whether the research shall be conducted or continued, of research subjects who are considered to be objectively unable to give informed consent upon receiving an explanation of the said research to be conducted or continued in easy-to-understand language according to their ability to understand.

(27) Personal Information

Personal information as defined in Article 2, paragraph (1) of the Personal Information Protection Act.

(28) Individual Identification Code

Individual identification code as defined in Article 2, paragraph (2) of the Personal Information Protection Act.

(29) Sensitive Personal Information

Sensitive personal information as defined in Article 2, paragraph (3) of the Personal Information Protection Act.

(30) Pseudonymized Personal Information

Pseudonymized personal information as defined in Article 2, paragraph (5) of the Personal Information Protection Act.

(31) Anonymized Personal Information

Anonymized personal information as defined in Article 2, paragraph (6) of the Personal

Information Protection Act.

(32) Information Related to Personal Information

Information related to personal information as defined in Article 2, paragraph (7) of the Personal Information Protection Act.

(33) Personal or Other Related Information

Personal information, pseudonymized personal information, anonymized personal information and information related to personal information.

(34) Deleted or Other Related Information

Deleted or other related information as defined in Article 41, paragraph (2) of the Personal Information Protection Act.

(35) Processing Method etc. Related Information

Processing method etc. related information as defined in Article 35, item (i) of the Enforcement Rules for the Act on the Protection of Personal Information (Rules of the Personal Information Protection Commission No. 3 of 2016; hereinafter referred to as the "Enforcement Rules for the Act on the Protection of Personal Information").

(36) Adverse Event

All undesirable or unintended injuries or illnesses or signs thereof (including abnormal laboratory values) occurring in a research subject, whether or not causally related to the research conducted.

(37) Serious Adverse Event

Of the above-defined adverse events, an event that:

(i) Results in death;

(ii) Is life-threatening;

(iii) Requires inpatient hospitalization or prolongation of existing hospitalization;

(iv) Results in persistent or significant disability or incapacity; or,

(v) Is a congenital anomaly or birth defect to offspring.

(38) Unexpected Serious Adverse Event

Of the above-defined serious adverse events, an event that is not consistent with the information in the research protocol, the document used for obtaining informed consent, etc., or is not consistent with the severity described in such, even if there is any description about the event.

(39) Monitoring

An act of overseeing the progress of research, and of determining whether the research is being conducted in compliance with these Guidelines and the research protocol, in order to ensure that the research is properly conducted. Such act is performed by an individual appointed by the principal investigator.

(40) Audit

An examination of research-related activities to determine whether the research has been conducted in compliance with these Guidelines and the research protocol, in order to assure the reliability of results of the research. Such examination is performed by an individual appointed by the principal investigator.

(41) Genetic Counseling

Providing support or assistance to the research subjects, etc., or their blood relatives, to make their own choices and undertake their own actions for their future lives, using knowledge of genetic medicine and counseling techniques, to repeatedly interact with and provide information to such research subjects, etc., or their blood relatives for the purpose of resolving or alleviating medical or psychological problems that may arise around genetic disorders.

Part 3 Scope of Application

1. Research applicable to these Guidelines

These Guidelines shall apply to any medical and biological research involving human subjects that is conducted by a Japanese investigator, etc., or is conducted in Japan. Of research that falls under the scope to which other guidelines are applicable, however, matters not set forth in such other guidelines shall be conducted in accordance with these Guidelines.

In addition, research falling under any of the following categories A through C shall not be applicable to these Guidelines:

A. Research conducted pursuant to the provisions of laws and ordinances;

B. Research included within scope of the code of conduct set forth by laws and ordinances; or,

C. Research utilizing only the specimens and/or information listed in the following:

(i) Specimens and/or information, the value of which has already been established academically, that are widely used in research and are generally available;

(ii) Existing information that is not information relating to an individual; and,

(iii) Anonymized personal information that has already been created.

2. Information on deceased individuals

These Guidelines shall apply mutatis mutandis to medical and biological research involving human subjects conducted by a Japanese investigator, etc., or conducted in Japan, which handles information pertaining to deceased individuals.

3. Research conducted outside Japan

(1) When conducting research outside Japan (including research conducted collaboratively with foreign research implementing entities), a Japanese investigator, etc. shall follow these Guidelines and also adhere to the provisions set forth in local laws, ordinances, guidelines, etc. of the country or the region where the research is conducted. When the provision(s) set forth in such local laws, ordinances, guidelines, etc. of the country or the region where the research is conducted are stricter than the provision(s) of these Guidelines, however, research shall be conducted in accordance with the provision(s) of the said local laws, ordinances, guidelines, etc. of the country or the region where the said research is conducted, in place of the relevant provision(s) of these Guidelines.

(2) When the provision(s) of these Guidelines are stricter than the provision(s) of local laws, ordinances, guidelines, etc. of the country or the region where the research is conducted and it is difficult to conduct the research in accordance with the provision(s) of these Guidelines, if all of the following matters are prescribed in the research protocol and the chief executive of the Japanese research implementing entity gives approval after deliberations by the relevant ethical review committee with respect to conduct of the research, the said research may be conducted in accordance with the provision(s) of local laws, ordinances, guidelines, etc. of the country or the region where the said research is conducted, in place of the relevant provision(s) of these Guidelines:

(i) Appropriate measures to be taken with respect to informed consent at the overseas research implementing sites; and,

(ii) Appropriate measures to be taken to protect personal information used in the research at the overseas research implementing sites.

(3) When only providing existing specimens and/or information from Japan to the investigator, etc. outside Japan, these Guidelines shall apply and the relevant provisions of Parts 8 and 9 shall be observed.

Chapter 2 Obligations of Investigator, etc.

Part 4 Basic Obligations of Investigator, etc.

1. Consideration for research subjects, etc.

(1) The investigator, etc. shall conduct research with the utmost respect for the life, health, and human rights of the research subjects.

(2) The investigator, etc. shall comply with laws, regulations, guidelines, etc., and shall properly conduct the research in accordance with the research protocol that has been reviewed by the ethical review committee and approved by the chief executive of the research implementing entity for the conduct of the said research.

(3) In principle, the investigator, etc. shall obtain informed consent prior to conducting research.

(4) The investigator, etc. shall respond appropriately and promptly to consultation, inquiries, complaints, etc. (hereinafter referred to as "consultation, etc.") of research subjects, etc., and other individuals concerned.

(5) The investigator, etc. shall not disclose information obtained while they are engaged in research without justifiable reason. The same shall apply even after the investigator, etc. are no longer engaged in the research.

(6) When conducting research on a group with certain characteristics, such as local residents, that may reveal unique characteristics of the said local residents, etc., the investigator, etc. shall explain the content and significance of the research to the research subjects, etc. and the said local residents, etc., and endeavor to obtain their understanding of the research.

2. Education and training

The investigator, etc. shall receive education and training related to the ethics of research as well as knowledge and skills necessary to conduct the research prior to its conduct. They shall also receive education and training during the research period on a regular basis as necessary.

Part 5 Obligations of Chief Executive of Research Implementing Entity

1. Overall supervision of research

(1) The chief executive of the research implementing entity shall take responsibility for the necessary supervision to ensure that the research he/she approved for conducting is conducted properly.

(2) The chief executive of the research implementing entity shall confirm, as necessary, that the research is being conducted properly in accordance with these Guidelines and the research protocol, and shall take necessary measures to ensure the proper conduct of the research.

(3) The chief executive of the research implementing entity shall ensure that those involved in the research work conduct the research with due respect for the life, health, and human rights of the research subjects.

(4) The chief executive of the research implementing entity shall not disclose, without any justifiable reason, information obtained during duties related to the research. The same shall apply, even after he/she has ceased to be engaged in the duties.

2. Establishment, etc. of systems and procedures for conduct of research

(1) The chief executive of the research implementing entity shall arrange systems and procedures (including matters relating to the handling of specimens and/or information)

necessary for the proper conduct of research.

(2) If a research subject incurs any health damage related to research conducted by the research implementing entity, the chief executive of the said research implementing entity shall ensure that necessary measures are taken appropriately, such as compensation for research-related health damage.

(3) The chief executive of the research implementing entity shall ensure that information on the conduct of research is notified to the research subjects, etc., or is made easily accessible by research subjects, etc., depending on the contents of the research to be conducted at the said research implementing entity.

(4) The chief executive of the research implementing entity shall ensure that the results of the research and other information related thereto are appropriately made public, after taking necessary measures to protect the human rights of the research subjects, etc. and other individuals concerned or the rights and interests of the investigator, etc. and other individuals concerned.

(5) The chief executive of the research implementing entity himself/herself shall, as necessary, verify and review whether the research conducted by the said research implementing entity complies with these Guidelines and shall take appropriate measures based on the results of such verification and reviews.

(6) The chief executive of the research implementing entity shall cooperate with investigations conducted by the ethical review committee.

(7) The chief executive of the research implementing entity shall take measures to ensure that the investigator, etc. of the said research implementing entity shall receive education and training related to the ethics of research, as well as knowledge and skills necessary to conduct the research. The chief executive of the research implementing entity himself/herself shall also receive such education and training.

(8) The chief executive of the research implementing entity may delegate the authority and duties set forth in these Guidelines to appropriate individual(s) who belong to the said research implementing entity, in accordance with the procedures established at the said research implementing entity.

Chapter 3 Proper Conduct of Research, etc.

Part 6 Procedures Related to Research Protocol

1. Preparation and revision of research protocol

(1) When the principal investigator intends to conduct research, he/she shall prepare a research protocol in advance. If the principal investigator intends to conduct research that differs from the content of the research protocol, he/she shall revise the research protocol in advance. When research is to be conducted using existing specimens and/or information for which consent has been obtained with respect to the matters listed in Part 8.5 (xxi), and when the content of the research within the scope of the said consent (including the recipient, etc.) has been specified, the research proposal concerning the content of the said research shall be prepared or revised.

(2) In preparing or revising the research protocol described in (1) above, the principal investigator shall ensure the ethical justification and scientific validity of the research. In addition, he/she shall comprehensively evaluate the burden on research subjects and the predicted risks and benefits, and shall take measures to minimize burdens and risks.

(3) The principal investigator who conducts multi-institutional joint research shall appoint a representative investigator from among the said principal investigators to represent work pertaining to the said multi-institutional joint research.

(4) When the representative investigator intends to conduct multi-institutional joint research, he/she shall prepare or revise a single research protocol after clarifying the roles and responsibilities of the principal investigators from each research implementing entity.

(5) When the principal investigator intends to entrust part of the work related to the research, he/she shall prepare or revise the research protocol after specifying the details of the said entrusted work.

(6) When entrusting part of the work related to research, the principal investigator shall conclude a contract in writing or by electromagnetic means (that is a method using an electronic data processing system or other information communication technology; the same shall apply hereinafter) concerning the matters to be observed by the entrusted party, and shall exercise necessary and appropriate supervision over the entrusted party.

(7) When the principal investigator intends to conduct research involving invasiveness (excluding minor invasiveness) that involves medical technique beyond usual medical practice, he/she shall take appropriate measures in advance, such as obtaining insurance coverage, in order to provide compensation for any health damage caused to research subjects in relation to the said research.

2. Submission of matters to ethical review committee for deliberation

(1) The principal investigator shall submit the matter to the ethical review committee for

deliberation with respect to the appropriateness of conducting the research.

(2) In principle, the representative investigator shall submit a matter to a single ethical review committee for deliberation to make a comprehensive review on the research protocol for multi-institutional joint research.

(3) After deliberations by the ethical review committee, the principal investigator shall submit the results of the deliberations, the documents submitted to the said ethical review committee, and any other documents requested by the chief executive of the research implementing entity, to the chief executive of the research implementing entity, in order to receive approval for conduct of the said research at the said research implementing entity.

(4) Notwithstanding the provisions of (1) to (3) above, if it is determined that research is urgently necessary to prevent the occurrence or spread of harm to public health, research may be conducted only with the permission of the chief executive of the research implementing entity, prior to deliberations by the ethical review committee on the conduct of the said research. In this case, the principal investigator shall submit the matter to the ethical review committee without delay after approval. If the ethical review committee expresses the opinions that the research should be suspended or terminated or that the research protocol should be revised, the principal investigator shall respect the said opinions and take appropriate measures such as suspending or terminating the research or revising the research protocol.

(5) Concerning multi-institutional joint research, if the principal investigator submits the matter to an individual ethical review committee regardless of the provisions of (2) above, the principal investigator shall provide the said ethical review committee with the information necessary for the review, including permission to conduct the research at the collaborative research implementing entities, the results of reviews by other ethical review committees, and the status of the progress of the said research.

3. Approval by chief executive of research implementing entity

(1) When the principal investigator requests approval for conduct of the research, the chief executive of the research implementing entity shall, while respecting the opinions of the ethical review committee, decide whether to approve or approval for conduct of the research and decide on other necessary measures concerning the research. In this case, the chief executive of the research implementing entity shall not give approval for conduct of the said research if the ethical review committee expresses the opinion that the conduct of the said research is inappropriate.

(2) If the chief executive of the research implementing entity learns of or obtains information that may affect continuing research being conducted at the said research implementing entity,

he/she shall promptly suspend the research, identify the cause, and take other appropriate measures.

(3) When the chief executive of the research implementing entity learns of or obtains information that may impair or threaten the appropriateness of research conducted or the reliability of research results, he/she shall promptly take necessary measures.

4. Registration of research summary

(1) The principal investigator shall register a summary of any research involving intervention, prior to its conduct, in the database maintained by the Ministry of Health, Labour and Welfare (Japan Registry of Clinical Trials: jRCT) and other public databases, and update the summary according to revisions of the research protocol and the progress of the research. In addition, the principal investigator shall also endeavor to register a summary of other research prior to the conduct thereof and update the summary at the time of revising the research protocol and according to the progress of the research.

(2) The obligation to register in (1) above shall not apply where the chief executive of the research implementing entity, in the opinion of the ethical review committee, determines that it is necessary to keep the research summary private in order to protect the human rights of the research subjects, etc. and other individuals concerned or the rights and interests of the investigator, etc. and other individuals concerned.

5. Ensuring proper conduct of research

(1) The principal investigator shall instruct and manage the investigators and other persons involved in conducting the said research so that the research is properly conducted in accordance with the research protocol and that the reliability of the results is ensured.

(2) When the principal investigator learns of the occurrence of a serious adverse event in the conduct of research involving invasiveness, he/she shall promptly take necessary measures.

6. Procedures after research is completed

(1) When the principal investigator completes (including terminates; the same shall apply hereinafter) research, he/she shall report to that effect and a summary of the research results to the ethical review committee and the chief executive of the research implementing entity in writing or by electromagnetic means without delay.

(2) When the research is completed, the principal investigator shall publicly announce the results of the said research without delay, after taking necessary measures to protect the human rights of the research subjects, etc. and other individuals concerned or the rights and interests of the investigator, etc. and other individuals concerned. Upon final publication of the results of

research involving invasiveness (excluding minor invasiveness) and intervention, the results shall be reported without delay to the chief executive of the research implementing entity.

(3) Upon completion of the research involving intervention, the principal investigator shall register the results of the said research without delay in the public database in which the summary of the said research was registered as in Section 4 (1). The principal investigator shall also endeavor to register the results of other research.

(4) When conducting research involving medical technique beyond usual medical practice, the principal investigator shall endeavor to ensure that the research subjects receive the best possible prevention, diagnosis, and treatment obtained from the results of the said research, even after the said research has been completed.

Part 7 Contents of Research Protocol

(1) Contents of research protocol (excluding cases as defined in (2) below) shall, in principle, include the matters below. Any of those matters may be omitted, however, when the chief executive of the research implementing entity gives approval for such after deliberations by the relevant ethical review committee.

(i) Title of the research;

(ii) Organizational framework for the research (including the names of all of the research implementing entities and cooperating research institutions, the names of the investigator, etc., and the names of persons who only provide existing specimens and/or information, and the names of institutions to which they belong);

(iii) Purpose and significance of the research;

(iv) Method and time period of the research;

(v) Enrolling criteria of research subjects;

(vi) Basis of scientific validity for conducting the research;

(vii) Procedures pursuant to the provisions of Part 8 below for obtaining informed consent, etc. (including information to be provided and consented to pursuant to the relevant provisions of Part 8, when obtaining informed consent);

(viii) Handling of personal or other related information (including the processing method, if the information is processed, and a statement to the effect that pseudonymized personal information or anonymized personal information is to be created, if such is the case);

(ix) Burdens placed on the research subjects and predicted risks and benefits, including comprehensive assessment of such burdens, risks and benefits, as well as measures to minimize those burdens and risks;

(x) Means for storing and disposing of specimens and/or information (including records related to information used in research);

(xi) Matters to be reported to the chief executive of the research implementing entity and procedures for such reports;

(xii) Status of research-related conflicts of interest of the research implementing entity, such as research fund resources, as well as research-related conflicts of interest of the investigator, etc., such as his/her individual income;
(xiii) Means to disclose information on research;
(xiv) Handling of results, etc. obtained from research;
(xv) Consultation system and services (including genetic counseling) for research subjects, etc. and other individuals concerned to receive research-related consultation;
(xvi) When obtaining informed consent from a representative, etc., procedures pursuant to the provisions of Part 9 below (including matters related to the criteria for selecting a representative, etc. and to be informed and consented to pursuant to the provisions of Parts 8 and 9 below);
(xvii) When obtaining informed assent, procedures pursuant to the provisions of Part 9 below (including information to be provided);
(xviii) When research is to be conducted in accordance with the provisions of Part 8.7, the method for determining whether all of the requirements listed in the said provision are met;
(xix) When the research involves any financial expenditure on or remuneration for the research subjects, etc., a statement to that effect and details of such;
(xx) When the research involves invasiveness, means to respond in cases of serious adverse event;
(xxi) When the research involves invasiveness, whether or not compensation will be offered for research-related health damage and details of such compensation;
(xxii) When the research involves any medical technique beyond usual medical practice, responses related to healthcare delivery for the research subjects after the research;
(xxiii) When part of work related to the research is entrusted, the content of work to be entrusted and means of supervision over the contractor(s);
(xxiv) With respect to specimens and/or information acquired from the research subject, when any of those may be used or provided to other research implementing entity(s) for the research in future that is not identified at the time of obtaining consent from the research subjects, etc., a statement to that effect, the contents of utilization assumed at the time of obtaining consent, and the method by which the research subjects, etc. confirm information on the research to be conducted and the research implementing entity scheduled to receive such specimens and/or information; and,
(xxv) When monitoring or audit is performed pursuant to the provisions of Part 14 below, organizational framework and procedures for such.

(2) In principle, the matters to be included in the research protocol when the collection and provision of specimens and/or information are to be conducted shall be as follows. Any of those matters may be omitted, however, when the chief executive of the research implementing entity gives approval for such after deliberations by the relevant ethical review committee.
(i) Organizational framework for collection and provision of specimens and/or information

(including the name(s) of the institution collecting and providing specimens and/or information and the investigator, etc.);

(ii) Purpose and significance of the collection and provision of specimens and/or information;

(iii) Method and time period for collection and provision of specimens and/or information;

(iv) Types of specimen and/or information to be collected and provided;

(v) Procedures pursuant to the provisions of Part 8 below for obtaining informed consent, etc. (including information to be provided and consented to pursuant to the relevant provisions of Part 8, when obtaining informed consent);

(vi) Handling of personal or other related information (including the processing method, if the information is processed, and a statement to the effect that pseudonymized personal information or anonymized personal information is to be created, if such is the case);

(vii) Burdens placed on the research subjects and predictable risks and benefits, including comprehensive assessment of such burdens, risks and benefits, as well as measures to minimize those burdens and risks;

(viii) Means for storing specimens and/or information and for their quality control;

(ix) Handling of specimens and/or information after collection and provision are completed;

(x) Status of research-related conflicts of interest of the institution collecting and providing specimens and/or information, such as fund resources for collection and provision, as well as research-related conflicts of interest of the investigator, etc., such as his/her individual income;

(xi) Responses to consultation, etc. made by the research subjects, etc. and other individuals concerned;

(xii) When the research involves any financial expenditure on or remuneration for the research subjects, etc., a statement to that effect and details of such;

(xiii) Handling of results, etc. obtained from the research; and,

(xiv) With respect to specimens and/or information acquired from the research subject, when any of those may be provided to other research implementing entity(s) for the research in the future that is not identified at the time of obtaining consent from the research subjects, etc., a statement to that effect, the content of utilization assumed at the time of obtaining consent, and the method by which the research subjects, etc. confirm information on the research implementing entity scheduled to receive such specimens and/or information.

Chapter 4 Informed Consent, etc.

Part 8 Procedures for Obtaining Informed Consent, etc.

1. Procedures for obtaining informed consent, etc.

When the investigator, etc. intends to conduct research, or when a person who only provides existing specimens and/or information intends to provide existing specimens and/or information, he/she shall, in principle, obtain informed consent in advance in accordance with the following procedures (1) through (5), respectively, as provided in the research protocol approved by the chief executive of the research implementing entity concerning the conduct of

the said research. When specimens and/or information are to be provided to a person located overseas (excluding countries specified by the Personal Information Protection Commission as foreign countries falling under all of the matters in Article 15, paragraph (1) of the Enforcement Rules for the Act on the Protection of Personal Information; the same shall apply hereinafter), the procedures in (6) below shall be followed, in addition to the procedures in (1), (3), or (4) below. However, this shall not apply to cases where existing specimens and/or information are provided or received in accordance with the provisions of laws and regulations.

(1) Cases where research is to be conducted by acquiring new specimens and/or information:

The investigator, etc. shall conduct research following the procedures in A or B below.

In addition, the investigator, etc. shall follow the procedures in A or B themselves, even when acquiring new specimens and/or information for the said research through a cooperating research institution. In addition, the cooperating research institution shall ensure that the said procedures have been taken.

A. Research involving invasiveness

The investigator, etc. shall obtain written informed consent, which includes information to be provided pursuant to the provisions of Section 5 below.

B. Research not involving invasiveness

(a) Research involving intervention

The investigator, etc. shall not necessarily be required to obtain informed consent in writing. When written informed consent is not obtained, however, the investigator, etc. shall obtain oral informed consent, with respect to the information provided pursuant to the provisions of Section 5 below, and prepare a record of methods for providing such information and its content, as well as details of consent obtained.

(b) Research not involving intervention

(i) Research utilizing specimens

The investigator, etc. shall not necessarily be required to obtain informed consent in writing. When written informed consent is not obtained, however, the investigator, etc. shall obtain oral informed consent, with respect to the information provided pursuant to the provisions of Section 5 below, and prepare a record of methods for providing such information and its content, as well as details of consent obtained.

(ii) Research not utilizing specimens

i. Cases where research is to be conducted by acquiring sensitive personal information

The investigator, etc. shall not necessarily be required to obtain informed consent. When informed consent is not obtained, however, the investigator, etc. shall, in principle, obtain appropriate consent from the research subjects, etc. However, if the research subjects, etc. are provided with an opportunity to refuse

conduct or continuation of the research, and if the requirements listed in Section 8 (1) (i) through (iii) are met, and if any of the following requirements apply, then sensitive personal information may be obtained and used after an appropriate measure is taken in accordance with the provisions of Section 8 (2):

a. The research implementing entity, which is an academic research institution or the equivalent, needs to acquire the said sensitive personal information for the purposes of academic research, and there is no risk of unreasonably infringing on the rights and interests of the research subjects; or,

b. There are special reasons for the research implementing entity to acquire such sensitive personal information to conduct the research, and it is difficult to obtain informed consent and appropriate consent from the research subjects, etc.

ii. Other cases

The investigator, etc. shall not necessarily be required to obtain informed consent or appropriate consent. When informed consent or appropriate consent is not obtained, however, the investigator, etc. shall notify the research subjects, etc. of the matters listed in Section 6 (i) through (xi) with respect to conducting the research, or make them easily accessible by the research subjects, etc., and provide the research subjects, etc. with an opportunity to refuse conduct or continuation of the said research. However, (3) B shall apply mutatis mutandis when information used in research (excluding sensitive personal information) is to be provided to collaborative research implementing entities.

(2) Cases where research is to be conducted utilizing existing specimens and/or information retained by the research implementing entity:

The investigator, etc. shall follow the procedures in A or B below:

A. Research utilizing specimens

The investigator, etc. shall not necessarily be required to obtain informed consent in writing. When written informed consent is not obtained, however, the investigator, etc. shall obtain oral informed consent, with respect to the information provided pursuant to the provisions of Section 5 below, and prepare a record of methods for providing such information and its content, as well as details of consent obtained. However, if any of the following requirements (a) through (d) applies, such procedures are not required:

(a) All of the said existing specimens and/or information meet any of the following requirements:

(i) If the said existing specimens are already in a state that does not allow identification of specific individuals, personal information is not obtained using the said existing specimens;

(ii) The information used in the said research is pseudonymized personal information (limited to information that has already been created);

(iii) The information used in the said research is anonymized personal information; or,

(iv) The information used in the said research is information related to personal information.

(b) Case (a) does not apply, and it is difficult to obtain informed consent, and one of the following requirements (i) or (ii) is met:

(i) Appropriate consent has been obtained after the matters listed in Section 6 (i) through (iii) and (vii) through (x) are notified to the research subjects, etc.;

(ii) Only the consent of the research subjects, etc. for another research for which the use in the said research was not specified at the time of acquiring the said existing specimens and/or information has been obtained, and all of the following requirements are met:

i. With respect to conduct of the said research, the matters listed in Section 6 (i) through (iii), (vii), and (viii) are notified to the research subjects etc., or are kept in a state where they are easily accessible by the research subjects, etc.; and,

ii. The consent is reasonably considered to be related to the purposes of the said research.

(c) Case (a) does not apply, and consent to the matters listed in Section 5 (xxi) has been obtained at the time of acquiring the said existing specimens and/or information; subsequently, the content of the research within the scope of the said consent is specified; information on the content of the said identified research is notified to the research subjects, etc., or is kept in a state where they are easily accessible by the research subjects, etc., and, in principle, the research subjects, etc. are provided with an opportunity to withdraw their consent to implementation of research.

(d) Any of cases (a) through (c) does not apply, and all of the following requirements (i) through (iii) are met:

(i) It is difficult to conduct the research without using the said existing specimens, and one of the following requirements is met:

i. The research implementing entity, which is an academic research institution or the equivalent, needs to handle the said existing specimens and/or information for academic research purposes, and there is no risk of unjustly infringing on the rights and interests of the research subjects; or,

ii. There are special reasons for conducting the said research, and it is difficult to obtain informed consent and appropriate consent from the research subjects, etc.

(ii) Concerning conduct of the research, the matters in Section 6 (i) through (iii) and (vii) through (x) are notified to the research subjects, etc., or are kept in a state where they are easily accessible by the research subjects, etc.; and,

(iii) In principle, the research subjects, etc. are provided with an opportunity to refuse conduct or continuation of the said research.

B. Research not utilizing specimens

The investigator, etc. shall not necessarily be required to obtain informed consent. When informed consent is not obtained, however, any of the cases in (a) to (d) below shall apply:

(a) The information used in the said research is pseudonymized personal information (limited to information that has already been created), anonymized personal information, or information related to personal information;

(b) If (a) does not apply and only the consent of the research subjects, etc. for another research for which the use in the said research was not identified at the time of acquiring the said information, and all of the following requirements are met:

(i) Concerning conduct of the said research, the matters listed in Section 6 (i) through (iii) and (vii) and (viii) are notified to the research subjects, etc., or are kept in a state where they are easily accessible by the research subjects, etc.; and,

(ii) The consent is reasonably considered to be related to the purposes of the said research.

(c) When (a) does not apply, and consent is obtained for the matters listed in Section 5 (xxi) at the time of obtaining information used in research and, subsequently, the content of research within the scope of the consent is specified, then information on the content of such identified research is notified to the research subjects, etc., or is kept in state where they are made easily accessible by the research subjects, etc., and, in principle, the research subjects, etc. are provided with an opportunity to withdraw their consent for the research to be conducted.

(d) None of (a) through (c) applies, and appropriate consent has been obtained after the matters listed in Section 6 (i) through (iii) and (vii) through (x) are notified to the research subjects, etc., or all of the requirements from (i) to (iii) listed below are met:

(i) Any of the following requirements is met:

i. The information used in the said research is pseudonymized personal information (excluding information that has already been created);

ii. The research implementing entity, which is an academic research institution or the equivalent, needs to handle information used in the said research for academic research purposes and there is no risk of an unjustly infringing on the rights and interests of the research subjects; or,

iii. There are special reasons for conducting the said research and it is difficult to obtain appropriate consent from the research subjects, etc.

(ii) Concerning conduct of the said research, the matters listed in Section 6 (i) through (iii) and (vii) through (x) are notified to the research subjects, etc., or are kept in a state where they are easily accessible by the research subjects, etc.; and,

(iii) In principle, the research subjects, etc. are provided with an opportunity to refuse conduct or continuation of the research.

(3) Cases where existing specimens and/or information are to be provided to other research implementing entity(s):

Persons who provide existing specimens and/or information to other research implementing entity(s) shall follow the procedures in A or B below:

A. When attempting to provide existing specimens and sensitive personal information

Informed consent is not necessarily required to be obtained in writing. When written informed consent is not obtained, oral informed consent shall be obtained concerning the matters explained in accordance with the provisions of Section 5 (including a statement to the effect that the said existing specimens and sensitive personal information will be provided), and a record shall be made of methods for providing such information and its content, as well as details of consent obtained. However, if it is difficult to follow these procedures and any of the following requirements (a) through (c) applies, the said procedures are not required:

(a) Only existing specimens are provided; the said existing specimens are provided in a form that does not allow identification of specific individuals; and, the research implementing entity to which the said existing specimens is provided does not obtain personal information using the said existing specimens.

(b) Provision (a) does not apply, and consent is obtained for the matters listed in Section 5 (xxi) at the time of obtaining existing specimens and sensitive personal information; subsequently, the content of the research (including the recipient) within the scope of the consent is specified; then information on the content of such identified research is notified to the research subjects, etc., or is kept in state where they are easily accessible by the research subjects, etc.,; and, in principle, the research subjects, etc. are provided with an opportunity to withdraw their consent for the research to be conducted.

(c) Item (a) or (b) does not apply, and appropriate consent has been obtained to the provision of the said existing specimens and sensitive personal information after the matters listed in Section 6 (i) through (vi) and (ix) through (xi) are notified to the research subjects, etc., or all of the following requirements (i) through (iii) are met:

(i) One of the following requirements is met (in the case where it is necessary to provide the said existing specimens, this is limited to cases where it is difficult to conduct the research without using the said existing specimens):

i. The research implementing entity, which is an academic research institution or the equivalent, needs to provide the said existing specimens and sensitive personal information to the collaborative research implementing entity for academic research purposes, and there is no risk of unjustly infringing on the rights and

interests of the research subjects;

ii. The said existing specimens and sensitive personal information are to be provided to the research implementing entity, which is an academic research institution or the equivalent; the said research implementing entity needs to handle them for academic research purposes; and, there is no risk of an unjustly infringing on the rights and interests of the research subjects; or,

iii. There are special reasons for providing the said existing specimens and sensitive personal information; and, it is difficult to obtain appropriate consent from the research subjects, etc.

(ii) Concerning the provision of the said existing specimens and sensitive personal information to other research implementing entity(s), the matters listed in Section 6 (i) through (vi) and (ix) through (xi) are notified to the research subjects, etc., or are kept in a state where they are easily accessible by the research subjects, etc.; and,

(iii) The research subjects, etc. are provided with an opportunity to refuse to provide the said existing specimens and sensitive personal information to other research implementing entity(s).

B. Other than A

When providing information used in research (excluding sensitive personal information), informed consent shall not be necessarily required. When informed consent is not obtained, however, appropriate consent shall be obtained in principle. However, if any of the following requirements (a) through (d) apply, the said procedures are not required:

(a) The information used in the said research is information related to personal information, and either of the following (i) and (ii) applies:

(i) The research implementing entity to which the information is to be provided is not expected to acquire such information related to personal information as personal information; or,

(ii) The research implementing entity to which the information is to be provided is expected to acquire the said information related to personal information as personal information, but any of the following requirements applies:

i. When, in provisions of A (c) (i) i through iii, “specimens and sensitive personal information” is read as “information related to personal information,” any of the provisions of A (c) (i) i through iii is met; or,

ii. The person providing the information to be used in the said research has confirmed that the appropriate consent has been obtained from the research subjects, etc. at the research implementing entity to which the information will be provided.

(b) It is difficult to obtain appropriate consent, and the information used in the said research is anonymized personal information.

(c) Provision (a) or (b) does not apply, and consent is obtained for the matters listed in Section 5 (xxi) at the time of acquiring the information to be used in the said research,; subsequently, the content of the research (including the recipient) within the scope of the said consent is specified; then information on the content of the said identified research is notified to the research subjects., or is kept in a state where they are easily accessible by the research subjects, etc.; and, in principle, the research subjects, etc. are provided with an opportunity to withdraw their consent for the research to be conducted.

(d) Any of the provisions (a) through (c) does not apply, and it is difficult to obtain appropriate consent; and when, in provisions of A (c) (i) through (iii), "specimens and sensitive personal information" is read as "information used in research," all of the provisions of A (c) (i) through (iii) are met.

(4) Procedures for persons, etc. who only provide existing specimens and/or information

Persons, etc. who only provide existing specimens and/or information shall meet all of the following requirements, in addition to the procedures in (3):

A. The chief executive of an institution to which a person who only provides existing specimens and/or information belongs (hereafter referred to as the "chief executive of the affiliated institution") shall establish a system and a rule (including a rule for the handling of specimens and/or information) to ensure that provision of existing specimens and/or information is conducted properly.

B. A person who only provides existing specimens and/or information shall, when providing existing specimens and/or information in accordance with (3) A (a) or B (a) (i), or (ii) i or (b), report that effect to the chief executive of the affiliated institution.

C. A person who only provides existing specimens and/or information intends to provide existing specimens and/or information in accordance with (3) A (b) or (c), or, B (a) (ii) ii, (c) or (d) shall receive approval by the chief executive of the affiliated institution after deliberations by the ethical review committee.

D. When a person who only provides existing specimens and/or information intends to provide existing specimens and/or information in accordance with to (3) A (b) or (c) or B (c) or (d), the chief executive of the affiliated institution shall notify the research subjects, etc. of information concerning the provision of the said specimens and/or information or ensure that such information is made easily accessible by the research subjects, etc.

(5) Cases where research is to be conducted based on existing specimens and/or information provided in accordance with the procedures in (3)

When conducting research based on existing specimens and/or information provided in accordance with the procedures in (3), the investigator, etc. shall follow the procedures in A and B below:

A. The investigator, etc. shall confirm all of the following:

(a) Details of the informed consent for the said existing specimens and/or information or the measures taken for providing the said existing specimens and/or information pursuant to the provisions of (3);

(b) The name, address, and name of the chief executive of the other institution to which the said existing specimens and/or information were provided; and,

(c) Acquisition history of the said existing specimens and/or information of the other institution that provided the said existing specimens and/or information.

B. When existing specimens and/or information are to be received (except for cases falling under (3) A (a) or B (a) (i) or (b)), the following requirements are met:

(a) When research is to be conducted with the provided existing information related to personal information because (3) B (a) (ii) applies, procedures similar to those described in (2)B shall be followed; or,

(b) When research is to be conducted with the provided existing specimens and/or information that can identify specific individuals because (3) A (b) or (c) or B (c) or (d) applies, the matters listed in Section 6 (i) through (iii) and (vii) through (x) are kept in a state that they are easily accessible by the research subjects, etc., and, in principle, the research subjects, etc. are provided with an opportunity to refuse conduct or continuation of the research.

(6) Handling of specimens and/or information to be provided to a person located in a foreign country

A. When specimens and/or information are to be provided to a person located in a foreign country (excluding those who have established a system that conforms to the standards set forth in Article 16 of the Enforcement Rules for the Act on the Protection of Personal Information; the same shall apply hereinafter in A and B) (including cases where all or part of the handling of the said specimens and/or information are entrusted to a person located in a foreign country), all of the information listed in B shall be provided to the research subjects, etc. in advance, and appropriate consent shall be obtained from the said research subjects, etc. However, this shall not apply in any of the following requirements (a) through (c).

(a) All of the specimens and/or information to be provided fall under either of the following (i) or (ii):

(i) All of the specimens and/or information (excluding information used in the research falling under (ii)) meet any of the following requirements, and the chief executive of the institution providing the said specimens and/or information are provided with a report concerning the provision of the same:

i. It is difficult to obtain appropriate consent; the specimens to be provided are in a state that does not allow identification of specific individuals; and, personal information is not acquired using the said specimens at the research implementing entity to which the specimens will be provided;

ii. It is difficult to obtain appropriate consent, and the information to be used in the research to be provided is anonymized personal information;

iii. The information to be used in the research to be provided is information related to personal information (except in cases where the research implementing entity to which the information is provided is expected to acquire the said information related to personal information as personal information).

(ii) The information to be provided for use in the research is information related to personal information (limited to cases where the research implementing entity to which the information is provided is expected to acquire the said information related to personal information as personal information); the person who provides the said information related to personal information confirms that the information meets any of the following requirements, or that consent has been obtained from the research implementing entity to which the personal information is to be provided; and, approval has been obtained by the chief executive of the institution that provides the said information related to personal information after deliberations by the ethical review committee.

i. The research implementing entity, which is an academic research institution or the equivalent, is required to provide the said information related to personal information to a person located in a foreign country that is the collaborative research implementing entity for the purposes of academic research; and, there is no risk of unjustly infringing on the rights and interests of the research subjects.

ii. The said information related to personal information is to be provided to a person located in a foreign country that falls under the category of academic research institution or the equivalent; the research implementing entity to which such information is provided needs to handle the information for academic research purposes; and, there is no risk of unjustly infringing on the rights and interests of the research subjects.

iii. There are special reasons for providing the said information related to personal information, and it is difficult to obtain appropriate consent from the research subjects, etc. at the research implementing entity to which such information related to personal information is to be provided.

(b) Sensitive personal information is acquired pursuant to the proviso of (1) B (b) (ii) i; such sensitive personal information is provided to a person located in a foreign country; and, approval has been obtained by the chief executive of the institution providing specimens and/or information after deliberations by the ethical review committee as to whether all of the following requirements are met.

(i) It is difficult to obtain appropriate consent;

(ii) When, in provisions of (a) (ii) i through iii, the term “information related to personal information” is read as “sensitive personal information,” any of the requirements

listed in (a) (ii) i through iii is met;

(iii) All of the requirements listed in Section 8 (1) are met, and appropriate measures are taken in accordance with the provisions of Section 8 (2); and,

(iv) All of the information listed in B is provided to the research subjects, etc.

(c) It is difficult to obtain appropriate consent; provision (a) or (b) does not apply; and, approval has been obtained from the chief executive of the institution to which the specimens and/or information are to be provided after deliberations by the ethical review committee as to whether all of the following requirements are met.

(i) When, in provisions of (a) (ii) i through iii, the term "information related to personal information" is read as "specimens and/or information," any of the requirements listed in (a)(ii)i through iii is met;

(ii) Concerning implementation of the said research and the provision of the said specimens and/or information to a person located in a foreign country, all of the information listed in B, and the matters listed in Section 6 (i) through (vi), (ix), and (x), are notified in advance to the research subjects etc., or are kept in a state where they are easily accessible by the research subjects, etc.; and,

(iii) In principle, the research subjects, etc. is provided with an opportunity to refuse to provide the said specimens and/or information.

B. Those who provide specimens and/or information to persons located in a foreign country shall provide the following information to the research subjects, etc., in accordance with the provisions of A:

(i) Name of the foreign country;

(ii) Information obtained by an appropriate and reasonable method concerning the system for protecting personal information in the foreign country; and,

(iii) Information on measures taken by the person concerned to protect personal information.

C. Those who provide specimens and/or information to persons located in a foreign country (limited to those who have established a system that conforms to the standards set forth in Article 16 of the Enforcement Rules for the Act on the Protection of Personal Information), if specimens and/or information are provided to the person concerned without obtaining appropriate consent of the research subjects, etc., shall take the necessary measures required by Article 28, paragraph (3) of the Personal Information Protection Act with respect to the handling of personal information, and shall provide the research subjects, etc. with information on such necessary measures upon request thereof.

2. Obtaining informed consent by electromagnetic means

The investigator, etc. or those who only provide existing specimens and/or information may

obtain informed consent by electromagnetic means in place of written informed consent in Section 1, by taking into consideration all of the following:

(i) Properly confirming the identities of research subjects, etc.;

(ii) Ensuring that research subjects, etc. have an opportunity to ask questions about the explanations, and that the said questions are adequately answered; and,

(iii) Making matters related to consent, including the explanations provided in Section 5, easily accessible even after informed consent has been obtained, and, in particular, providing written documents to the research subjects, etc. if they so request.

3. Records concerning the provision of specimens and/or information

(1) Providing specimens and/or information

The principal investigator or a person who only provides the specimens and/or information shall prepare a record of the provision of the said specimens and/or information and retain it for a period of three (3) years from the date of the provision of the said specimens and/or information to which the said record pertains. In addition, a person who only provides specimens and/or information at a cooperating research institution shall report the provision of such specimens and/or information to the chief executive of the said cooperating research institution.

(2) Receiving specimens and/or information

When receiving specimens and/or information from other research implementing entity(s), etc., the investigator, etc., shall confirm that appropriate procedures have been taken by the person providing the said specimens and/or information, and prepare a record concerning the provision of the said specimens and/or information.

The principal investigator shall retain the said records prepared by the investigator, etc. for a period of five (5) years from the date of the report concerning the completion of the said research.

4. Revising research protocol

When the investigator, etc. intend to conduct research by revising the research protocol, they shall, in principle, take the procedures for informed consent, etc. as stipulated in Section 1 above with respect to the revised part. However, in cases where approval has been obtained by the chief executive of the research implementing entity after deliberations by the ethical review committee, this shall not apply to the revised part pertaining to the said approval.

5. Matters to be explained

When obtaining informed consent from the research subjects, etc., information to be provided to the research subjects, etc. shall, in principle, include the matters below. Any of those matters may be omitted, however, when the chief executive of the research implementing entity gives approval for that after deliberations by the relevant ethical review committee.

(i) Title of the research and the fact that approval of the chief executive of the research implementing entity has been given concerning its conduct;

(ii) The name of the cooperating research institution pertaining to the said research subjects; the name of the person who only provides the existing specimens and/or information and the name of the affiliated institution; and, the names of all of the principal investigators and their affiliated institutions;

(iii) Purpose and significance of the research;

(iv) Method and time period of the research (including purposes for utilizing and handling of specimens and/or information acquired from the research subjects);

(v) Reasons why asked to be enrolled in the research;

(vi) Burdens placed on the research subjects and predictable risks and benefits;

(vii) The fact that research subjects, etc. may withdraw their consent at any time, even after they have given consent, when the research is to be conducted or continued (when it may be difficult to take measures that follow withdrawal by the research subjects, etc., a statement to that effect and the reason for the difficulty);

(viii) The fact that the refusal or withdrawal of consent by the research subjects, etc. when the research is to be conducted or continued does not cause any disadvantage to such research subjects, etc.;

(ix) Means to make information on the research public;

(x) The fact that research subjects, etc. can request and obtain or read the research protocol and documents concerning method of the research, to the extent such does not interfere with the protection of personal or other related information of other research subjects, etc. or the originality of the said research, as well as the procedure to obtain or read such protocols and documents;

(xi) Handling of personal or other related information (including the processing method, if the information is processed, and a statement to the effect that pseudonymized personal information or anonymized personal information is to be created, if such is the case);

(xii) Means for storing and disposing of specimens and/or information;

(xiii) Status of research-related conflicts of interest of the research implementing entity, such as research fund resources, as well as research-related conflicts of interest of the investigator, etc., such as his/her individual income;

(xiv) Handling of results, etc. obtained through research;

(xv) Response to consultation, etc. (including genetic counselling) made by the research subjects, etc. and other individuals concerned;

(xvi) When specimens and/or information are to be provided to a person located in a foreign country, the information stipulated in Section 1 (6) B.

(xvii) When the research involves any financial expenditure on or remuneration for the research subjects, etc., a statement to that effect and details of such;

(xviii) When the research involves medical technique beyond usual medical practice, description of alternative procedure(s) or course(s) of treatment;

(xix) When the research involves medical technique beyond usual medical practice, response related to the healthcare delivery to the research subjects after the research;

(xx) When the research involves invasiveness, whether or not compensation will be offered for research-related health damage and details of such compensation;

(xxi) With respect to specimens and/or information acquired from the research subject, when any of those may be used or provided to other research implementing entity(s) for the research in the future that is not identified at the time of obtaining consent from the research subjects, etc., a statement to that effect, the contents of utilization assumed at the time of obtaining consent, and the method by which the research subjects, etc. confirm information on the research to be conducted and the research implementing entity scheduled to receive such specimens and/or information; and,

(xxii) When the research involves invasiveness (excluding minor invasiveness) and intervention, the fact that the monitor(s), the auditor(s), and the ethical review committee will be granted direct access to the specimens and/or information acquired from the research subjects, without violating the confidentiality of the research subjects, to the extent necessary.

6. Matters to be notified to research subjects, etc. or be kept in a way that is easily accessible by the research subjects, etc.

In the provisions set forth in Section 1, the matters to be notified to research subjects, etc. or to be in a way that is easily accessible by the research subjects, etc. include the matters below:

(i) The purposes and methods for utilizing specimens and/or information (including methods in cases where the specimens and/or information are provided to other entity(s));

(ii) The categories of specimens and/or information used or provided;

(iii) The scheduled date of commencement of use or provision;

(iv) The name of the institution providing specimens and/or information and the name of its chief executive;

(v) Method for obtaining specimens and/or information to be provided;

(vi) The name of the principal investigator (the representative investigator in the case of multi-institutional joint research) of research using the specimens and/or information to be provided and the name of the research implementing entity to which he/she belongs;

(vii) The scope of utilizing persons;

(viii) Name or title of the person responsible for managing the specimens and/or information;

(ix) The fact that, at the request of the research subjects, etc., the utilization of specimens and/or information identifying the research subject or the provision of such specimens and/or information to other research implementing entity(s) will be suspended;

(x) The method for receiving requests made by the research subjects, etc. as set forth in (ix); and,

(xi) When the specimens and/or information are to be provided to a person located in a foreign country, the information stipulated in Section 1 (6) B.

7. Research procedures in emergency situations involving an obvious life-threatening risk to a research subject

When the investigator, etc. considers that the research subject fulfills all of the following conditions, in accordance with specifications prescribed in the research protocol, the investigator, etc. may conduct research without obtaining the consent of the research subjects, etc. When the said research is conducted, however, the investigator, etc. shall promptly follow procedures to obtain informed consent in writing or by electromagnetic means including the information to be provided pursuant to the provisions of Section 5 above.

(i) The research subject is facing an emergency involving obvious life-threatening risk;

(ii) When the research involves intervention, usual medical practice is unlikely to achieve sufficient therapeutic effects in the research subject and there is sufficient possibility of saving the life of the research subject in a life-threatening condition by conducting the said research;

(iii) Burdens and risks placed on the research subject are minimized; and,

(iv) The representative or the prospective representative cannot immediately be contacted for consent.

8. Simplification of procedures concerning informed consent, etc.

The procedures for informed consent may be simplified in accordance with the provisions of Section 1 or Section 4 if all of the requirements listed in (1) (i) through (iv) below are met and the measures listed in (2) (i) through (iii) below are taken:

(1) When the investigator, etc. intends to conduct research that meets all of the following requirements, he/she may simplify some of the procedures as provided in Sections 1 and 4, in accordance with the research protocol approved by the chief executive of the research implementing entity for conducting the said research:

(i) The research to be conducted does not involve invasiveness (excluding minor invasiveness);

(ii) Omission of procedures pursuant to the provisions of Sections 1 and 4 above is not contrary to the interests of the research subjects;

(iii) If procedures pursuant to the provisions of Sections 1 and 4 above are not omitted, it will be difficult to conduct the research or the value of the said research will be significantly undermined; and,

(iv) The research to be conducted is recognized as being of high social significance (only in cases where specimens and/or information are provided to a person located in a foreign country in accordance with Section 1 (6) A (b)).

(2) When any procedure(s) is to be omitted pursuant to the provisions of (1) above, the investigator, etc. shall take appropriate measures from among those defined below.

(i) Make an announcement to the population to which the research subjects, etc. belong, with respect to the purposes of collecting and utilizing specimens and/or information, as well as details (including the method) of such collection and utilization;

(ii) Offer an ex-post explanation to the research subjects, etc. promptly (including such explanation made to the group to which the subjects, etc. belong); and,

(iii) In the case that the specimens and/or information are collected or used continuously for a long period, the investigator, etc. shall endeavor to make a public announcement, with respect to the situation of such collection or utilization, including the purposes and methods of collection or utilization of the said specimens and/or information, in order to make it widely known to society.

9. Withdrawal of consent, etc.

When a research subject, etc. offers withdrawal or refusal of consent corresponding to any of the following, the investigator, etc. shall, without delay, take measures in accordance with the said withdrawal or refusal, as well as provide an explanation on such measures to the said research subjects, etc. However, the investigator, etc., are not necessarily required to take the said measures when it is difficult and the chief executive of the research implementing entity approves that the said measures should not be taken after deliberations by the ethical review committee. In this case, the investigator, etc. shall endeavor to provide an explanation to the research subjects, etc. concerning the fact that measures in accordance with the said withdrawal or refusal will not be taken, along with the reasons, and to obtain the understanding of the research subjects, etc.

(i) Withdrawal of all or part of consent for the said research to conduct or continue;

(ii) Refusal of all or part of the research to conduct or continue, based on information concerning the research, that is notified or made easily accessible (including refusal pursuant to the provisions of Part 9.1 (1) B (a) (ii));

(iii) Refusal of all or part of the research to conduct or continue, in accordance with procedures for obtaining informed consent pursuant to the provisions of Section 7 above; or,

(iv) Refusal by a research subject, concerning the said research to which his/her representative has given consent, of all or part of the research to conduct or continue, in accordance with procedures for obtaining informed consent from the said research subjects.

Part 9 Procedures, etc. for Obtaining Informed Consent from a Representative, etc.

1. Requirements for obtaining informed consent from a representative, etc.

(1) When the investigator, etc. or persons who only provide existing specimens and/or information obtains informed consent from a representative, etc. pursuant to the provisions of Part 8 above, all of the requirements as defined below shall be met.

A. The research protocol describes the following matters:

(i) Criteria for selecting representative, etc.; and,

(ii) Information to be provided to the representative, etc. (including the reason why the said person should be considered a research subject, when research subjects correspond to either B (a) or B (b) below).

B. The research subject shall correspond to any of (a) through (c) below:

(a) The research subject is a minor. When the research subject has completed junior high school or other relevant schooling, or is 16 years or older, and is considered to have sufficient capacity to make judgments concerning the research to be conducted on him/herself, as well as the following matters are prescribed in the research protocol and the chief executive of the research implementing entity approves the research to be conducted after deliberations by the relevant ethical review committee, informed consent shall be obtained not from a representative but from the said research subject;

(i) The research to be conducted does not involve invasiveness; and,

(ii) Information on conduct of the research, including the purposes of the research and the handling of specimens and/or information, is kept in a state where it is easily accessible by persons with parental authority or guardians of minors, and that the said persons will be provided with an opportunity to refuse conduct or continuation of the said research.

(b) The research subject is an adult, but is objectively considered to be unable to give informed consent.

(c) The research subject is a decedent, however, excluding cases where conduct of research is contrary to the subject's explicit will as expressed during his/her lifetime.

(2) When obtaining informed consent from a representative etc. pursuant to the provisions of Part 8 above, the investigator, etc. or the persons who only provide existing specimens and/or information shall select representative, etc. in accordance with the criteria pursuant to the provisions of (1) A (i) above and provide information to the said representative, etc. pursuant to the provisions of Part 8.5 and of (1) A (ii) above.

(3) When having obtained informed consent from a representative, etc., and the research subject has completed junior high school or other relevant schooling, or is 16 years or older, and is considered to have sufficient capacity to make judgments concerning the research to be conducted on him/herself, the investigator, etc., or the persons who only provide existing specimens and/or information shall obtain informed consent also from the said research subject.

2. Procedures, etc. for obtaining informed assent

(1) Even when having obtained informed consent from a representative, but when the research subject is considered to be able to express his/her will concerning the research to be conducted on him/herself, the investigator, etc. or the persons who only provide existing specimens and/or information shall endeavor to obtain informed assent from the said research subject. The same shall not apply to cases where informed consent is obtained from the research subject pursuant to the provisions of Section 1 (3) above.

(2) When conducting research for which procedures for obtaining informed assent will be

predicted pursuant to the provisions of (1) above, the principal investigator shall, in advance, prescribe information to be provided and the means to provide to research subjects, in the research protocol.

(3) When a research subject expresses his/her will to refuse to have all or part of the research to be conducted or continued, in the course of the procedures for obtaining informed assent pursuant to the provisions of (1) above, the investigator, etc. or the persons who only provide existing specimens and/or information shall endeavor to respect such will. This, however, shall not apply when direct benefits to the health of the research subject are expected if the said research is conducted or continued, and when the representative gives consent to it.

Chapter 5 Handling Results, etc. Obtained from Research

Part 10 Explanation of Results, etc. Obtained from Research

1. Procedures, etc. for explaining results, etc. obtained from research

(1) Based on the characteristics of the research to be conducted and the results, etc. to be obtained from the said research, the principal investigator shall establish a policy for explaining the results, etc. obtained from the said research to the research subjects, and shall include such policy in the research protocol. In establishing the said policy, all of the following matters shall be taken into consideration:

A. Whether the said results of the research are sufficient in terms of accuracy and certainty as information for evaluating the health status, etc. of the research subjects;

B. Whether the said results are important to the health, etc. of the research subjects; and,

C. Whether the explanation of the said results, etc. is likely to cause a significant hindrance to the proper conduct of the research work.

(2) When obtaining the informed consent from research subjects, etc., the investigator, etc. shall explain thereto the policy on explaining the results, etc. obtained from the said research in (1) above to obtain their understanding. If the research subjects, etc. do not wish to be informed of the results, etc. obtained through the said research, their wishes shall be respected. However, even if the research subjects, etc. do not wish to be informed of the results of the research, if the results are found to have a serious effect on the lives of the research subjects or blood relatives thereof, and if effective measures are available, the investigator, etc. shall report to the principal investigator.

(3) Upon receiving a report pursuant to the provisions of (2) above, the principal investigator shall determine the necessity of an explanation, the method for providing the explanation, and the content of the explanation, to the research subjects, etc., including the following points, and submit the matter to the ethical review committee.

(i) Effects on the lives of the research subjects and their blood relatives, etc.;

(ii) Availability of effective treatments and the health status of the research subjects;

(iii) Possibility that blood relatives of the research subjects will suffer from the same disease; and,
(iv) Details of the explanation of the results of the research at the time of informed consent.

(4) Based on deliberations by the ethical review committee in (3) above, the investigator, etc. shall provide a sufficient explanation to the research subjects, etc. and confirm the intentions thereof. If they still do not wish to receive an explanation, the investigator, etc. shall not provide an explanation.

(5) Without the consent of the research subjects, etc., the investigator, etc. shall not, in principle, explain the results, etc. obtained through research on the research subjects to persons other than the research subjects, etc. However, this shall not apply to cases where blood relatives, etc. of the research subjects desire an explanation of the results, etc. obtained from the research, and the principal investigator, after deliberations by the ethical review committee as to whether or not such explanation is necessary based on the reasons and necessity for requesting such explanation, determines that such explanation is necessary.

2. Consultation system, etc. for research

When handling the results, etc. obtained from research, the principal investigator shall establish a system that enables the research subjects, etc. to receive appropriate consultation concerning the said research, taking into consideration the characteristics of the results, etc. and giving due consideration to the medical or psychological effects, etc. of the research. In addition, it is important, in establishing the system, for the principal investigator to work closely with the physicians in charge of medical treatment, and in cases where genetic information is handled, efforts shall be made to ensure collaboration with persons who provide genetic counseling and genetic medicine specialists.

Chapter 6 Ensuring Reliability of Research

Part 11. Appropriate Handling and Reporting of Research

1. Ensuring ethical justification and scientific validity of research

(1) If the investigator, etc. learns, or obtains information, that the research undermines or may undermine its ethical justification or scientific validity (except in the cases described in (2) below), he/she shall promptly report the fact or provide such information to the principal investigator.

(2) If the investigator, etc. learns, or obtains information, that the research undermines or may undermine the appropriateness of its conduct thereof or the reliability of research results, he/she shall promptly report the fact or provide such information to the principal investigator or the chief executive of the research implementing entity.

(3) If a serious concern arises from the perspective of respecting the human rights of the research subjects, etc., or from the perspective of conducting research, such as leakage of research-related information, the investigator, etc. shall promptly report it to the principal investigator or the chief executive of the research implementing entity.

2. Managing and supervising research progress and identifying and reporting adverse events, etc.

(1) The principal investigator shall endeavor to ensure the proper conduct of the research and the reliability of the research results, including obtaining necessary information concerning the conduct of the research.

(2) If the principal investigator receives a report according to Section 1 (1) that is considered to affect the continuation of the research (except for cases falling under (3)), he/she shall report it to the chief executive of the research implementing entity without delay and, as necessary, suspend or terminate the research or revise the research protocol.

(3) If the principal investigator receives a report according to Section 1 (2) or (3), he/she shall promptly report it to the chief executive of the research implementing entity and, as necessary, suspend or terminate the research, or revise the research protocol.

(4) The principal investigator shall terminate the research if it is determined that the anticipated risks are greater than the expected benefits of the said research, or that adequate results have been obtained, or that adequate results will not be obtained from the said research.

(5) The principal investigator shall report the progress of the research and the occurrence of adverse events associated with the conduct of the research to the ethical review committee and the chief executive of the research implementing entity in accordance with the research protocol.

(6) When conducting multi-institutional joint research, the principal investigator shall share necessary information related to the said research with the principal investigators of the collaborative research implementing entities.

(7) Upon receiving a report pursuant to Section 1 (2) or (3) or Section 2 (2) or (3), the chief executive of the research implementing entity shall promptly take appropriate measures, including terminating the research or investigating the cause, after deliberations by the ethical review committee, as necessary. In this case, before deliberations by the ethical review committee, the chief executive of the research implementing entity shall instruct the principal investigator to suspend the research or take provisional measures, as necessary.

3. Reporting, etc. to Ministers

(1) Upon becoming aware that the research being conducted or any research conducted in the past by the research implementing entity does not conform to these Guidelines (including reports pursuant to Section 1 (2) or (3) or Section 2 (2) or (3)), the chief executive of the said research implementing entity shall promptly submit the matter to the ethical review committee and take the necessary action, and, if the degree of such nonconformity is serious, shall report the status and results of any response taken to the Minister of Health, Labour and Welfare (to the Minister of Education, Culture, Sports, Science and Technology and the Minister of Health, Labour and Welfare for the research implementing entity under the jurisdiction of the Ministry of Education, Culture, Sports, Science and Technology; and, to the Minister of Health, Labour and Welfare and the Minister of Economy, Trade and Industry for the research implementing entity under the jurisdiction of the Ministry of Economy, Trade and Industry; hereinafter simply referred to as "Ministers") and make a public announcement.

(2) The chief executive of the research implementing entity shall provide cooperation with the inspection carried out by the Minister(s) or entity(s) entrusted with the duties by the Minister(s) (hereinafter referred to as the "Minister(s), etc.") to confirm that the research conducted by the said research implementing entity complies with these Guidelines.

Part 12 Managing Conflicts of Interest

(1) When conducting research, the investigator, etc. shall report to the principal investigator concerning the status of conflicts of interest related to the said research, such as individual income, etc., and make an appropriate response to ensure the transparency of such.

(2) When conducting research that may be related to any commercial activity, such as that to confirm the effectiveness or safety of medicine or medical device, the principal investigator shall understand the status of the said research-related conflicts of interest and describe it in the research protocol.

(3) The investigator, etc. shall provide information concerning the status of conflicts of interest described in the research protocol pursuant to the provisions of (2) above, to the research subjects, etc. in the course of procedures for obtaining informed consent pursuant to the provisions of Part 8 above.

Part 13 Storing Specimens and/or Information, etc. Related to Research

(1) The investigator, etc. shall ensure that information used in research and records related to such specimens and/or information used in research (including records related to the provision of specimens and/or information; hereinafter referred to as "information, etc.") are accurate.

(2) When storing specimens and/or information, etc., the principal investigator shall prescribe

means for storage in the research protocol in accordance with the operating procedures pursuant to the provisions of (3) below; instruct and manage the investigator, etc. to ensure that they retain accurate information, etc.; and, perform the necessary management in order to prevent leakage, mishandling, theft, loss, etc. of such specimens and/or information, etc.

(3) The chief executive of the research implementing entity shall prepare operating procedures for storing specimens and/or information, etc. and exercise the necessary supervision in order that such specimens and/or information, etc. related to the research he/she approved for conducting are stored properly.

(4) The principal investigator shall report to the chief executive of the research implementing entity concerning the management status pursuant to the provisions of (2) above, in accordance with the operating procedures pursuant to the provisions of (3) above.

(5) The chief executive of the research implementing entity shall endeavor to ensure that information, etc. of the said research implementing entity is stored for as long a period as possible and regarding research that involves invasiveness (excluding minor invasiveness) and intervention, the said chief executive shall exercise the necessary supervision to ensure that such information, etc. is stored appropriately until at least five (5) years have passed from the date completion of the said research is reported or three (3) years have passed from the date that the final publication of the research results is reported, whichever is later. The above provision shall apply to the storage of pseudonymized personal information, deleted or other related information (limited to information that can be used to restore the personal information used to create pseudonymized personal information, in the case of information concerning the processing method used pursuant to Article 41, paragraph (1) of the Personal Information Protection Act), and anonymized personal information, as well as information on processing methods, etc. (regarding deleted or other related information or processing methods etc. related information, excluding cases where such information is destroyed). Furthermore, with respect to records related to the provision of specimens and/or information, the said chief executive shall exercise the necessary supervision to ensure that such records are stored appropriately for three (3) years from the date of provision in the case of providing specimens and/or information, and for five (5) years from the date completion of the said research is reported in the case of receiving specimens and/or information.

(6) When disposing of specimens and information, etc., the chief executive of the research implementing entity shall exercise the necessary supervision to ensure that appropriate measures are taken to prevent specific individuals from being identified.

Part 14 Monitoring and Auditing

(1) The principal investigator shall endeavor to ensure the reliability of research, and when

conducting research that involves invasiveness (excluding minor invasiveness) and intervention, shall perform monitoring and, as necessary, an audit, in accordance with the specifications prescribed in the research protocol approved by the chief executive of the research implementing entity.

(2) The principal investigator shall offer the necessary instructions and management to those engaged in monitoring or auditing to ensure that such monitoring and auditing are appropriately carried out in accordance with the specifications prescribed in the research protocol approved by the chief executive of the research implementing entity for the conduct of the said research.

(3) The principal investigator shall not appoint those engaged in conducting and monitoring the research, which is subject to the audit, to execute such audit.

(4) Those engaged in monitoring shall report to the principal investigator concerning the results of the said monitoring. In addition, those engaged in the audit shall report to the principal investigator and the chief executive of the research implementing entity concerning the results of the said audit.

(5) Those engaged in monitoring and those engaged in auditing shall not disclose, without justifiable reason, any information obtained while performing their duties. The same shall apply even after they cease to be engaged in the duties.

(6) The chief executive of the research implementing entity shall support the execution of monitoring and auditing pursuant to the provisions of (1) above and take necessary measures for the said execution of such monitoring and auditing.

Chapter 7 Response to a Serious Adverse Event

Part 15 Response to a Serious Adverse Event

1. Response to be made by the investigator, etc.

When the investigator, etc. learns of a serious adverse event while conducting research that involves invasiveness, the investigator, etc. shall follow the procedures pursuant to the provisions of Section 2 (1) and Section 3 below, take relevant measures such as providing explanations to the research subjects, etc. and report to the principal investigator promptly.

2. Response to be made by principal investigator

(1) When the principal investigator intends to conduct research involving invasiveness, he/she shall describe in advance, in the research protocol, the procedures to be followed by the investigator, etc. in the occurrence of a serious adverse event, and shall take necessary measures to ensure that the said procedures are followed properly and smoothly.

(2) When a cooperating research institution is asked to acquire specimens and/or information for the research, the principal investigator shall receive a prompt report of any serious adverse event that occurs in a research subject.

(3) If the principal investigator learns of the occurrence of a serious adverse event in the conduct of research involving invasiveness, he/she shall promptly obtain the opinions of the ethical review committee on the said adverse event and on the continuation of the research, and then report to the chief executive of the research implementing entity to that effect, and take appropriate measures in accordance with the procedures, etc., pursuant to the provisions of (1) above and Section 3. In addition, the principal investigator shall promptly share the information concerning the occurrence of the said adverse event with the investigator, etc. involved in conducting the said research.

(4) If the representative investigator learns of the occurrence of a serious adverse event in the conduct of research involving invasiveness in multi-institutional joint research, he/she shall promptly share the information concerning the occurrence of the said adverse event, including the responses described in (3) above, with the principal investigator of the collaborative research implementing entity(s) conducting the said research.

(5) When any unexpected serious adverse event occurs while conducting research involving invasiveness (excluding minor invasiveness) and intervention, and if the said unexpected serious adverse event may be in direct consequence of the said research, the principal investigator of the research implementing entity where the said adverse event has occurred shall promptly report to the chief executive of the research implementing entity; shall promptly report the status and results of the measures taken pursuant to the provisions of (2) and (3) above to the Minister of Health, Labour and Welfare; and, shall make a public announcement.

3. Response to be made by the chief executive of the research implementing entity

When conducting research involving invasiveness, the chief executive of the research implementing entity shall prepare operating procedures detailing what should be done by the investigator, etc. in response to a serious adverse event and take necessary measures in order that a response will be made properly and smoothly in accordance with the said operating procedures.

Chapter 8 Ethical Review Committee

Part 16 Organizing, etc. Ethical Review Committee

1. Qualifications for organizing ethical review committee

The organizer of the ethical review committee shall meet the following qualifications:

(i) Having the capacity to appropriately perform administrative work related to review;
(ii) Having the capacity to sustainably operate the ethical review committee; and,
(iii) Having the capacity to operate the ethical review committee in a neutral and fair manner.

2. Obligations of organizer of ethical review committee

(1) The organizer of the ethical review committee shall prescribe the organizational structure of the said committee and rules for operating the committee, as well as ensure that members of the ethical review committee and other individuals engaged in administrative work perform their duties in accordance with the said rules.

(2) The organizer of the ethical review committee shall appropriately retain review materials concerning the research that the said ethical review committee has examined until completion of the said research is reported (when the research involves invasiveness (excluding minor invasiveness) and intervention, the review materials shall be retained for five (5) years from the date completion of the said research is reported).

(3) When beginning operations of the ethical review committee, the organizer of the said committee shall make public, in the Ethical Review Committee Reporting System, its organization, provisions for its operation, and list of members of the committee.

In addition, the said organizer shall similarly make public, in the Ethical Review Committee Reporting System, the status of the said committee's meetings held and a summary of the committee's reviews at least once a year. With respect to the summary of the committee's reviews, however, any of the contents may be omitted from such publication when the committee considers that confidentiality is required in order to protect the human rights of the research subjects, etc. and other individuals concerned or the rights and interests of the investigator, etc. and other individuals concerned.

(4) The organizer of the ethical review committee shall take necessary measures to ensure that members of the said ethical review committee and other individuals engaged in administrative work receive education and training concerning relevant reviews and other related duties.

(5) The organizer of the ethical review committee shall provide cooperation with the inspection carried out by the Minister(s), etc. on compliance of the said ethical review committee's organization and operation with these Guidelines.

Part 17 Roles, Responsibilities, etc. of Ethical Review Committee

1. Roles and responsibilities

(1) When the principal investigator asks for deliberations with respect to the appropriateness of conducting research or other matters, the ethical review committee shall review the

matters, neutrally and fairly, in accordance with these Guidelines, including information on any conflicts of interest of the research implementing entity and the investigator, etc. concerning the research from ethical and scientific viewpoints, and shall present its opinions in writing or by electromagnetic means.

(2) With respect to the research reviewed pursuant to the provisions of (1) above, the ethical review committee shall conduct necessary investigations from ethical and scientific viewpoints, and shall provide the principal investigator with necessary opinions concerning the research, including revisions to the research protocol and termination of the said research.

(3) Regarding research it reviews pursuant to the provisions of (1) above, for research that involving invasiveness (excluding minor invasiveness) and intervention, the ethical review committee shall conduct necessary investigations to ensure the appropriateness of conducting the said research and the reliability of the results of the research, and shall provide the principal investigator with necessary opinions concerning the said research, including revisions to the research protocol and termination of the research.

(4) Members of the ethical review committee, experts, and individuals engaged in administrative work shall not disclose, without justifiable reason, any information obtained while performing their duties related to the committee. The same shall apply, even after they cease to be engaged in the duties.

(5) When a member of the ethical review committee or an individual engaged in administrative work learns of the occurrence of any serious concern with respect to the human rights of the research subjects, etc. or with respect to the appropriateness for conducting the research the committee reviews pursuant to the provisions of (1) above, such as divulging information related to such research, as well as with respect to the neutrality or fairness of its reviews, the said member or individual shall report promptly to the organizer of the committee.

(6) Members of the ethical review committee and individuals engaged in administrative work shall receive education and training to acquire the knowledge necessary to undertake reviews from ethical and scientific viewpoints prior to being engaged in reviews or other related duties. They shall also receive education and training subsequently, on a regular basis, as necessary.

2. Composition and quorum, etc.

(1) The composition of the ethical review committee shall comply with all of the following requirements in order that the duties of the committee, such as reviewing research protocols, are executed appropriately. Those members as defined in each of the groups of (i) to (iii) below cannot concurrently hold the same status in other groups. The same requirements shall

apply to the quorum of the committee's meetings.

(i) The committee shall have a member who is an expert in natural science, such as a medicine and medical care professional, etc.;

(ii) The committee shall have a member who is an expert in humanities and social sciences, such as a professional in ethics and law, etc.;

(iii) The committee shall have a member who can reflect the opinions of the general public, including viewpoints on research subjects;

(iv) The committee shall have at least two members who do not belong to the institution to which the organizer of the committee belongs;

(v) The committee shall have both male and female members; and,

(vi) The committee shall have five or more members.

(2) The investigator, etc. engaged in the research that is subject to deliberation shall not be present when deliberation and adoption of opinions are carried out at a meeting of the committee. When so requested by the said ethical review committee, however, the investigator, etc. may attend a meeting to provide information on the said research.

(3) The principal investigator who submits a matter on which the ethical review committee deliberates shall not be present when deliberation and adoption of opinions are carried out at a meeting of committee. When it is necessary to do so in order to understand details of the said deliberations by the ethical review committee, however, the said principal investigator may attend a meeting by obtaining the said committee's consent.

(4) The ethical review committee may invite nonmembers with expertise in specialist areas to provide assistance depending on matters subject to review and content of such.

(5) When reviewing the research protocol for which research subjects require special consideration and presenting its opinions on such research, the ethical review committee shall, as necessary, seek the opinions of experts on such research subjects.

(6) The ethical review committee shall endeavor to adopt its opinions unanimously.

3. Expedited review, etc.

(1) Under any of the following circumstances the ethical review committee may delegate reviews to member(s) designated by the said committee (hereinafter referred to as "expedited review") and adopt their opinions. The results of the said expedited review shall be considered to be the conclusion of the entire ethical review committee and shall be reported to other members of the committee.

(i) Review of multi-institutional joint research conducted after the entire scope of the research has already been reviewed by the ethical review committee as specified in Part

6.2 (5), which provided opinions to the effect that conduct is appropriate;
(ii) Review of minor revisions to research protocol;
(iii) Review of research that does not involve invasiveness and intervention; or,
(iv) Review of research that involves minor invasiveness, and does not involve intervention.

(2) The ethical review committee may include, in its report, matters falling under (1) (ii), which the ethical review committee has previously approved as requiring only confirmation, by stipulating in advance the specific content and operation, etc., of such matters in the regulations specified in Part 16.2 (1).

4. Review of research to be conducted by other research implementing entity(s)

(1) When the principal investigator requests a review by an ethical review committee established outside his/her own research implementing entity, the said ethical review committee shall have enough information concerning the organizational framework for the research, to undertake a review and present its opinions.

(2) If, after having reviewed research conducted by another research implementing entity(s), the ethical review committee is requested by the said principal investigator to continue reviewing the said research, it shall review the same and provide its opinions.

Chapter 9: Basic Responsibilities Concerning Personal Information and Specimens and/or Information of Deceased Individuals

Part 18 Protecting Personal or Other Related Information.

1. Handling of personal or other related information.

With respect to the handling of personal or other related information., including prohibition of inappropriate acquisition and use of personal information, assurance of accuracy, etc., safety control measures, reporting of leaks, etc., and responding to requests for disclosure, etc., the investigator, etc. and the chief executive of the research implementing entity shall comply with the provisions of these Guidelines, in addition to the rules and regulations, etc. applicable to businesses handling personal information, administrative entities, as provided in the Personal Information Protection Law.

2. Handling of specimens

With respect to the handling of specimens, the investigator, etc. and the chief executive of the research implementing entity shall comply with the provisions of these Guidelines and endeavor to take necessary and appropriate measures in accordance with the provisions of the Personal Information Protection Act and related ordinances.

3. Handling of specimens and/or information of the deceased individuals

With respect to specimens and/or information that can identify specific individuals regarding

deceased individuals, the investigator, etc. and the chief executive of the research implementing entity shall, in consideration of the dignity of the deceased individuals and the feelings of the bereaved family, etc., endeavor to handle such specimens and/or information appropriately and take necessary and appropriate measures in accordance with the provisions of the Personal Information Protection Act and related ordinances, etc., in addition to the provisions of these Guidelines.

Chapter 10 Supplementary Provisions

Part 19 Effective Date

These Guidelines shall take effect as of July 1, 2023.

Part 20 Transitional Measures

(1) With respect to any research that is being conducted at the time of enforcing these Guidelines in accordance with the provisions of these Guidelines prior to their revision or the Ethical Guidelines for Epidemiological Research, the Ethical Guidelines for Clinical Research, the Ethical Guidelines for Human Genome/Gene Analysis Research, or the Ethical Guidelines for Medical and Health Research Involving Human Subjects prior to their abolishment, the provisions then in force may remain applicable, provided that the provisions of the Personal Information Protection Act and related regulations and guidelines are complied with.

(2) With respect to any research that is being conducted prior to enforcing these Guidelines in accordance with the provisions of these Guidelines prior to their revision or the Ethical Guidelines for Epidemiological Research, the Ethical Guidelines for Clinical Research, the Ethical Guidelines for Human Genome/Gene Analysis Research, or the Ethical Guidelines for Medical and Health Research Involving Human Subjects prior to their abolishment, the investigator, etc. and the chief executive of the research implementing entity or the organizer of the ethical review committee shall not be precluded from conducting research or managing the ethical review committee in accordance with the provisions of these Guidelines, respectively.

Part 21 Review

These Guidelines shall be reviewed in their entirety as necessary or approximately five (5) years after their enforcement.