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 he research could not be complete without human specimen provision from said donor, and principles of proxy consenter 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 consenter 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 consenter 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 consenter 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 consenter 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 consenter 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 consenter 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 Consenter Or Equivalent Person>

The following conditions shall be met in order that informed consent from a proxy consenter 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 consenter 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 consenter.

- 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 consenter or equivalent person, give explanations to the donor, proxy consenter 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 consenter 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 consenter 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 consenter 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 consenter 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 consenter 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 consenter 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 consenter, 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 consenter or an equivalent person of a donor (excluding a proxy consenter 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 consenter 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 consenter requests genetic information of the minor to be disclosed, principal investigators may disclose the information to the proxy consenter. 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 consenter, 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 consenter 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 consenter 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