

**ETHICS GUIDELINES
FOR
HUMAN GENOME/GENE ANALYSIS RESEARCH**

March 29, 2001

**Ministry of Education, Culture, Sports, Science and Technology
Ministry of Health, Labour and Welfare
Ministry of Economy, Trade and Industry**

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INTRODUCTION

The promotion of scientific research is an important element achieving a society in which people can live healthy and fulfilling lives. In this context, human genome/gene analysis research begun in the latter half of the twentieth century has made significant contributions to the progress of both life science and health care science and is starting to play an important role in the development of the health and welfare of humanity and the growth of new industries.

It is also true that human genome/gene analysis research depends largely on research activities targeted at individuals, and that genetic information obtained in the course of research reveals genetic predispositions of both donors (those persons who provide a human specimen for human genome/gene analysis research) and their blood relatives, which might cause various ethical, legal or social problems. Therefore, research must be conducted properly on the basis of respect for human dignity and human rights as well as understanding and cooperation from society. For these purposes, the protection of the rights of individual donors should be given priority over scientific or societal benefits in accordance with ethical standards stipulated in such documents as the Helsinki Declaration of the World Medical Association. It is also essential that society be given adequate explanation of the less positive aspects of research and that research be conducted on the basis of this understanding. As Japan has yet to fully establish standards regarding overall human genome/gene analysis research that could respond to the aforementioned demands, it has become an urgent issue to establish such specific guidelines so that human dignity will be respected, the human rights of donors and their families or blood relatives will be protected and research will be conducted properly.

The present ethics guidelines to be applied to overall human genome/gene analysis research were jointly prepared and are presented to society at large by the Ministry of Education, Culture, Sports, Science and Technology, the Ministry of Health, Labour and Welfare and the Ministry of Economy, Trade and Industry, as stipulated in the "Fundamental Principles of Research on the Human Genome" (issued by the Bioethics Committee of the Council for Science and Technology on June 14, 2000), which in turn was established based on such documents as the "Universal Declaration on the Human

Genome and Human Rights" by the United Nations Educational, Scientific and Cultural Organization (UNESCO), and also with reference to the "Guidelines for Bioethical Problems Associated with Genetic Analysis Research" (from the Advanced Medical Technology Evaluation Committee of the Health Sciences Council on April 28, 2000).

Any and all parties who are involved in human genome/gene analysis research are required to comply with the present Guidelines.

<Note>

With the enforcement of the present Guidelines, the "Guidelines for Bioethical Problems Associated with Genetic Analysis Research" shall be abolished and replaced with the present Guidelines.

PART I: BASIC IDEAS

1. Basic Principles

The present Guidelines were established, based on the special characteristics of human genome/gene analysis, and are to be applied to all human genome/gene analysis research and observed in every research locale. The following matters are set as basic principles of the present Guidelines so that human dignity and human rights will be protected and research will be promoted properly based on an understanding from and cooperation of society:

<Note>

Recognizing the special characteristic of human genome/gene analysis research various problems might be raised as a result of genetic information obtained in the course of research possibly revealing genetic predispositions of both donors and their blood relatives, the definitions and scope of research to which the present Guidelines should apply are stipulated under 14 (3) below.

(1) respect for human dignity

(2) adequate prior explanation and informed consent on the basis of free will

- (3) thorough protection of personal information
- (4) conduct of socially beneficial research that contributes to the knowledge , health and welfare of humanity
- (5) priority of individual human rights protection over scientific or societal benefits
- (6) guarantee of the propriety of research through preparation of and compliance with research protocols pursuant to the present Guidelines as well as prior review and authorization by the ethics review committee established as an independent body
- (7) guarantee of transparency of research through on-site investigation of research progress by third parties as well as release of research results into the public domain

2. Scope of Application

The present Guidelines shall apply to human genome/gene analysis research and require researchers and equivalent persons to comply with them.

<Subrule 1: Subrule Concerning Research Conducted Prior To The Enforcement Of The Present Guidelines>

Although the present Guidelines do not apply to ongoing human genome/gene analysis research begun prior to the enforcement of these Guidelines, such research should be conducted in line as closely as possible with them.

<Subrule 2: Subrule Concerning Collaborative Research With Overseas Institutions>

1. In conducting collaborative research with an overseas institution, the ideas prescribed in these Guidelines shall still be observed and human dignity and human rights shall be respected, with regard to the process of human specimen provision, the significance of human genome/gene analysis research, etc. in the country where such research is conducted.

2. Research shall, in principle, be conducted pursuant to the criteria under these

Guidelines while observing laws, guidelines and the like stipulated in the country where such research is conducted.

3. When guidelines in the country where such research is conducted are more rigorous than these Guidelines, research shall be conducted in line with the more rigorous guidelines.

The issue of clinical examinations or equivalent human genome/gene analyses which are conducted in the course of a medical treatment and whose results are medically established as instruments to be utilized directly for the medical treatment of donors and their blood relatives will have to be carefully discussed in the future as a matter regarding medical treatment, and the present Guidelines therefore do not apply. However, medical doctors giving treatment should, with the purposes of these Guidelines in mind, take appropriately responsible measures on their own with regard to human genome/gene analysis, referring to guidelines etc. prepared by pertinent academic societies or other authorized organizations.

PART II: DUTIES OF RESEARCHERS AND EQUIVALENT PERSONS

3. Basic Duties of All Researchers and Equivalent Persons

(1) All researchers and equivalent persons shall conduct human genome/gene analysis research for the purposes of elucidating life phenomena, preventing diseases, improving diagnosis and treatment protocols, promoting health, etc.

(2) All researchers and equivalent persons shall ensure the societal usefulness of their human genome/gene analysis research and shall pay attention to the protection of individual human rights by prioritizing them over scientific or societal benefits.

(3) All researchers and equivalent persons shall make it a basic practice to conduct human genome/gene analysis research only after providing adequate explanation to donors, their proxy consenters or equivalent persons and obtaining informed consent based on their free will.

(4) All researchers and equivalent persons shall not, in the absence of any justifiable reason, divulge personal information obtained in the course of their profession. This shall continue to apply after they resign from their profession.

(5) All researchers and equivalent persons shall strive to protect personal information and shall also respond in good faith to questions, complaints, etc. concerning the handling of personal information.

(6) All researchers and equivalent persons shall, when any serious doubt in terms of the protection of human rights of donors or equivalent persons arises, such as an unexpected divulgence of personal information, immediately report this to both the director of their research institution and a principal investigator.

(7) All researchers and equivalent persons shall conduct human genome/gene analysis research in compliance with these Guidelines and with respect for human dignity and human rights by, for instance, conducting research in accordance with a research protocol as authorized by the ethics review committee and approved by the director of their research institution.

(8) All researchers and equivalent persons shall strive to guarantee transparency of research through, for instance, securing of the proper process for research conduct, on-site investigations by qualified external persons, appropriate responses to inquiries from donors or equivalent persons regarding research progress and the release of research results into the public domain.

(9) All researchers and equivalent persons shall, in consideration of the fact that human specimen provision is based on goodwill, make efforts to limit the amount of human specimen provision from people by, for instance, properly preserving and utilizing specimens already provided.

4. Duties of Directors of Research Institutions

(1) Directors of research institutions shall assume the final responsibility for the conduct

of human genome/gene analysis research in their institution and shall oversee principal investigators and research conductors so that they will conduct research properly in accordance with a research protocol. In doing so, the directors of research institutions shall strive to have all parties concerned with their institution understand thoroughly that they should protect the human rights of donors and equivalent persons as much as possible and that they may be subject to penalties, such as disciplinary actions, if they violate these Guidelines, a research protocol or the like.

<Subrule Concerning Examples Of Directors Of Research Institutions>

The following positions are examples of directors of research institutions:

- Hospital Director
- Public Health Care Center Director
- Dean of Faculty of Medicine
- Director of Laboratory.

(2) Directors of research institutions shall take adequate measures for the prevention of personal information divulgence.

<Subrule Concerning Measures For Personal Information Protection>

Processes, equipment and regimes shall be arranged to pursue the rigorous management of personal information. In using computers, for instance, some measures should be taken for this purpose; one example is to separate computers processing personal information from other computers.

(3) Directors of research institutions, such as human specimen collecting institutions, that handle personal information shall designate a personal information custodian for the purpose of protecting personal information in human genome/gene analysis research. Directors may, as required, also designate, upon specifying a chain of command, a co-custodian or an assistant who conducts actual operations under the supervision of a personal information custodian.

<Subrule Concerning Requirements For Personal Information Custodians>

1. A personal information custodian/co-custodian shall be a person, such as a medical doctor or pharmacist, who is prohibited from divulging confidential information obtained in the course of their profession under Article 134 of the Criminal Code (Law No.45 of 1907), Article 100 of the National Public Service Law (Law No.120 of 1947) or any other provision of law.

2. A personal information custodian/co-custodian may not simultaneously hold the position of principal investigator or research conductor conducting human genome/gene analysis research (excluding human specimen provision) using human specimens to be provided by the personal information custodian/co-custodian.

(4) Directors of research institutions shall establish an ethics review committee as an advisory board to review the propriety of conducting human genome/gene analysis research etc. When, however, it is difficult to set up an ethics review committee for reasons such as the small size of a human specimen collecting institution, an ethics review committee established by a collaborative research institution, a public service corporation or an academic society may be substituted for an internal one.

<Subrule 1: Subrule Concerning The Establishment Of An Ethics Review Committee>

When a committee with the similar function already established in a research institution is reorganized as an ethics review committee meeting the present Guidelines, it does not have to be renamed as an Ethics Review Committee.

<Subrule 2: Subrule Concerning Handling Of Collaborative Research>

In the case of collaborative research, authorization for a research protocol shall be obtained from the ethics review committee of each institution, and the director of each research institution shall, in consulting the propriety of conducting research, obtain important information, such as the progress of authorization for the research protocol in other research institution(s), progress in obtaining informed consent and progress of anonymization, and submit the information to the ethics review committee of his/her research institution.

(5) Directors of research institutions shall, with regard to any research protocol or alteration thereof, respect the opinions of the ethics review committee in determining whether or not to approve it. Directors of the research institutions shall not approve the conduct of research for which the ethics review committee submits the opinion of authorization denial.

(6) Directors of research institutions shall keep track of the progress of human genome/gene analysis research by, for instance, receiving a research progress report on a regular basis, at least annually, and implementing an on-site investigation by qualified external persons on a regular basis, at least annually, and shall order the research altered or discontinued based on the ethics review committee submitting the opinion of alteration or discontinuation, or if necessary for any reason.

<Subrule Concerning On-Site Investigation By Qualified External Persons>

1. Directors of research institutions shall, with regard to the progress of the process for obtaining informed consent and progress of personal information protection, have on-site investigations conducted to check that those processes are conducted in accordance with the relevant research protocol.

2. Director of research institutions shall have principal investigators and research conductors cooperate with on-site investigations.

3. External investigators shall not, in the absence of any justifiable reason, divulge information obtained in the course of an on-site investigation. This shall continue to apply after they resign from their positions.

(7) Directors of research institutions shall deliver to a personal information custodian a copy of an approved research protocol, a copy of regular reports regarding research progress and a copy of on-site investigation results conducted by qualified external persons.

(8) Directors of research institutions shall deliver to the ethics review committee a copy of regular reports regarding research progress and a copy of on-site investigation results conducted by qualified external persons.

(9) Directors of research institutions shall properly respond to complaints, inquiries, etc. from donors and equivalent persons by, for instance, setting up a special route to receive such complaints etc.

(10) Directors of human specimen collecting institutions shall, in principle, anonymize a human specimen when providing it to an external institution, (When the human specimen collecting institution also conducts human genome/gene analysis research, its research division shall be considered to be an external institution).

<Subrule Concerning Provision Of Unanonymized Human Specimens To External Institutions>

When a donor, proxy consentor or equivalent person agrees to the provision of an unanonymized human specimen to an external institution and, at the same time, a research protocol authorized by the ethics review committee and approved by the director of a research institution allows for the provision of unanonymized human specimens to external institutions, anonymization is not required.

(11) Directors of human specimen collecting institutions shall, as required, ensure that donors and their families or blood relatives will be able to receive genetic counseling by, for instance, establishing a pertinent genetic counseling system or explaining about genetic counseling and making referral to pertinent genetic counseling services.

<Subrule Concerning Referral To Genetic Counseling Organizations>

When a human specimen collecting institution does not have an internal genetic counseling system, the institution shall, if a donor and his/her family or blood relative desires genetic counseling, make referral to pertinent genetic counseling services.

5. Duties of Principal Investigators

(1) Principal investigators shall, prior to conducting human genome/gene analysis

research, prepare a research protocol and seek approval from the director of his/her research institution. Such a procedure must also be followed prior to altering a research protocol.

(2) Principal investigators shall, in preparing a research protocol, thoroughly take into account such factors as the necessity of the research and the research method intended to prevent disadvantage to donors and equivalent persons, in consideration of various impacts that donors and equivalent persons would be expected to experience as a result of the proposed human genome/gene analysis research.

<Subrule Concerning Cases When Donors Have A Disease Or The Like Causing A Mental Disorder, Intellectual Disability Or Equivalent Condition>

When a donor has a monogenic disease or the like, for which a treatment or prevention protocol has not been established and which, at the same time, causes a mental disorder, intellectual or severe physical disability, principal investigators shall take particular caution in examining such factors as the necessity of the research, medical/psychological impacts on the donor, and the propriety of the research method proposed, and the ethics review committee shall take particular caution in reviewing such factors.

(3) Principal investigators shall prepare a research protocol in full consideration of the special characteristics of human genome/gene analysis research. In particular, such matters as the process and method of obtaining informed consent, the method of personal information protection, the results expected from research and principles of the disclosure, the method of preservation and use of human specimens, and the principles of genetic counseling shall be described clearly.

<Subrule Concerning Items To Be Described In Research Protocols>

The following items shall, in general, be described in a research protocol, but adjustments are permitted according to the details of the research:

- donor selection policy (specific selection method which can be regarded as

reflecting the reasonableness in making selection; when a donor has a disease, a drug response abnormality or the like, the means to inform the donor of the disease name or an equivalent description of the condition)

- significance, objective(s) and method of research (targeted disease, analytical methods, etc.; if addition or alteration is expected in the future, the details thereof; in case of a monogenic disease or an equivalent, the necessity of the research, measures intended to prevent disadvantage, etc.), period of research, expected results and risk, and the means for personal information protection (including the handling thereof when not anonymized)

- types and quantities of human specimens

- name(s) of collaborative research institution(s)

- name(s) of principal investigator(s) etc.

- process and method for obtaining informed consent

- written explanation and consent form(s) to obtain informed consent

- when it is difficult to obtain informed consent from a donor himself/herself, the significance of the targeted research, the reason why the research could not be complete without human specimen provision from said donor, and principles of proxy consent selection

- principles of regarding disclosure of genetic information

- in the case of using an existing specimen, whether or not consent has been obtained, the details thereof, the timing of provision, and the extent of compliance with the present Guidelines

- in the case of receiving a human specimen or genetic information from another research institution, the details of informed consent

- in the case of providing a human specimen or genetic information or contracting out a part of the research to an external institution, matters such as the anonymization method (including details of a contract(s) concerned)

- method of human specimen preservation and its necessity (including the possibility of use in other research and details of expected research)

- in the case of providing a human specimen to a cell, gene or tissue bank, the bank name(s), the anonymization method, etc.

- method of human specimen disposal and anonymization method therein

- necessity of genetic counseling and a system thereof

- method of research fund-raising

(4) Principal investigators shall oversee research conductors so that they will properly conduct human genome/gene analysis research by, for instance, having all research conductors observe matters described in an approved research protocol.

(5) Principal investigators shall, with regard to the progress of human genome/gene analysis research, report to the director of their research institution in writing on a regular basis, at least annually.

<Subrule Concerning Reporting Items>

Principal investigators shall, in general, include the following items in regular reports on research progress to be submitted to the director of their research institution, but adjustments are permitted according to the details of the research:

- quantities of human specimens provided
- quantities of human specimens or genetic information provided to external institution(s) and the reason for such provision
- quantities of human specimens on which human genome/gene analysis research was conducted
- research results and progress
- whether or not any problems arose
- in a human specimen collecting institution, quantities of anonymized human specimens as well

(6) Principal investigator shall, in principle, conduct human genome/gene analysis research by using anonymized human specimens or genetic information.

<Subrule Concerning Research Using Unanonymized Specimen/Information>

When a donor, proxy consentor or equivalent person agrees and, at the same time, a research protocol authorized by the ethics review committee and approved by the director of a research institution allows not to anonymize human specimens or genetic information, anonymization is not required.

(7) Principal investigators shall not, in principle, provide an unanonymized human specimen or genetic information to an external institution.

<Subrule Concerning Provision To External Institutions Without Anonymization>

When a donor, proxy consentor or equivalent person agrees to provision without anonymization and, at the same time, a research protocol authorized by the ethics review committee and approved by the director of a research institution allows not to anonymize human specimens or genetic information, it is permitted to provide unanonymized human specimens or genetic information to an external institution.

(8) Principal investigators shall, in contracting out a part of work in human genome/gene analysis research, in principle, anonymize human specimens or genetic information to be provided to the contractor concerned.

<Subrule Concerning Contracting-Out Without Anonymization>

When a donor, proxy consentor or equivalent person agrees and, at the same time, a research protocol authorized by the ethics review committee and approved by the director of a research institution allows not to anonymize human specimens or genetic information, anonymization is not required.

(9) Principal investigators shall, both on a regular basis and in response to a request from parties including donors, explain clearly or release into the public domain the progress and results of human genome/gene analysis research. This shall not, however, apply to a part that is essential for the protection of human rights of a donor or equivalent person and/or intellectual property rights of researchers.

6. Duties of Personal Information Custodians

(1) Personal information custodians (including co-custodians; the same definition shall hereinafter apply) shall, in principle, anonymize human specimens or genetic information

prior to conducting human genome/gene analysis research, based on a request from a principal investigator. When, however, a person such as a principal investigator operates an anonymizing process as an assistant, a personal information custodian shall oversee that the process is conducted properly.

<Subrule Concerning Exceptions To Human Specimen Anonymization>

When a donor, proxy consentor or equivalent person agrees and, at the same time, a research protocol authorized by the ethics review committee and approved by the director of a research institution allows not to anonymize human specimens, anonymization is not required.

(2) Personal information custodians shall not, in principle, provide to an external institution personal information that was removed at the time of anonymization.

<Subrule Concerning The Provision Of Personal Information To External Institutions>

When a donor, proxy consentor or equivalent person agrees and, at the same time, a research protocol authorized by the ethics review committee and approved by the director of a research institution allows not to anonymize, it is permitted to provide personal information to an external institution.

(3) A personal information custodian, in addition to conducting the anonymizing process, shall rigorously control information containing personal information by, for instance, properly supervising a principal investigator who uses unanonymized human specimens.

7. Duties and Composition of Ethics Review Committees

(1) An ethics review committee shall, in accordance with the present Guidelines, review the appropriateness of conducting a research protocol or any other related matter, include a review on relevant ethical and scientific viewpoints, and express, in writing, its opinions to the director of the concerned research institution.

(2) An ethics review committee may, with regard to research in progress, express to the

director of the research institution its opinions on alteration, discontinuation of or any other treatment to the research protocol as it deems necessary.

(3) Members of an ethics review committee shall not, in the absence of any justifiable reason, divulge information obtained in the course of their duty. This shall continue to apply after the member resigns from the duty.

(4) An ethics review committee shall be properly composed of and operated by members from various backgrounds so that it will be able to perform review work in a fair and impartial manner from an independent standpoint, based on an interdisciplinary and pluralistic approach.

<Subrule 1: Subrule Concerning The Composition Of Ethics Review Committees>

- An ethics review committee shall be composed of persons expertized in the fields of human/social sciences, including ethics and law, and in the field of natural science, and from the general public.

- It is desirable that at least half of members should be external persons; when, however, this is difficult to realize, at least two external members must be placed on the committee.

- At least half of external members shall be persons expertized in the fields of human/social sciences or from the general public.

- An ethics review committee shall be composed of both male and female members.

<Subrule 2: Subrule Concerning The Operation Of Ethics Review Committees>

- When an ethics review committee deliberates or votes on an item, attendance by at least one member in the fields of human/social sciences or one member from the general public is required.

- The director of a research institution, a principal investigator and a research conductor of the research being reviewed shall not participate in deliberation or voting by the ethics review committee. They may, however, in response to a request from the ethics review committee, attend the meeting and provide

explanations.

<Subrule 3: Subrule Concerning Operation Regulations>

Operation regulations shall be established with regard to the following matters:

- chairman selection method
- requisites for convening
- requisites for decision-making
- retention period of review records
- matters related to release into the public domain

(5) An ethics review committee may, if it desires, establish a fast-track review process to be conducted either by members pre-appointed by the chairman or by its subcommittee. Results of fast-track reviews shall be reported to all the members other than those who performed the review or, in case of a subcommittee, to its umbrella organization, the ethics review committee.

<Subrule Concerning The Fast-Track Review Process>

1. The following matters shall, in general, be allowed to be delegated to review by a fast-track review process:

- review of minor alteration to an already authorized research protocol
- review of a research protocol that is classified under a research protocol already authorized by the ethics review committee
- review of a collaborative research protocol to be conducted by another research sharing institution after the research protocol has already been authorized by the ethics review committee of the principal research institution

2. An ethics review committee member who received a report on results of a fast-track review may request to the chairman, upon giving reasons, for a separate review by the ethics review committee with regard to the said matter. In this case, the chairman shall, provided that he/she acknowledges that there are reasonable grounds to do so, immediately hold an ethics review committee meeting and review the matter.

(6) With regard to an ethics review committee, matters regarding the composition thereof

and regulations regarding its operations must be released into the public domain and that its proceedings must also, in principle, be released into the public domain.

<Subrule 1: Subrule Concerning The Release Of Matters Regarding Ethics Review Committee Composition>

The following matters shall be released into the public domain with regard to the composition of an ethics review committee:

- composition of the ethics review committee (including its subcommittees)
- names and organizations of members and positions

<Subrule 2: Subrule Concerning The Release Of Committee Proceedings>

1. Committee proceedings shall be released into the public domain in such a manner that its details will be understood.
2. If the proceedings contain a part that might interfere with the protection of human rights of parties including donors, the originality of research or intellectual property rights, that part may be kept undisclosed on the basis of a decision by the ethics review committee. In such cases, the ethics review committee shall make public the reasons for non-disclosure.

PART III: BASIC STANCE TOWARDS DONORS

8. Informed Consent

(1) Principal investigators (excluding those who conduct research by receiving human specimens from other research institutions; the same definition shall hereinafter apply in Section 8 (excluding (4) and (7))) shall not select a person who will receive a request for a human specimen in an unreasonable, improper or unfair manner.

<Subrule Concerning The Informing Process When A Donor Has A Disease>

When a person who will receive a request for a human specimen has or may have a disease or a drug response abnormality, the person shall have already been informed of the disease name or an equivalent description of the condition.

(2) Principal investigators shall receive a human specimen after giving to a donor adequate explanation of such matters as the significance, objective(s), method and expected results of research, disadvantage that the donor might incur, and the method of preservation and use of a human specimen, and upon obtaining written consent made on the basis of free will.

(3) When obtaining informed consent from a donor under the preceding Rule (2) is difficult, a principal investigator may obtain informed consent from a proxy consentor or an equivalent person of the donor only if the importance of intended research is great and, at the same time, the ethics review committee acknowledges and the director of the research institution approves that research would not be complete without receiving a human specimen from the donor.

<Subrule 1: Subrule Concerning Cases When Informed Consent Is Obtained From Proxy Consentor Or Equivalent Person>

The following conditions shall be met in order that informed consent from a proxy consentor or an equivalent person be permitted, when obtaining informed consent from a donor himself/herself is difficult. In any case where these conditions are met, a principal investigator shall describe in a research protocol the importance of the targeted research, the reason why the research would not be complete without receiving a human specimen from the donor and principles of the selection of a proxy consentor or an equivalent person, and shall have the research protocol authorized by the ethics review committee and approved by the director of his/her research institution:

- when it is judged objectively that a donor is not capable of giving effective informed consent for a reason such as dementia
- when a donor is a minor. In this case, however, a principal investigator shall still give adequate explanation to the donor himself/herself in plain language and make efforts to obtain an understanding. When a donor is a minor at the age of 16 years or older, principal investigators shall also obtain informed consent from the donor together with consent from the proxy consentor.
- when a donor is a deceased person and there is no contradiction to his/her explicit antemortem intention

<Subrule 2: Subrule Concerning Basic Principles Of Proxy Consenter Selection>

Principal investigators shall, in describing principles of proxy consenter selection in a research protocol, take into account such matters, in general, as the family composition of a donor and situation facing the donor, based on the consideration that someone who is thought to be able to speak for the donor in terms of putative intentions and benefits of the donor should be selected as a proxy consenter, among persons listed below:

1. voluntary guardian, persons in parental authority and, if any, appointed guardian or curator
2. donor's spouse, adult children, parents, adult siblings and grandchildren, grandparents and relatives living with the donor, and those persons who are considered to be equivalent to these persons

<Subrule 3: Subrule Concerning Basic Principles Of Selection of Surviving Family Members>

Principal investigators shall, in describing principles of selection of a surviving family member in a research protocol, take into account such matters, in general, as the family composition of a deceased donor, the situation facing the donor, and his/her customs, based on the consideration that someone who is thought to be able to speak for the donor in terms of antemortem putative intentions of the donor should be selected as a surviving family member, among persons listed below:

- deceased donor's spouse, adult children, parents, adult siblings and grandchildren, grandparents and relatives living with the donor, and those persons who are considered to be equivalent to these persons

(4) A donor, proxy consenter or equivalent person may withdraw, in writing, informed consent that he/she has given, at any time without incurring any disadvantage.

(5) When a donor, proxy consenter or equivalent person withdraws informed consent, principal investigators shall, in principle, anonymize the human specimen(s) and research

results related to the said donor and dispose of them.

<Subrule Concerning Exemptions Of Disposal>

1. When either of the following conditions is met, disposal of human specimen(s) and research results is not required:

- the human specimen(s) has/have been anonymized in an unlinkable fashion
- there is a compelling reason not to. For instance, when the possibility of personal information revelation is extremely small even if the information remains unanonymized and, at the same time, the disposal process would be extremely burdensome.

2. When research results have already been made public, disposal of research results is not required.

(6) Principal investigators shall, in the process of obtaining informed consent from a donor, proxy consentor or equivalent person, give explanations to the donor, proxy consentor or equivalent person by furnishing a written document describing the necessary matters in order to obtain an adequate understanding. When a donor has a monogenic disease etc., principal investigators shall give explanations, including information related to the use of genetic counseling and, as required, provide an opportunity for genetic counseling.

<Subrule Concerning The Content Of Explanatory Document>

The following matters shall, in general, be described in an explanatory document directed to a donor, proxy consentor or equivalent person, but adjustments are permitted according to the details of the research:

- that human specimen provision is voluntary
- that a person who received a request for human specimen provision will not be treated in a disadvantageous manner because of his/her refusal
- that a donor, proxy consentor or equivalent person may withdraw, in writing, informed consent that he/she has given, at any time without incurring any disadvantage
- that, when a donor, proxy consentor or equivalent person withdraws his/her consent, the human specimen(s) and research results related to the withdrawal

will be disposed of unless, for instance, they have been anonymized in an unlinkable fashion

- reason(s) for selection as a donor
- significance, objective(s) and method of research (targeted disease, analytical method, etc.; if addition or alteration is expected in the future, the details thereof; in the case of a monogenic disease or an equivalent, the necessity of research, measures intended to prevent disadvantage, etc.), period of research
- when obtaining informed consent from a donor is difficult, the significance of the targeted research, the reason why the research could not be complete without human specimen provision from the donor
- name and position of the principal investigator
- expected research results and expected risk and/or disadvantage to a donor or equivalent person (including disadvantage in social life, such as social discrimination)
- that a donor, proxy consentor or equivalent person may, when so desired, obtain or access documents on the research protocol and research method if doing so does not hinder the protection of personal information of other donors or equivalent persons or the securing of research originality
- whether a human specimen to be provided or genetic information derived therefrom will be anonymized in a linkable or unlinkable fashion, and the specific method of anonymization. When anonymization is not possible, the details of and reason(s) for this
- whether or not the provision of a human specimen or genetic information derived from the specimen to other institutions is possible. If so, that the ethics review committee would review the handling of personal information, the name(s) of the receiving institution(s), the propriety of use in the receiving institution(s).
- method of anonymization etc. to be applied in the case when a part of research is contracted out
- matters regarding disclosure of genetic information
- that research outcomes might generate intellectual property rights, such as patent rights, in the future. Name(s) of any organization(s) to which such intellectual property rights, such as patent rights, would belong to, were it to be

generated.

- that genetic information derived from human specimens might, upon anonymization, be made public in an academic society etc.
- method of preservation and use of human specimens
- method of preservation, use or disposal of human specimens after the completion of research (including the possibility of use in other research and details of expected research)
- when a human specimen might be provided to a human cell, gene or tissue bank for distribution as general research material, academic significance of the bank(s) concerned, name(s) of the organization(s) operating the bank(s), method(s) of anonymization for the human specimen to be provided, and name(s) of person(s) in charge of the bank(s)
- information related to use of genetic counseling (for instance, that genetic counseling is available in the case of monogenic diseases etc.)
- method of research fund-raising
- that human specimen provision is gratuitous
- information regarding, for instance, where inquiries, complaints, etc. should be filed

(7) When principal investigators receive a human specimen or genetic information from another research institution, they shall confirm the details of informed consent related to the human specimen or genetic information through a written document or its equivalent from the research institution.

(8) When principal investigators, prior to conducting human genome/gene analysis research, obtains informed consent from a donor, proxy consentor or equivalent person with the expectation that a human specimen and/or personal information will be used in human genome/gene analysis research or related medical research, the principal investigator shall clearly state the specific research objective(s) expected at that point in time and shall explain and provide an understanding of how personal information will be controlled and protected, including the possibility of anonymization.

9. Disclosure of Genetic Information

(1) When a donor, with regard to human genome/gene analysis research through which genetic information of each individual donor could be revealed, requests his/her own genetic information to be disclosed, principal investigators shall, in principle, disclose the requested information. This shall not, however, apply if there is no adequate significance in providing genetic information and informed consent to non-disclosure has been obtained from the donor.

<Subrule Concerning Disclosure Of Genetic Information>

1. When a donor, in spite of having agreed to non-disclosure of genetic information at the time of giving informed consent, requests *ex post facto* for disclosure, principal investigators shall disclose genetic information of the donor unless the following condition is met. When the genetic information is not disclosed, the principal investigator shall provide the reason(s) for non-disclosure to the donor in plain language.

- that it is described in a research protocol that the targeted research is human genome/gene analysis research or equivalent intending to elucidate the association between a certain disease and genes or the function of a certain gene by mutually comparing genetic information of a large number of people or genes and, at the same time, lacks significance in informing an individual donor of genetic information as such information is not accurate or certain enough to evaluate his/her state of health etc., and that the research protocol has been authorized by the ethics review committee and approved by the director of the concerned research institution

2. Principal investigators may, when a minor-aged donor requests his/her own genetic information to be disclosed, disclose the information to the minor upon adequate consideration of potential psychological impacts etc. of disclosure. When, however, the minor is under the age of 16 years, principal investigators shall determine the intention of his/her proxy consentor and respect that intention. The principal investigator shall also report to the director of his/her research institution when, as a result of disclosing the minor's genetic information, the donor might disadvantage himself/herself or there is concern of discrimination against the donor, custody relinquishment, or negative impacts

on treatments. The director of the research institution shall, prior to disclosure, seek opinions of the ethics review committee regarding the propriety of disclosure and details and method thereof and also seek dialogue with the minor and his/her proxy consentor, if necessary.

(2) When a donor, with regard to human genome/gene analysis research through which genetic information of donors could be revealed, does not want his/her own genetic information to be disclosed, principal investigators shall not disclose the information.

<Subrule Concerning Non-Disclosure Of Genetic Information>

Principal investigators shall, even if a donor does not want his/her own genetic information to be disclosed, report to the director of his/her research institution when it is discovered that the genetic information has a serious impact on the life of the donor and his/her blood relatives and, at the same time, there is an effective treatment protocol. The director of the research institution shall seek the opinions of the ethics review committee regarding the propriety of disclosure and details and method thereof, including consideration of, in particular, the following matters, and shall, based on those opinions, consult with the principal investigator, medical doctor in charge of treating the donor and the director of the medical institution to which the doctor belongs. The principal investigator shall, based on consultation results, confirm the intention of the donor after giving him/her adequate explanations and, if the donor still does not want the genetic information to be disclosed, shall not disclose it.

- impact on life of the donor and his/her blood relatives
- whether or not there is an effective treatment protocol and the donor's state of health
- possibility that blood relatives are afflicted with the same disease etc.
- details of explanation about the disclosure of research results given at the time of informed consent

(3) Principal investigators shall not, in the absence of consent from a donor, in principle, disclose genetic information of the donor to any person other than the donor.

<Subrule Concerning Disclosure To Persons Other Than The Donor>

1. When a proxy consentor or an equivalent person of a donor (excluding a proxy consentor of a minor) requests genetic information of the donor to be disclosed, the director of a research institution shall, after presenting to the ethics review committee the reason(s) for or the necessity of the disclosure request by the proxy consentor or equivalent person, determine a response based on the opinions of the ethics review committee.

2. When a donor is a minor and his/her proxy consentor requests genetic information of the minor to be disclosed, principal investigators may disclose the information to the proxy consentor. When, however, the minor is 16 years of age or older, the principal investigator shall confirm his/her intention and respect that intention. The principal investigator shall also report to the director of his/her research institution when, as a result of disclosing the minor's genetic information, there is concern of discrimination against the donor, custody relinquishment, or negative impacts on treatments. The director of the research institution shall, prior to disclosure, seek opinions of the ethics review committee regarding the propriety of disclosure and details and method thereof and also seek dialogue with the minor and his/her proxy consentor, if necessary.

3. Principal investigators may, even if a donor does not want his/her own genetic information to be disclosed to his/her blood relatives, inform a blood relative of the donor of information related to a disease or a drug response abnormality containing a genetic predisposition derived from genetic information of the donor himself/herself if all of the following conditions are met:

1) that it is discovered that the genetic information has a serious impact on lives of the donor's blood relatives and, at the same time, there is an effective treatment protocol

2) that the director of the research institution seeks opinions of the ethics review committee regarding the propriety of disclosure and details and method thereof, including consideration of, in particular, the following matters, and, based on those opinions, reaches a conclusion, upon consultation with the principal investigator, that necessary information should be provided to the blood relative:

a. possibility that the blood relative is afflicted with the same disease etc.

- b. impact on lives of blood relatives
 - c. whether or not there is any effective treatment protocol, and the blood relative's state of health
 - d. details of explanation about disclosure of research results given at the time of informed consent
- 3) that the principal investigator, based on the conclusion under 2), seeks the understanding of the donor again and makes efforts to obtain consent regarding the provision of necessary information to the blood relative
 - 4) that the intention of the donor's blood relative to request for information provision is confirmed upon an adequate explanation

(4) Principal investigators shall, in disclosing genetic information regarding a monogenic disease etc., disclose the information in adequate consideration of medical or psychological impacts etc. while keeping in close contact with a medical doctor in charge of treatments, and shall also, if necessary, offer an opportunity for genetic counseling.

<Note>

The significance of the genetic information being disclosed depends largely on the medical examination and treatment, and it is necessary to have close contact with a medical doctor in charge of treatments, especially a doctor specializing in medical genetics. Therefore, the person who should disclose the information might be either the medical doctor in charge of medical examinations and treatments who would disclose it as a part of the medical examinations and treatments, or the principal investigator who would do so under the direction of the doctor.

10. Genetic Counseling

(1) Objective

The objective of genetic counseling in human genome/gene analysis research is to help a donor, his/her family/families or blood relative(s) through dialogue so that they can make free choices in their future, by offering accurate information, deepening their

understanding of genetic diseases etc., and reducing their anxieties or worries concerning human genome/gene analysis research, genetic diseases, etc.

(2) Method of Counseling

Genetic counseling shall be provided by and in cooperation with medical doctors, health care professionals and others who have adequate knowledge of medical genetics and are well-experienced in genetic counseling.

<Note>

Matters regarding the establishment of a genetic counseling system for reference to directors of human specimen collecting institutions are prescribed in 4 (11), matters regarding the description of principles of genetic counseling in research protocols are in 5 (3), items to be explained and matters regarding genetic counseling opportunity offering at the time of obtaining informed consent are in 8 (6), and matters regarding genetic counseling opportunity offering at the time of disclosing genetic information are in 9 (4).

PART IV: HANDLING OF HUMAN SPECIMENS

11. Use of Existing Specimens

(1) The propriety of using a human specimen provided and preserved before the conduct of any human genome/gene analysis research shall be determined, in accordance with the provisions under (2) to (4) and upon authorization from the ethics review committee, by the director of a research institution with consideration of whether or not consent has been obtained from a donor, proxy consentor or equivalent person, details thereof and the timing of provision of the specimen.

(2) For an existing specimen provided after the enforcement of the present Guidelines, the director and a principal investigator of a research institution shall carefully make judgment on the use, and the ethics review committee shall carefully review the propriety of the use in research, in accordance with the philosophy of the present Guidelines.

(3) A Group A human specimen (a human specimen for which consent, including consent for the use in human genome/gene analysis research, was obtained at the time of provision) may be used in human genome/gene analysis research within the scope of the obtained consent.

(4) A Group B human specimen (a human specimen on which consent has been obtained at the time of provision, but only for research that does not articulate its use in human genome/gene analysis research) or a Group C human specimen (a human specimen for which consent for its use in research has not been obtained) may not, in principle, be used in human genome/gene analysis research unless consent from a donor, proxy consentor or equivalent person is newly obtained in accordance with the process etc. prescribed in the present Guidelines.

<Subrule 1: Subrule Concerning The Use Of Group A Human Specimens Provided After The Enforcement Of The Present Guidelines>

The director of a research institution and a principal investigator shall make judgment on how a Group A human specimen should be handled, in consideration of how extensively, regarding the use in other human genome/gene analysis research, the significance or objective(s) of the intended human genome/gene analysis research, method of anonymization, etc. were referred to when consent was obtained at the time of the provision thereof, and the timing of the obtaining of the consent, etc., and the ethics review committee shall review, also in consideration of these matters, how the existing specimen should be handled.

<Subrule 2: Subrule Concerning The Use Of Group B Human Specimens Provided Prior To The Enforcement Of The Present Guidelines>

A Group B human specimen provided prior to the enforcement of the present Guidelines may be used in human genome/gene analysis research when any of the following requirements is met but only if such use is authorized by the ethics review committee and approved by the director of the research institution:

1) causing risk or disadvantage to a donor or equivalent person is not possible

because the specimen has been anonymized in an unlinkable fashion

2) the specimen has been anonymized in a linkable fashion, the possibility of causing risk or disadvantage to a donor or equivalent person as a result of human genome/gene analysis research is extremely low, the intended research is deemed highly useful, and conducting the intended research in another way is virtually impossible or extremely difficult

<Subrule 3: Subrule Concerning The Use Of Group B Human Specimens Provided After The Enforcement Of The Present Guidelines>

A Group B human specimen provided after the enforcement of the present Guidelines may be used in human genome/gene analysis research only when, in addition to the fulfillment of the aforementioned requirements described in <Subrule 2>, an opportunity for donors, proxy consenters and/or equivalent persons to refuse the use thereof is guaranteed and the use in human genome/gene analysis research is authorized by the ethics review committee and approved by the director of the research institution, in consideration of how extensively, particularly regarding research to be conducted by using specimens that are anonymized in a linkable fashion, the significance or objective(s) of other human genome/gene analysis research, the method of anonymization, etc. were referred to when consent was obtained at the time of the provision of the Group B human specimen, the timing of the obtaining of the consent, etc.

<Subrule 4: Subrule Concerning The Use Of Group C Human Specimens Provided Prior To The Enforcement Of The Present Guidelines>

A Group C human specimen provided prior to the enforcement of the present Guidelines may be used in human genome/gene analysis research when any of the following requirements is met but only if the use is authorized by the ethics review committee and approved by the director of the research institution:

1) causing risk or disadvantage to a donor or equivalent person is not possible because the specimen has been anonymized in an unlinkable fashion

2) the specimen has been anonymized in a linkable fashion and all of the following requirements are met:

a. the possibility of causing risk or disadvantage to a donor or equivalent person

as a result of human genome/gene analysis research is extremely low

- b. the intended human genome/gene analysis research using the specimen will make a significant contribution to the public interest
- c. conducting the intended research in another way is virtually impossible
- d. measures are taken to have information related to the progress of human genome/gene analysis research made public and also to guarantee an opportunity for donors, proxy consenters and/or equivalent persons to make inquiries and/or refuse the use of a human specimen in research.

<Subrule 5: Subrule Concerning The Use Of Group C Human Specimens Provided After The Enforcement Of The Present Guidelines>

A Group C human specimen provided after the enforcement of the present Guidelines may be used in human genome/gene analysis research only when, in addition to the fulfillment of the aforementioned requirements in <Subrule 4> and particularly regarding research to be conducted by using specimens that are anonymized in a linkable fashion, the number of applicable cases is limited and, at the same time, the use is authorized by the ethics review committee and approved by the director of the research institution, based on the grounds that the use is imperative because of, for instance, the urgent need to conduct the research.

12. Methods of Human Specimen Preservation and Disposal

(1) General Principles for Preservation

Principal investigators shall, in preserving a human specimen in their research institution, observe matters agreed to by a donor, proxy consentor or equivalent person and comply with a method prescribed in the research protocol.

(2) Provision to Human Cell, Gene or Tissue Banks

Principal investigators shall, in providing a human specimen to a human cell, gene or tissue bank, ensure that the human specimen will be anonymized in an unlinkable fashion

when the bank distributes it as a general research specimen or its equivalent and shall also observe matters agreed to by the donor, proxy consentor or equivalent person concerned, including consent for provision to such banks.

(3) Disposal of Human Specimens

Principal investigators shall, when the preservation period of a human specimen prescribed in a research protocol expires, except when they are preserving the human specimen in accordance with a research protocol or the specimen is provided to a human cell, gene or tissue bank, observe matters agreed to by the donor, proxy consentor or equivalent person concerned and dispose of the human specimen after anonymizing it.

PART V: REVISION

13. Revision

The present Guidelines shall be revised, as required or in approximately five years after the enforcement thereof, upon conducting an examination of the entire contents.

PART VI: DEFINITIONS OF TERMS

14. Definitions of Terms

(1) Human Specimen

"Human specimen" means any blood, tissue, cell, body fluid and/or excrement to be used in human genome/gene analysis research, any portion of a human body, such as DNA, extracted or medical information of a donor (including specimens provided by deceased persons). Any tissue, cell, body fluid or excrement as well as DNA, etc. extracted whose scientific value is fixed and, at the same time, which is adequately recognized as research outcomes, is used commonly and broadly in research and is commonly available shall, however, be excluded.

<Note 1>

It is supposed that the prerequisite for human specimen provision from a person who has been recognized to be brain-dead under the Organ Transplantation Law (Law No.104 of 1997) be considered adequately met if such human specimen provision is received after the so-called "three indications of death", namely, absence of heartbeat, absence of breathing and absence of dilation of the pupils of the eyes, are observed as a result of organ removal.

<Note 2>

Although it shall be indeed necessary to meet the purposes of the present Guidelines when conducting research by receiving provision of fertilized eggs, embryos, fetuses, ES cells, etc., it shall not be considered suitable to conduct such research solely on the basis of the compliance with the present Guidelines; careful separate examination is still required therein, from an ethical point of view etc.

(2) Medical Information

"Medical information" means information including disease names, drug names, examination results, etc. which are obtained in the course of medical examinations and treatments.

(3) Human Genome/Gene Analysis Research

"Human genome/gene analysis research" means research conducted by using human specimens for the purpose of elucidating structures or functions of the human genome and genes that commonly exist in cells of a donor and possibly inheritable. To simply provide a human specimen for use in such research shall also be included in the definition.

<Subrule Concerning The Scope Of Human Genome/Gene Analysis Research Covered By The Present Guidelines>

1) The present Guidelines shall apply to human genome/gene analysis research intending to analyze structures or functions of base sequences of DNA or complementary DNA derived from mRNA or the like by using a tissue, such as

leukocytes, of a donor, a main example of which is research that analyzes what is called germline mutation or polymorphism. On the other hand, the present Guidelines shall not, in principle, apply to research that targets mutation of a genome or a gene that appears *a posteriori* only on a affected region of a disease, such as cancer, and is not inherited to the next generation (this refers to research that analyzes what is called somatic mutation, which includes research that analyzes normal tissues to corroborate the existence of a mutation), research regarding gene expression or research regarding structures or functions of proteins. When, however, the aforementioned research is conducted for the purpose of elucidating information regarding a genome or a gene to be possibly inherited to descendants, the present Guidelines shall apply. It is still desired that appropriate measures should be taken, based on the purposes of the present Guidelines, in conducting research regarding somatic mutation, gene expression or structures or functions of proteins to which the present Guidelines do not apply.

2) Research whose main objective is not to conduct human genome/gene analysis research but which partially involves human genome/gene analysis research shall also be included in the definition.

3) Research that secondarily uses a human specimen or genetic information obtained in the course of medical examinations and treatments shall also be included in the definition.

4) As clinical trials and post-marketing surveillance studies of pharmaceutical products conducted in accordance with the Pharmaceutical Affairs Law (Law No.145 of 1960) are already regulated by the "Ministerial Ordinance Concerning Good Clinical Practice (Ordinance of Ministry of Health No.28 of 1997)" and the "Ministerial Ordinance Concerning Good Post-Marketing Surveillance Practice (Ordinance of Ministry of Health No.10 of 1997)", the present Guidelines shall not apply to them. Similarly, the present Guidelines shall not apply to the production of medical equipment and clinical trials and post-marketing surveillance studies conducted for the purpose of applying for import approval, all of which are prescribed in the Medicine Law.

5) The present Guidelines shall not apply to genetic structure analysis training, such as biology training for educational purposes, that is conducted in the study

field of a gene whose structure and function is already known and, at the same time, does not involve the use of a human specimen or analysis results beyond training purposes.

(4) Genetic Information

"Genetic information" means information that reflects the genetic characteristics or constitution of an individual person, which is obtained in the course of human genome/gene analysis research conducted by using a human specimen or is already contained in a human specimen.

(5) Personal Information

"Personal information" means information of individuals containing their name, birth date or any other description, through which a specific individual could be identified (including information that could be easily collated with other information and a specific individual could thereby be identified).

<Note 1>

On what legal grounds personal information of deceased persons should be protected is a subject of discussion. The standpoint taken in the present Guidelines is that personal information of deceased persons should also be protected in consideration of the human dignity of the deceased persons, sentiments of surviving family members and the fact that the genetic information is common to their blood relatives.

<Note 2>

Although personal information may typically include a name, birth date, address and phone number of a person as well as a symbol, such as a medical record number given to each individual patient, it would have to be judged on an individual basis whether or not a certain piece of information should be considered personal information under the present Guidelines.

(6) Anonymization

"Anonymization" or "to anonymize" means to remove, in part or in whole, from the personal information of a certain person, information through which a specific individual could be identified and to give instead a symbol or a number that has no relevance to the person, for the purpose of preventing the personal information from being divulged externally in violation of law, the present Guidelines or a research protocol. When it is impossible to identify a specific person only through a certain piece of information included in a human specimen but it is possible to identify the person by combining information available elsewhere, such as in some list, "anonymization" or "to anonymize" means to remove, in part or in whole, the information that is necessary to complete such combination and to make it impossible to identify the person. Anonymization would be implemented either of the following ways:

a. anonymization in a linkable fashion

anonymization implemented through a method where a corresponding list of an individual and a newly-given symbol or number is maintained so that the person may be identified as necessary

b. anonymization in an unlinkable fashion

anonymization implemented through a method where no corresponding list aforementioned in a. is maintained, so that an individual could not be identified

(7) Personal Information Custodian

"Personal information custodian" means a person in charge of controlling and anonymizing personal information, under the direction of the director of a research institution in which personal information is handled, including human specimen collecting institutions, so that personal information of donors or equivalent persons will not be divulged outside of the institution.

(8) Informed Consent

"Informed consent" means consent regarding provision and handling of a human specimen which a person who has been requested to provide a human specimen gives on the basis of his/her free will after receiving adequate prior explanations from a principal

investigator with regard to human genome/gene analysis research and understanding the significance, objective(s), method, expected results, etc. of the said research and possible disadvantage to parties including donors. Under the present Guidelines, informed consent shall be given in writing.

(9) Proxy Consenter or Equivalent Person

A "proxy consenter or equivalent person" means a person who gives informed consent in place of another person who has been requested to provide a human specimen when the latter person is incapable of giving informed consent. When a donor is a deceased person, his/her surviving family member shall be a "proxy consenter or equivalent person". When surviving family members are to be excluded from the definition, the expression "proxy consenter" shall be used.

<Note>

As a proxy consenter or equivalent person is, first and foremost, a person who decides whether or not to agree to human specimen provision etc. by a donor in place of the donor from a viewpoint of human rights protection for the donor, it is necessary to examine separate measures with regard to genetic issues of proxy consenters or equivalent persons themselves.

(10) Minor

A "minor" means an unmarried person under the age of 20 years.

(11) Research Institution

A "research institution" means an institution that conducts human genome/gene analysis research (including human specimen collecting institutions).

(12) Human Specimen Collecting Institution

A "human specimen collecting institution" means a research institution that collects

human specimens from people, such as medical institutions or public health centers.

(13) Collaborative Research Institution

A "collaborative research institution" means a public or private research institution, including a university, that collaboratively conducts human genome/gene analysis research described in a research protocol. When a research institution receives a human specimen from another human specimen collecting institution, the human specimen collecting institution shall also be included in the definition.

(14) External Institution

An "external institution" means a research institution or the like other than the research institution at issue. When a human specimen collecting institution also conducts human genome/gene analysis research in a different division within the institution by using the internal human specimen collection, the research division shall be considered to be an external institution.

(15) Ethics Review Committee

An "ethics review committee" means a council-type body established as an advisory board for the director of a research institution for the purposes of investigation and discussion of the propriety of conducting human genome/gene analysis research and other related matters, involving both an ethical viewpoint, such as human rights protection for donors or equivalent persons, and a scientific viewpoint.

(16) Researcher or Equivalent Person

A "researcher or equivalent person" means a person involved in human genome/gene analysis research, such as principal investigators, research conductors (including those who conduct operations of receiving human specimen provision), those who conduct genetic counseling, those who conduct operations of protecting personal information, directors of research institutions, etc.

(17) Principal Investigator

A "principal investigator" means a researcher in a research institution who carries out human genome/gene analysis research as well as supervises related operations and, at the same time, has sufficient knowledge of the usefulness and limitations of human genome/gene analysis research and of bioethics.

(18) Research Conductor

A "research conductor" means a person who conducts human genome/gene analysis research in accordance with the direction or contract by a principal investigator and, at the same time, has the necessary knowledge and skills according to the details of the operation concerned, such as researchers, medical doctors, pharmacists, nurses, clinical laboratory technologists, etc.

(19) Donor

A "donor" means a person who provides a human specimen for human genome/gene analysis research. When a person who is supposed to have relevance to genetic information of a donor, including his/her families, blood relatives or proxy consentor or equivalent person, is to be included in the definition, the expression "donor, proxy consentor or equivalent person" shall be used.

(20) Genetic Counseling

"Genetic counseling" means targeting, supporting or assisting in the solution or relief of various medical or psychological problems that could arise with regard to a hereditary disease through repeated dialogue and information offering by making use of knowledge of medical genetics and counseling techniques.

(21) Existing Specimen

An "existing specimen" means a human specimen provided and preserved prior to the conduct of human genome/gene analysis research. Existing specimens can be divided into the following categories, according to the extent of consent obtained at the time of human specimen provision:

a. Group A human specimen

"Group A human specimen" means a human specimen for which consent has been given at the time of human specimen provision, including the use in human genome/gene analysis research.

b. Group B human specimen

"Group B human specimen" means a human specimen for which consent has been given at the time of human specimen donation, but only for research that does not articulate the use in human genome/gene analysis research, under such expression as "agree to the use in medical research".

c. Group C human specimen

"Group C human specimen" means a human specimen for which consent for the use in research has not been given at the time of human specimen provision.

(22) Human Cell, Gene or Tissue Bank

A "human cell, gene or tissue bank" means a non-profit business that conducts quality control of provided human cells, genes, tissues, etc. and distributes them to unspecified researchers as research material.

PART VII: SUBRULES

15. Subrules

In addition to those subrules prescribed in the present Guidelines, matters required with regard to the enforcement of the present Guidelines shall be separately prescribed.

PART VIII: DATE OF ENFORCEMENT

16. Date of Enforcement

The present Guidelines shall take effect as of April 1, 2001.