

FUNDAMENTAL PRINCIPLES
OF RESEARCH ON THE HUMAN GENOME

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Bioethics Committee

Council for Science and Technology

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Preface

Stunning recent developments in the life sciences, and the progress in the technology that has underpinned these developments, are deepening our scientific understanding of what it is that constitutes human life. At the same time these developments makes great contributions to the improvement of our life, in increasing levels of health and enhancing the prevention, diagnosis and treatment of disease. Humankind has thus reaping tremendous benefit from this steady march forward. However, through these advancements, it is becoming possible for humans to place their mark, one could even say interfere, in the inner workings of all stages of life from birth to death. The result has been the emergence of various ethical, legal and social issues, leading to a renewed awareness of the human dignity and. We cannot focus exclusively on what benefits may be gained through the developments of life sciences in areas of human health and the fight against disease, but must also look at the ethical values and principles involved and carefully evaluate whether problems may arise. Herein lies the reason why a heightened awareness of bioethics as an important aspect of human society has begun to take centre stage in recent periods.

Progress in research into the human genome, often referred to as the blueprint of human life, is deeply approaching the origin of the human life and thus opening up the possibility of a total transformation both in how we view what it is that makes us human and in how we view life itself. It also has the potential to shake the entire system of values that we hold as a society. This scenario makes it imperative that we consider what limits should be set, on how far human genome research should be permitted to go, and of what nature this research should be. The human genome research is at the brink of unlocking the entire genetic code of human being. From now on, our objective is to determine those genetic factors involved in specific traits and the aetiology of disease based on research into the differences between individual genomes. This research leads to further developments of biomedicine, from which a new approach to medical care will emerge whereby treatment would be tailored specifically to each individual. However, as this research requires the provision of numerous samples from many participants, whose genetic information will be revealed in the results obtained during the course of this research, there is concern that far more and even bigger problems will arise in this research in the future. It is for this reason that an urgent establishment of fundamental ethical norms, based on bioethical considerations, is needed for human genome research.

The Bioethics Committee of the Council for Science and Technology, since its inception of considered the questions of the application of cloning technology into humans and of the research on human embryonic stem cells, and have addressed the basic ideas on each of them. Then in light of the situation described above, A Sub-Committee on the Human Genome Research was newly created in December 1999 to examine the approach to be taken in the human genome research, and, following the discussion therein, reached to proclaim hereby the “Fundamental Principles of Research on the Human

Genome.”

These Fundamental Principles define the ethical framework that should be respected by those who are engaged in human genome research, such as scientists and physicians. They also presents the basic conception to be understood both by those individuals who are providing research samples and by the society as a whole. The Fundamental Principles, therefore serve as “the Constitution” in human genome research, and relevant guidelines must be formulated based on these Fundamental Principles to provide a more detailed rules that should be adhered to in the course of research. Furthermore, the Fundamental Principles should be revised as the needs arise, following the future development of genome research and the advancement of the societal understanding and awareness of bioethical considerations, . Furthermore, various issues have to be dealt with in the area of practical applications stemming from human genome research, such as in medical diagnosis, prevention and treatment, so that appropriate guidelines must also be set down to cover these issues. We hope that the ideas contained in these Fundamental Principles will be reflected in these future guidelines.

The bioethical principles are, needless to say, founded on the premise of the basic understanding of the life sciences and of the broad reflections on the life of human being. However, development in the life sciences is moving at an incredibly rapid pace, and we must face and solve a wide range of problems on even a daily basis. Until now Japan has not been fully aware of bioethical understanding and lacking adequate framework for bioethical debate. Therefore, it is important that, on one hand, measures be put into place to create an understanding in society of the issues that are arising, and on the other hand, to build a foundation within the education system covering the life sciences and bioethics from an early juncture, and, at the same token, to keep promoting debates and efforts directed towards achieving a social consensus on these issues. It is our fervent hope that the proclamation of these Fundamental Principles will further enhance the awareness of bioethical consideration and to grow up the firm foundation for the research on the life sciences in which all and every researchers and physicians fully respect the human dignity and human rights, in order to build up the society where progress is in harmony balance with welfare and happiness.

June 14th, 2000

Bioethics Committee

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Basic Ideas

1. **Science**, as one of the intellectual activities of humanity that aims at the pursuit of truth, underlies the future development of human society. Freedom of research, which is the pillar of science, is a part of freedom of thought, which, in turn, is a core component of fundamental human rights. Science, however, is not an autonomous entity that is independent of society but one that is confined within the sphere of human society. Thus, scientific research should conform to the respect for human dignity, should interact with various social factors, and should fully understand that there might be oppositions or conflicts between scientific interests and other social interests.
2. **Life science** aims at the elucidation of phenomena concerned with the life of living organisms, and especially at understanding humanity from a biological point of view. The applications of the results of research in life science, including medical treatments and agriculture, have made a significant contribution to the progress of the health and welfare of humanity. The application of findings derived from research on the human genome in particular shed light on the possibility of the prevention and treatment of diseases that have defied traditional medical approaches. However, it is a concern that progress in life science may precipitate various problems at the interface with society. We, humanity, have a history in which we have seriously neglected considerations of human dignity and human rights in the name of research. After the Second World War, these acts of violation were reflected on with deep regret, and so that such past errors are not repeated, all nations and related international organizations have been constantly making various efforts from the viewpoint of bioethics, beginning with the pronouncement of the Nuremberg Code. Medical practitioners and researchers, too, alerted by the Declaration of Helsinki and other pronouncements, have come to realize that human dignity and human rights should be respected in their research. In relation to research on the human genome, which is the focus of the present Fundamental Principles, the “Universal Declaration on the Human Genome and Human Rights” was adopted in 1997 at the General Conference of UNESCO (the United Nations Educational, Scientific and Cultural Organization). This Declaration was endorsed by the General Assembly of the United Nations and accepted in various countries as the first pronouncement on universal ethical principles concerning research on the human genome.
3. **Research on the human genome** made rapid progress as a result of the Human Genome Project, which began in earnest in 1990. This research aims to analyse the structures and functions of the human genome, investigate the biological functions of humans, and understand the mechanisms underlying human life. Based on this information, human genome research further aims to contribute to the protection of human life and health and to the prevention and

treatment of disease. Great strides have been made in research on genetic polymorphism in particular, due to the accelerated decoding of DNA sequences. Research on the genetic information collected from individuals enables the aetiology of diseases to be determined, novel strategies for the prevention, diagnosis, and treatment of diseases to be developed, and also for new medicines to be developed. Some of the findings generated by this research are now being put to practical use.

4. **Research on the human genome and its outcomes**, however, may give rise to serious ethical, legal and social issues because, on the one hand, they may lead to the manipulation of “life”, while on the other hand, they may bring about the risk of violating the dignity and human rights of an individual on account of his/her personal genetic characteristics. Thus, it is imperative that all these issues are guarded against and that the full understanding of the public is gained with regard to research activities on the human genome and the application of the outcomes of such activities.
5. **The “Fundamental Principles”** were established in order that research on the human genome might be conducted in an appropriate manner without violating human dignity or human rights. The principles are mainly aimed at researchers and medical practitioners concerned with the human genome. These principles also provide the basis for the understanding of research on the human genome that the public, and especially those persons providing research samples, and their blood relatives and families, are expected to have. It should be noted that research on the human genome is intricately related to the diagnosis and treatment of diseases based on the genetic information it provides. National guidelines on genetic diagnosis and gene therapy need to be established separately in addition to the “Fundamental Principles of Research on the Human Genome”.

Chapter 1 The human genome, and research on the human genome

Principle 1 The significance of the human genome

1. The human genome is the heritage of humanity.
2. The human genome is the blueprint of human life. It provides all members of humanity with a biological basis as a human being and it also underlies the uniqueness and diversity of each human being.
3. The existence of a human being is not determined only by his/her genome.
4. Conveying the fundamental information of human life from parents to children, from children to grandchildren, et cetera, the human genome builds the fundamental structures and functions of an individual as a human being. At the same time, however, the human genome is acted on by various influences in the natural and social environment.

Principle 2 Diversity of the human genome and the dignity and human rights of individuals

The human genome differs from one individual to another. The diversity of genetic characteristics signifies the originality and uniqueness of each individual and the plurality of humanity as a whole. Thus, it is imperative that, regardless of their genetic characteristics, all individuals or groups of individuals are respected for their dignity and human rights, and that they are equal to one another and are not subjected to any form of discrimination.

Principle 3 Due consideration of ethical, legal, and social issues

It is considered that since research on the human genome and the applications of its outcomes have the potential to significantly change the way in which human beings think about human life and living, it may have an extremely serious impact on society. Therefore, due consideration should be given to ethical, legal and social issues in research and its applications.

Principle 4 Participants, and their families and blood relatives

Research on the human genome inevitably requires research samples that are provided by human subjects. Therefore, this type of research can be conducted only with a high regard for the dignity and human rights of the persons providing research samples (hereafter, “participants”), and their families and blood relatives.

Chapter 2 Rights of participants

Section 1 Informed consent

Principle 5 Basic Conditions

1. A research sample may be collected from an individual subject for research on the human genome only after the participant has first been given a sufficient explanation of the research, and has then given, of his/her own free will, his/her consent (informed consent).
2. The consent should be expressed in writing.
3. An individual who is requested to provide a research sample but does not consent to that request should not be disadvantaged as a result of his/her refusal.

Principle 6 Individuals who do not have the capacity to consent

In the event that research on the human genome is to be conducted using samples from participants including an individual who does not have the capacity to consent, it should be demonstrated in advance that the research in question requires a research sample from that particular individual, and his/her informed consent should be obtained from his/her representative.

Principle 7 Diversity of research

1. In the procedure for obtaining informed consent, the information and explanation about the research should be presented using the most appropriate method given the objectives and particulars of the research, in view of the fact that research on the human genome, and especially the identification of the genetic information of individuals, is associated with a high risk of ethical, legal and social issues.
2. In all research projects, the procedures used to obtain informed consent should be clearly described in the research plan and undergo prior review by the Ethics Committee.

Principle 8 Comprehensive consent, and unlinked and unidentified research samples

1.
 - (a) If a participant consents to provide a research sample for genome analysis in a particular research project and, at the same time, anticipates and consents to the use of the same sample in other genome analyses or related medical research, then the research sample may be used for the latter “studies aimed at other purposes.”
 - (b) In this case, sufficient information, which clearly outlines the anticipated objectives of the research at that point in time, should be given to the participant so that s/he can thoroughly understand the significance and consequences of the fact that the sample provided will be used in “studies aimed at other purposes,” as defined in the preceding sub-paragraph.
 - (c) In the cases described in the preceding two sub-paragraphs, protocols pertaining to the management and protection, including anonymity, of genetic and other personal information of the participant should be explained in detail, and strict confidentiality should be guaranteed.
2. If it is expected that the sample provided will be handled anonymously, the method of explanation used in the procedure of obtaining informed consent may be appropriately simplified on the condition that it is guaranteed that the sample can not be linked to the donor.
3. In the cases described in the preceding two paragraphs, the comprehensive consent and the simplified method of explanation can be used only when the source of the research sample to be used, and the actual protocols and method used in the procedure of obtaining informed consent are described in the research plan and when these issues are reviewed in advance by the Ethics Committee concerned.

Principle 9 Existing samples

1. Existing samples that were provided prior to the taking effect of the present Fundamental Principles, and for which informed consent was not obtained at the time of provision, may be

used only after consent is obtained.

2. Existing samples that were provided prior to the taking effect of the present Fundamental Principles, and for which informed consent was obtained at the time of provision, may be used only within the scope of the said consent.
3. Notwithstanding the preceding two paragraphs, if the research to be undertaken requires the use of an existing sample for which informed consent was not obtained at the time of provision, or if the research to be undertaken is beyond the scope of the consent obtained, the said sample should not be used prior to the proposed research undergoing a review by the Ethics Committee. The Ethics Committee should determine the conditions for the use of existing samples, including requirements for re-obtaining informed consent, taking the following points into consideration: the anonymity of the sample, the possibility of linking the sample to its donor, the nature of the sample, the research plan and details of the said research, the potential impact on the participant, et cetera, and measures for the protection of personal information.
4. In the case of existing samples, personal information, including genetic information, should be kept strictly confidential and rigorously protected. Researchers and research institutions should establish a system for the control of personal information.
5. Existing samples that are entrusted to organizations specialized for storage, such as human material banks, or that are already on the market, may be dealt with in the same manner as for general samples for scientific research.

Principle 10 Withdrawal of informed consent

1. The consent for a donated sample to be used for research may be withdrawn providing that the said sample can be linked to its participant.
2. A participant should not be disadvantaged even if s/he withdraws his/her informed consent.

Section 2 Genetic information of participants

Principle 11 The protection and control of genetic information and establishment of a control system

1. The genetic information of participants should be kept in strict confidence and under full protection.
2. Researchers and research institutions should keep in strict confidence and control the personal information of the participants, identifying the information with which the participant can be linked to the research sample, and the genetic information of the individuals that is obtained as a result of the research. They should also protect the said information with the utmost caution. To this end, research institutions should establish and consolidate systems and procedures required to control and protect genetic information along with other personal information and

identifying information.

3. All research institutions should make the importance of protecting the personal information in research on the human genome common knowledge to all researchers and personnel involved in the research. The significance of personal information and the necessity for its protection should be thoroughly understood by all.

Principle 12 Leakage of personal information

1. Any research organization and any researcher should take necessary measures in order to prevent the leakage of the personal information.
2. When a leak of the personal information is discovered, firm steps should be taken, including a disadvantageous demotion, against the very persons who divulged the information, the researchers undertaking the study in question, the managers of the personal information, the supervisor of the research organization and the people who are concerned with the information divulged.
3. A person who has suffered a leakage of his/her personal information or who has sustained damages from that leakage has legal rights to receive compensation or indemnity.

Principle 13 Right to be informed

A participant has the right to be informed of his/her genetic information resulting from the research.

Principle 14 Right not to be informed

A participant has the right not to be informed of his/her genetic information resulting from the research. The findings of the research may not be made known to the participant against his/her will.

Principle 15 Disclosure of information to blood relatives

1. In principle, blood relatives or families of participants may be informed of the genetic information of the participant only when a participant gives his/her own permission. Personal information pertaining to a participant may not be disclosed to his/her blood relatives or family against his/her will.
2. Notwithstanding the principle described in the preceding paragraph, if the genetic information obtained from the research leads to the conclusion that a portion of the genetic characteristics of the participant is or may be connected to the aetiology of a disease, this conclusion may be disclosed to his/her blood relatives following authorization by the Ethics Committee, and only if preventive measures or treatment have already been established for the disease in question.

Principle 16 Prohibition of discrimination

The genetic information of a participant forms the basis of his/her diversity as a member of humanity. The participant should not be subjected to any discrimination on account of any genetic characteristic in his/her genetic information that is obtained from the research.

Section 3 Other rights and interests

Principle 17 Gratuitousness and related principles

1. All research samples should be provided gratuitously.
2. In the event that an outcome obtained as a consequence of a research project becomes the subject of intellectual property rights or other rights, these property rights are not attributed to the participant.

Principle 18 Reparation for damages

A participant has the right to receive compensation or indemnity if s/he incurs damages during the course of any research on the human genome that involves the use of a sample provided by that participant, or in relation to that research.

Principle 19 Social and psychological support

On providing a research sample, or on knowing or being informed of the results of the research, a participant, and his/her blood relatives and family, must have access to all pertinent social and psychological support, including genetic counselling.

Chapter 3 Fundamental requisites of research on the human genome

Principle 20 Human dignity and freedom of research

1. Research that violates human dignity should not be undertaken.
2. Freedom of scientific research should be respected.
3. Research on the human genome and its applications should be conducted with full respect for human dignity and human rights.

Principle 21 Requisites of research and establishment of research plans

1. Research on the human genome should be designed so that useful and beneficial outcomes can be expected in the fields of biology, genetics and medicine.
2. Research on the human genome should be conducted on the basis of a clear and detailed plan of research.
3. Information regarding DNA sequence data should be released into the public domain.

Principle 22 Establishment and observance of protocols for conducting research

Research on the human genome is diverse depending on the objectives and subjects of each project. Adequate research protocols regarding the specific conditions detailed in the research plan should be established while respecting the present “*Fundamental Principles of Research on the Human Genome*.” All researchers and personnel involved in the implementation of the research should observe the said protocol.

Principle 23 Ethics Committee

1. On undertaking any research on the human genome, its research plan should undergo prior review by an independent, multidisciplinary and pluralist Ethics Committee.
2. The Ethics Committee should examine a submitted research plan on the human genome from ethical, legal and social points of view, in addition to its scientific merit, and comprehensively evaluate whether the implementation of the project should be approved or not.
3. The Ethics Committee should guarantee its transparency in its organization and reviewing deliberations.

Chapter 4 Relationship with society

Principle 24 Understanding and support by society and accountability

1. Research on the human genome makes a significant contribution to the life and health of humanity and of each individual, and to the welfare of society.
2. Public support for the advancement of research on the human genome, with recognition of the role played by the said research in society now and in the future, is desirable. This support should be underpinned by a sound understanding of the present “*Fundamental Principles of Research on the Human Genome*” (especially the significance of the human genome outlined in Principles 1 to 3).
3. All people involved in research on the human genome have a general accountability to society on all aspects of the research in order to improve the understanding and recognition of the public as described above.

Principle 25 Public disclosure of outcomes of the research and return of benefits to society

1. All beneficial outcomes in the fields of biology, genetics and medicine obtained from research on the human genome should be returned to society. In principle, they should be disclosed to the public.
2. All outcomes of research on the human genome should be employed for the development of science, the elimination of human suffering, the prevention and cure of diseases, and the improvement of health.

Principle 26 Appropriate measures

Appropriate measures should be taken so that research on the human genome can be adequately and effectively promoted in accordance with the “*Fundamental Principles of Research on the Human Genome*.” In addition, general, adequate and prompt decisions and countermeasures should be taken regarding the various ethical, legal and social issues that may arise from research on the human genome and its outcomes.

Principle 27 Dissemination of education and provision of information

Bearing in mind that research on the human genome will have a serious impact on life, living and the future of humanity and of each individual, education on the human genome and its research, including bioethics, should be widely promoted. Endeavours should be made to spread information concerning research on the human genome and its applications.

Supplementary provision

These “*Fundamental Principles of Research on the Human Genome*” should be revised as appropriate in the light of the future progress of research on the human genome and the understanding of such research by the public and social trends in this regard.

Explanatory Notes

Introduction

1. The aims of the explanatory notes

These explanatory notes were written to help better understanding of the “Fundamental Principles of Research on the Human Genome” (hereafter the Fundamental Principles) and their appropriate application in the scene of actual research.

Research on the human genome is conducted in order to comprehend systematically how human beings are organized according to the human genome, the blueprint of human life, and also includes the explication of the aetiology of disease in its objectives. To begin with, most of the research dealt with the decoding of the entire DNA sequences of the human genome and was defined as a novel bioscience based on the elucidation of the complete structure of the genome and the genetic information it contains. Now the decoding of the entire human genome is near completion, the research is mainly directed at the determination of responsible elements in the genome for various diseases and the understanding of their aetiology, both by functional analysis of the genome and genomic products (such as RNA, proteins) and by studying the plurality of the genomic structure at an individual level.

The present Fundamental Principles are written as a “constitution” for research on the human genome. These Fundamental Principles serve as the ethical norms that each researcher, medical practitioner, or other personnel concerned with the research should observe on the implementation of research on the human genome, and are, at the same time, the basic concepts that all participants who provide samples for the research, and their blood relatives and families, and also the general public, should be aware of. In order to embody these ideas better and to facilitate actual understanding and application of the Principles, the present explanatory notes describe the background and objective of each Principle, possibilities of acceptable exceptions notwithstanding the Principles, and other subjects expected to help in the understanding of each Principle.

2. The scope of subjects of the Fundamental Principles

As described above, the present Fundamental Principles deal with a field of research that promotes knowledge about the human genome, and are aimed specifically at what is termed “research on the human genome.” Therefore, clinical or industrial applications of the outcomes of such research on the human genome for diagnoses and treatments are not the direct subjects

of these Principles, and each should be controlled by its own appropriate guidelines. However, the Fundamental Principles described here are for consultation and use in a wide variety of situations, since they represent the basic principles for research in biosciences in general.

3. The “Basic Ideas”

In the section titled “Basic Ideas,” the background and reasoning behind the Fundamental Principles are described. In particular, the second half appeals for research on the human genome to be executed in an appropriate manner, with due consideration given to the reduction of any negative impacts that genetic information could elicit concerning various ethical, legal and social issues, while fostering its positive aspects, reflected, for example, in its considerable contribution to the health and welfare of humanity.

* In the present Explanatory Notes, “human” refers to a biological classification, “humanity” reflects humankind in the general sense, and “human being” is used when an individual or a group of individuals is considered.

Chapter 1 The human genome, and research on the human genome

In this chapter, the significance and social status of the human genome and the concepts of research on the human genome are described.

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| <i>Principle 1</i> <i>The significance of the human genome</i> |
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| <ol style="list-style-type: none">1. <i>The human genome is the heritage of humanity.</i>2. <i>The human genome is the blueprint of human life. It provides all members of humanity with a biological basis as a human being and it also underlies the uniqueness and diversity of each human being.</i> |
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The first two points made under Principle 1 describe the significance of the human genome. The word “heritage” in the first point is used in a similar sense to that implied in the phrase “world heritage,” symbolically indicating that the human genome is “an important entity, which human beings inherit from generation to generation,” and that this justifies each human being’s place as a member of humanity. However, this should not imply a proprietary right through which humanity jointly possesses the human genome as “a material, i.e. a property.” Thus, research and the applications that neglect the biological basis of humanity should never be permitted. As each individual has his/her own genome, humanity as a whole has the human genome. In this sense, donation of research samples from a variety of individuals for research on individual genomes and the human genome is extremely important. No one,

however, should be forced to donate a research sample on the pretext that his/her genome, being a part of the human genome, is the common property of humanity. The genome of an individual belongs to him/herself, and his/her consent is necessary when providing a research sample. This is the reason that the word “property” was avoided. The expression used here, the “heritage of humanity,” is also employed in “*Universal Declaration on the Human Genome and Human Rights*” of UNESCO (the United Nations Educational, Scientific and Cultural Organization), and at the ELSI (Ethical, Legal and Social Issues) Committee of HUGO (the Human Genome Organisation, an organization of scientists participating in the Human Genome Project).

The “blueprint of life” indicates that the organizations of humanity are built according to the genetic information involved in the human genome. Each individual has his/her own genome, his/her own original blueprint, hence s/he is a unique existence, different from any other individual, diverse in his/her own ways.

3. *The existence of a human being is not determined only by his/her genome.*
4. *Conveying the fundamental information of human life from parents to children, from children to grandchildren, et cetera, the human genome builds the fundamental structures and functions of an individual as a human being. At the same time, however, the human genome is acted on by various influences in the natural and social environment.*

The third point aims at eradicating the theory known as genetic determinism, which states that the figure, form, personality, life and death of an individual are entirely determined by his/her genome. The human genome is the basic blueprint of humanity in biological terms, but it differs from one person to another, as described in Principle 2, and represents the individuality and diversity of each person. At the same time, genes are acted on differently by the influence of the environment, as described in the fourth point, and a human being is never defined solely by his/her genome. An accurate understanding by the general public about the human genome is appealed for in this fourth point and also in Principle 2.

Principle 2 ***Diversity of the human genome and the dignity and human rights of individuals***
The human genome differs from one individual to another. The diversity of genetic characteristics signifies the originality and uniqueness of each individual and the plurality of humanity as a whole. Thus, it is imperative that, regardless of their genetic characteristics, all individuals or groups of individuals are respected for their dignity and human rights, and that they are equal to one another and are not subjected to any form of discrimination.

Continued from Principle 1, it is emphasized that the genetic characteristics of a person reflect nothing but his/her biological features, and that these characteristics indicate the individuality of each

human being; there is no superiority or inferiority implied. The public should fully understand this point and respect the human dignity and human rights of any individual or group of individuals. All human beings are equal to one another, and any discrimination according to their genetic characteristics is prohibited.

The “dignity” can be attributed both to individuals and to humanity as a whole, separating them from, for example, other animals. The “human rights” of this Principle refer comprehensively to what are called “fundamental human rights,” including those of individuals. Here, prohibition of discrimination is included as one of the general principles.

Respect for genetic characteristics, however, does not imply a denial of medical treatments of diseases with genetic predisposition, and especially not genetic treatments. Although the equality of the value of genetic characteristics should be recognized in general, medical care aims at mitigating any physical or mental disadvantages, or burdens that cause inconvenience, in leading an ordinary social existence. Therefore it is reasonable to study the genome and make use of its outcomes for medical treatments.

Principle 3 *Due consideration of ethical, legal, and social issues*

It is considered that since research on the human genome and the applications of its outcomes have the potential to significantly change the way in which human beings think about human life and living, it may have an extremely serious impact on society. Therefore, due consideration should be given to ethical, legal and social issues in research and its applications.

Concerning the human genome, it should be borne in mind that not only the research itself but also its applications can have an impact on society. The present Fundamental Principles are the ethical norms concerning the research, but also suggest that consideration should be taken of the social impact of the applications. On account of this, all people and organizations concerned, including those of private parties, should thoroughly respect the subjects of these Fundamental Principles.

Principle 4 *Participants, and their families and blood relatives*

Research on the human genome inevitably requires research samples that are provided by human subjects. Therefore, this type of research can be conducted only with a high regard for the dignity and human rights of the persons providing research samples (hereafter, “participants”), and their families and blood relatives.

It is because the research samples are donated from individuals who cooperate with the research, and because the genetic information of those individuals is analysed with the use of the research samples, that particular considerations should be made on ethical, legal and social issues concerning

research on the human genome. In this sense, the protection of the participants is specially stipulated in this Principle, in addition to the protection of the general public as described in Principle 3.

The said participants include not only patients but also healthy volunteers when that is required for the research. A person could be deemed to be one of the said “family” in view of his/her domestic status relative to the participant, e.g. cohabitation, without regard for his/her marital status.

Chapter 2 Rights of participants

In this chapter, the status of participants who contribute to research on the human genome and donate samples that are indispensable for the research is defined. The participants who provide genetic information that is directly analysed deserve the most careful consideration when discussing the ethical, legal and social issues relating to research on the human genome.

Section 1 Informed consent

In this section, “informed consent” is defined as an expression of the self-discretion that is fundamental to the protection of the human rights of the participants.

| <i>Principle 5</i> | <i>Basic Conditions</i> |
|---------------------------|---|
| 1. | <i>A research sample may be collected from an individual subject for research on the human genome only after the participant has first been given a sufficient explanation of the research, and has then given, of his/her own free will, his/her consent (informed consent).</i> |
| 2. | <i>The consent should be expressed in writing.</i> |
| 3. | <i>An individual who is requested to provide a research sample but does not consent to that request should not be disadvantaged as a result of his/her refusal.</i> |

Here, the general principles of informed consent are defined. The basis of informed consent is that an explanation should be given to each person who is going to provide a research sample so that s/he can fully understand the research, and to obtain the consent in writing of that person’s own free will. Actual procedures and formality of the consent should follow the present Fundamental Principles and guidelines set separately.

The person who explains the proposed research to the participant, for the purpose of obtaining their informed consent, should be careful that the participant fully understands the experiments in which his/her sample will be used, and the significance of the act of providing the material. On this occasion, objectives, methods and potential outcomes of the research, and also any disadvantages and losses that the participant might incur, should be explained in a clear and understandable way using written explanations, slides, video tapes, and any other medium that may be appropriate. It should be taken into account that participants do not always have a good knowledge of research on the human genome. For

this reason, explanations should be given in several steps, each time confirming that the participant has understood up to that point. An explanation using written material, for example, is desirable because it can give the participants as much time as they need before they make a decision to consent, and can indicate particular points for reflection. Explanations given to a group of participants in a seminar are only allowed as a supplement to the individual explanation given to each participant, if it is thought that this will facilitate his/her understanding. Unless there is a particular need, such group explanations should remain auxiliary to the formal procedure for obtaining informed consent from individuals.

Including such protocols as are described in Principles 7 and 8, the protocols and methods for obtaining participants' informed consent should be described in research plans. On the basis of the submitted research plans, the Ethics Committee will judge whether the protocols and methods are appropriate. The consent should be given in writing and a suitable record kept. However, if a participant has difficulty or is unable to consent in writing for a particular reason, such as difficulty in writing or motor functions, appropriate alternative methods, e.g. audio-visual recording, should be prepared. Alternative methods should be chosen in place of written consent only if there is such an impediment for the participant, and not for the sake of convenience for the researchers.

When a discrepancy is found between the contents of the explanations and the details of the research plans or the actual implementation of the research, it is deemed that effective consent has not been obtained.

Principle 6 ***Individuals who do not have the capacity to consent***

In the event that research on the human genome is to be conducted using samples from participants including an individual who does not have the capacity to consent, it should be demonstrated in advance that the research in question requires a research sample from that particular individual, and his/her informed consent should be obtained from his/her representative.

If participants for research include an individual who is incapable of giving his/her informed consent, it should be demonstrated that the research requires the sample from that particular individual. An individual incapable of giving his/her own consent should not be involved whenever the research could be conducted equally well without the participation of that individual. The study in question should, preferentially, be beneficial for the said individual, or at the least not give rise to any loss or disadvantage to him/her.

It is desirable that the definition of "individuals who do not have the capacity to consent" should be universally stipulated by law or national guideline. Whether or not an individual has the capacity to consent should be judged as scientifically and objectively as is possible. Thus, a medical practitioner who is unconnected with the research in question should make the actual decisions from a third-party standpoint.

The person who serves as a representative and gives his/her informed consent in place of that of a participant who is unable to give his/her own consent should be selected as the law provides: that is, being in parental authority when the participant is a minor, and otherwise being the legal guardian of the participant. In such a case when there is no pertinent person as provided by law, an adequate representative should be appointed, taking into consideration the human rights and the highest interests of the participant. The procedures to select the representative should be clearly described in research plans and undergo the review of the Ethics Committee. When giving consent on behalf of the participant, the representative should take sufficient precautions that the rights and interests of the participant are protected and would never be infringed.

In a case when the participant is a minor above a certain age, it is desirable that consent also be obtained from the participant him/herself.

Principle 7 Diversity of research

1. *In the procedure for obtaining informed consent, the information and explanation about the research should be presented using the most appropriate method given the objectives and particulars of the research, in view of the fact that research on the human genome, and especially the identification of the genetic information of individuals, is associated with a high risk of ethical, legal and social issues.*
2. *In all research projects, the procedures used to obtain informed consent should be clearly described in the research plan and undergo prior review by the Ethics Committee.*

As described in the “Basic Ideas,” research on the human genome and its outcomes may give rise to ethical, legal or social issues. In particular, the fact that the genetic information of a participant him/herself is determined may bring up various issues for the participant him/herself, his/her family or his/her blood relatives. Before informed consent is obtained, it is important to inform participants sufficiently and make certain that they understand all aspects of the research and the potential ethical, legal and social issues that may arise from it, including the points described above. Research on the human genome, however, consists of various studies with different objectives, subjects and methods. The standardization of protocols employed by different studies, including that of obtaining informed consent, would likely be impossible, or at the least be a hindrance to the research. It is required that certain protocols be set concerning the undertaking of research on the human genome so that the most rational and effective methods of research can be employed. The basis of informed consent is, as described in Principle 5, to allow the participant to exercise their self-discretion in the form of their consent, having first been adequately informed; therefore it is prerequisite to ensure the thorough understanding of the participant him/herself. On the condition that this prerequisite is met, different procedures for obtaining informed consent and experimental methods may be employed in each study on the human genome.

When it is difficult to give full explanations to each participant, for instance in cases of genome analyses involving large groups of participants, expedients should be designed by which each participant can sufficiently understand the objectives and particulars of the research, for example through holding a seminar. Within the guidelines set here for obtaining informed consent, simplification of the protocol for giving an explanation is permitted, when appropriate, either if the scope of the consent is not limited to a particular genome analysis project but extended to other genome analysis projects or to other related medical research (termed “comprehensive consent”), or if the provided research sample is made anonymous so that it is not possible to link the donor with his/her personal information (refer to points 1 and 2 of Principle 8).

In some research projects the associated medical benefits are not expected to emerge until after the research has continued for a relatively long period, during which time the link between each research sample and its donor must be maintained. Examples of this are large-scale epidemiological projects that deal with large groups of subjects and require follow-up surveys. Although explanations should, in principle, be given individually to participants prior to obtaining their consent, explanations of a collective nature, such as seminars, are also allowed, on the condition that the personal information of each participant is strictly managed and protected, taking into account the benefits expected from the outcome of the research both for the participants and for society, and in view of the possibility that the formal procedures for obtaining informed consent, such as informing participants individually, may bring about excessive burdens in the execution of the research. When such a form of explanation is planned in research that will use samples not anonymous of their donors, this should be clearly described in the research plan and undergo the review of the Ethics Committee. The Committee should judge whether or not the form of explanation in the submitted research plan is appropriate, taking the following points into account: the significance of the consent obtained from the participants; the medical and scientific importance of the research in question; and the appropriateness of the management and protection of the personal information of participants. Concerning long-term, large-scale research projects involving groups of subjects and using samples that will remain linked with their donors, the Ethics Committee should conduct the review with particular prudence.

Explanations given to groups of participants may also be beneficial for the participants themselves because such an environment can enable them to exchange information among themselves, bringing psychological relief (easiness) to any anxiety that they may feel. Besides that, distribution of detailed written explanations, individual explanations over the phone, and so forth, could be employed as strategies for obtaining informed consent as the occasion demands. Diverse protocols and methods for obtaining informed consent will emerge in the future as the research progresses.

The expedient methods described above, which are not based upon the formal procedures and methods for obtaining informed consent, can be adapted only when the proposed research on the human genome is expected to contribute greatly to the improvement of human health, the elucidation of the

aetiology of disease, and the prevention and treatment of diseases, and when the swift, rational and effective execution of the study itself is beneficial for the researchers, the participants, and society. It should not be done for the convenience of the research or for the curtailment of labour. Such simplification of explanations for the sake of researchers’ convenience impairs the validity of the informed consent. Thus, each study may be undertaken on the condition that the procedures and methods used for obtaining informed consent are clearly described in the research plans and undergo the review of the Ethics Committee. Whenever a participant asks to be informed individually, this should be satisfied from the original standpoint of obtaining informed consent. Even when the information is given using a simplified procedure, the consent should be individually obtained in writing. Simplification of the consent itself is not permitted under any circumstance.

However, there are situations in which the information should be given with the utmost prudence, concerning the basis of informed consent as described in the explanatory notes for Principle 5; for example, if a participant is not him/herself capable of giving consent, as described in Principle 6, or if a patient is suffering from a severe disease without knowing the difficulty of the treatment.

Regardless of the procedure used, the confidentiality of the personal genetic information should be carefully protected. Without this guarantee, the research plan should not be approved and the research should not be undertaken.

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| <p>Principle 8 <i>Comprehensive consent, and unlinked and unidentified research samples</i></p> <p>1. <i>(a) If a participant consents to provide a research sample for genome analysis in a particular research project and, at the same time, anticipates and consents to the use of the same sample in other genome analyses or related medical research, then the research sample may be used for the latter “studies aimed at other purposes.”</i></p> <p> <i>(b) In this case, sufficient information, which clearly outlines the anticipated objectives of the research at that point in time, should be given to the participant so that s/he can thoroughly understand the significance and consequences of the fact that the sample provided will be used in “studies aimed at other purposes,” as defined in the preceding sub-paragraph.</i></p> <p> <i>(c) In the cases described in the preceding two sub-paragraphs, protocols pertaining to the management and protection, including anonymity, of genetic and other personal information of the participant should be explained in detail, and strict confidentiality should be guaranteed.</i></p> |
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This principle defines exceptional cases of protocols concerning informed consent. Although this could be included in Principle 7, it is considered to be worth a separate mention.

Here, conditions of the “comprehensive consent” described in the explanatory notes for the previous principle are defined. In principle, a participant consents to provide a research sample for a

particular genome analysis within a particular research project. However, in view of the preciousness of provided samples, they may be used in other genome analyses or related medical research, on the condition that the participant anticipates and consents also to this further use of the sample. In this case, the personal information of the participant should be kept in the strictest confidence not only during the execution of the initial study, but also while the sample is stored in anticipation of other studies, and when it is used in studies aimed at other purposes.

Comprehensive consent should not be solicited simply for the sake of convenience or saving of labour. In accordance with the general principle of obtaining informed consent, detailed information should be given about other genome analyses and related medical research that are anticipated at that time, regardless of whether any of them are actually undertaken later. The studies aimed at other purposes described in this Principle are confined to genome analyses or related medical research. In order to use the sample for any other purpose besides those already stated, the formal procedures of informed consent should be followed.

In any case, a research project requiring comprehensive consent should not be approved by the Ethics Committee, as in the case of Principle 7, unless the confidentiality of the personal information of the participant (including genetic information and identifying information) is guaranteed.

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| <p>2. <i>If it is expected that the sample provided will be handled anonymously, the method of explanation used in the procedure of obtaining informed consent may be appropriately simplified on the condition that it is guaranteed that the sample can not be linked to the donor.</i></p> |
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This second point defines the simplification of explanations in the case of unlinked and unidentified research samples.

If a research sample is completely disconnected from the name of its donor, its donor has been made unidentifiable immediately on their provision of it, and it has been managed thereafter so that it cannot be traced back to its donor (i.e. it is an unlinked and unidentified research sample), then the sample is completely detached from the donor in all stages of the execution of the research, and in the presentation and publication of its results. The research sample was once a physical part of the donor, but there is no longer any link between the individual and the sample and personal genetic information produced from the genome analysis. In this case, disclosure of the genetic information due to the research would not disadvantage the participant because the information, although it would still pertain only to that participant, could not be connected to him/her. The simplification of the protocols that have been outlined in the current Fundamental Principles for giving explanations may be acceptable in research using unlinked and unidentified samples, following an assessment of the importance of the research from a medical point of view and the possibility that the participants may be disadvantaged due to their not having been informed in accordance with the formal procedures. The basis of informed consent is that the

participant fully understands the objectives, details and significance of the study concerned, and expresses his/her free will to cooperate with the research, thus the procedures and methods for giving explanations can be simplified on the condition that the aforementioned points are observed.

For instance, in a genome analysis project involving a group of subjects and using unlinked and unidentified samples, the adherence to the use of individual explanations prior to obtaining consent may impose excessive burdens on the researchers compared to the potential benefits of the outcome of the research. In such cases, individual explanations may be replaced by alternative forms of explanation, such as seminars, distribution of detailed written information, or presentation of audio-visual material. Whenever a participant makes a request to be informed individually, this should be satisfied in accordance with the principle of informed consent.

Nevertheless, the actual consent itself should not, under any circumstance, be simplified, but always be carried out on an individual basis and in writing.

3. *In the cases described in the preceding two paragraphs, the comprehensive consent and the simplified method of explanation can be used only when the source of the research sample to be used, and the actual protocols and method used in the procedure of obtaining informed consent are described in the research plan and when these issues are reviewed in advance by the Ethics Committee concerned.*

The aforementioned simplification of explanations, whether in the case of obtaining comprehensive consent, or of unlinked and unidentified samples, is exception to the principle of informed consent and can be put into practice only after the Ethics Committee has judged whether the research fulfils the necessary and sufficient conditions of the procedures for obtaining informed consent.

Principle 9

Existing samples

1. *Existing samples that were provided prior to the taking effect of the present Fundamental Principles, and for which informed consent was not obtained at the time of provision, may be used only after consent is obtained.*
2. *Existing samples that were provided prior to the taking effect of the present Fundamental Principles, and for which informed consent was obtained at the time of provision, may be used only within the scope of the said consent.*
3. *Notwithstanding the preceding two paragraphs, if the research to be undertaken requires the use of an existing sample for which informed consent was not obtained at the time of provision, or if the research to be undertaken is beyond the scope of the consent obtained, the said sample should not be used prior to the proposed research undergoing a review by the Ethics Committee. The Ethics Committee should determine the conditions for the use of existing*

samples, including requirements for re-obtaining informed consent, taking the following points into consideration: the anonymity of the sample, the possibility of linking the sample to its donor, the nature of the sample, the research plan and details of the said research, the potential impact on the participant, et cetera, and measures for the protection of personal information.

4. *In the case of existing samples, personal information, including genetic information, should be kept strictly confidential and rigorously protected. Researchers and research institutions should establish a system for the control of personal information.*
5. *Existing samples that are entrusted to organizations specialized for storage, such as human material banks, or that are already on the market, may be dealt with in the same manner as for general samples for scientific research.*

Careful consideration is required for samples that were provided prior to the taking-effect of the present Fundamental Principles (hereafter, “existing samples”), and Principle 9 describes the basic ideas concerning these. The existing samples were provided before the concepts of bioethics and informed consent were sufficiently understood by either researchers or the general public, and the conditions of information and consent might not meet the current, new criteria. Therefore, by the strictest interpretation, they should not be used but be destroyed immediately. However, the existing samples are precious as research samples, and appropriate use of the samples can be expected to contribute to the improvement of human health or eradication of diseases. Thus, if a research project using such a sample is deemed vital, and the research does not cause any disadvantage to the donor of that sample, it is suggested that the inadequate consent obtained at the time of provision can be compensated for by clarifying the above points in the research plan, which should then undergo review by the Ethics Committee.

In relation to the inadequacy of the informed consent obtained for the use of existing samples, such samples should not be used simply for the sake of convenience or saving of labour, as described in the explanatory notes for Principle 7.

As stated in Principle 7, the confidentiality of personal information, including genetic information, should be protected rigorously. Unless this can be guaranteed, the research plan in question should not be approved, the implementation of the research should not be permitted, and the existing samples should be destroyed.

Among existing samples, such as tissues, cells, body fluids, and excretions, and the DNA extracted from them, which have already generated good scientific results, have established their scientific values, are generally and widely used, and are generally available, certain samples have definite and proper sources, are stored in cell and tissue banks or on the market, and are equally available for all researchers. In research using such a sample, this sample may be dealt with in the same manner as for

general samples in scientific research, and it is unnecessary to trace it back to its donor to obtain their consent because the sample, in view of its nature, is not likely to violate the human dignity or human rights of its donor.

Principle 10 ***Withdrawal of informed consent***

1. *The consent for a donated sample to be used for research may be withdrawn providing that the said sample can be linked to its participant.*
2. *A participant should not be disadvantaged even if s/he withdraws his/her informed consent.*

In principle, consent can be withdrawn on the condition that the sample can still be attributed to its donor. The consent cannot be withdrawn once the sample has become unidentifiable, it is no longer linked to its donor, or it is stored in such a way that the linking is impossible. This information about the right to withdrawal of consent, and its limits, should be given in advance of obtaining the donor's informed consent. Samples that are stored in banks or are commercially available cannot become the subjects of withdrawal of consent.

Care should be taken that a participant would not be disadvantaged by the withdrawal of his/her informed consent.

When the consent to use a sample is withdrawn, the sample itself and the results derived exclusively from it should be destroyed.

Section 2 **Genetic information of participants**

Principle 11 ***The protection and control of genetic information and establishment of a control system***

1. *The genetic information of participants should be kept in strict confidence and under full protection.*
2. *Researchers and research institutions should keep in strict confidence and control the personal information of the participants, identifying the information with which the participant can be linked to the research sample, and the genetic information of the individuals that is obtained as a result of the research. They should also protect the said information with the utmost caution. To this end, research institutions should establish and consolidate systems and procedures required to control and protect genetic information along with other personal information and identifying information.*
3. *All research institutions should make the importance of protecting the personal information in research on the human genome common knowledge to all researchers and personnel involved in the research. The significance of personal information and the necessity for its protection*

should be thoroughly understood by all.

The conditions concerning the control system set in research institutions for the safekeeping and protection of the personal information related to provided samples, the identifying information and the genetic information of individuals, and those conditions concerning the transfer of the samples should be determined in the “guidelines” concerned with the application and enforcement of the present Fundamental Principles.

When each research institution considers its system for safekeeping and protection of personal information, it should take the following factors into account, in addition to conforming to prescriptions of law and ordinances:

- (1) the separation of personal information, including genetic information, of individuals and identifying information with which the donor can be linked to the research sample;
- (2) the appointment of custodians of the personal information, who will protect identifying information and personal information, and manage the separation and connection of the different categories of information;
- (3) the establishment of protocols and systems to manage personal information rigorously under the direction of the custodians;
- (4) the provision for a researcher to gain access to identifying information through the custodians of the personal information when that researcher needs to identify a sample under study and its donor;
- (5) the establishment of penal codes regarding the leakage of personal information, and the preparation of a system for compensation and indemnity for damages incurred resulting therefrom.

Rigorous management and protection of personal information are not achieved solely by enforcing the protocols and systems. The personal information can be totally secure only when every researcher and personnel related to the research fully understands and realizes the significance of protecting that personal information. Improving the awareness of those people concerned is vital. One countermeasure relating to the aforementioned issue (3) is, for example, to manage personal information with a computer isolated from any other computers, and to store the information rigorously in a data bank using external memory media.

If a research institution was to offer a sample that can be linked to a particular individual to another institution, whether domestic or foreign, the recipient institution should also have its own established system for custody and protection of personal information. The sample should not be offered to any institution whose system is inadequate.

Personal information could be disclosed within a limit provided for by law, for example, in the case of a criminal investigation.

Principle 12 **Leakage of personal information**

1. *Any research organization and any researcher should take necessary measures in order to prevent the leakage of the personal information.*
2. *When a leak of the personal information is discovered, firm steps should be taken, including a disadvantageous demotion, against the very persons who divulged the information, the researchers undertaking the study in question, the managers of the personal information, the supervisor of the research organization and the people who are concerned with the information divulged.*
3. *A person who has suffered a leakage of his/her personal information or who has sustained damages from that leakage has legal rights to receive compensation or indemnity.*

This Principle forms a counterpart to Principle 11. Concerning research on the human genome, the protection of personal information and prevention of its leakage are paramount, having priority over the acquisition of informed consent. Since the genetic information of an individual obtained from research on the human genome may contain information that indicates the individuality of that person, its leakage may result in violation of his/her human rights. In this regard, research institutions should establish measures to prevent the leakage of personal information, and, if a leakage occurs, they should observe their duty and take immediate and firm countermeasures.

A person, who is damaged by the leakage of his/her personal information, is entitled to receive appropriate compensation or indemnity. It should be noted that, in this case, the leakage alone could lead to the violation of human rights since, even if it does not bring about any actual damage, the leakage itself can be considered as damage.

If those persons responsible for the leakage can not prepare adequate compensation or indemnity, the research institution should offer compensation or indemnity. In view of the violation of human rights due to the leakage, some form of social relief measures should be prepared.

Principle 13 **Right to be informed**

A participant has the right to be informed of his/her genetic information resulting from the research.

This Principle presents the concept that the genetic information of an individual belongs to one but the individual him/herself and that each individual has right to know about his/her own genetic

information. Participants should have explained to them both their right to be informed and their right not to be informed at the time of obtaining their informed consent.

A participant has the right to know about his/her genetic information revealed during the course of the research, whether or not s/he is able to understand it, and whether or not it is useful to him/her. A participant has no right to the genetic information stemming from a sample s/he has provided, when that sample has become unlinked during the course of the research and is no longer attributable to the donor, and this should also be explained to the participant prior to obtaining their informed consent.

Genetic information obtained from research will not always lead directly to diagnoses. Even if a participant exercises his/her right to be informed, this will not always mean that the participant can obtain practically useful information. It is desirable that the researchers or medical practitioners fully explain to participants the meaning and usefulness of the genetic information obtained from the research, and the differences between research and diagnosis, and that they urge participants to understand and judge for themselves, before exercising their right to be informed, how genetic information arising as a primary result of research differs from any diagnosis coming from the interpretation of that information.

In the case of large-scale research projects, the genetic information of a single participant is not sufficient by itself to confer accuracy or reliability on a diagnosis, and it is not worth informing the participant of that diagnosis because, although it may be traceable to that participant, the personal information is stored in an unlinked condition, and so selecting his/her information from the entire group's data will greatly increase the burdens on the researchers. New forms of research may arise in which the right of participants to be informed cannot be easily exercised, nor would it be meaningful to do so. The actual implementation of the right to be informed in such a case should be determined in the guidelines concerned with the application and enforcement of the present Fundamental Principles.

As mentioned above, evaluation of the significance of each result of the research belongs in the domain of clinical diagnosis and is beyond the limit of the present Fundamental Principles. Guidelines should be drawn up separately for genetic diagnosis.

Principle 14 Right not to be informed

A participant has the right not to be informed of his/her genetic information resulting from the research. The findings of the research may not be made known to the participant against his/her will.

In relation to the right to be informed described in Principle 13, a participant also has the right not to be informed of the results of the research when s/he does not wish to know them. Researchers should explain to participants their right not to be informed, as well as their right to be informed, prior to obtaining their informed consent.

However, when the genetic information obtained from the research indicates that a portion of the genetic characteristics of the participant is or may be connected to the aetiology of a disease or to the

susceptibility to a drug, in other words, when the participant has already contracted a disease with a genetic predisposition, or carries such predisposition, it may be desirable that the participant be informed about the genetic information and its implications for his/her own benefit, if preventive measures or treatment for the disease, or the prediction of harmful side-effects, have already been established. If such a possibility is anticipated from the objectives or particulars of the research, the researchers should explain, at the time of obtaining informed consent, all such factors relating to the research in question, as follows: the significance of results obtained from the genome analysis; the possibility that genes that are not initially targeted may be found and analysed; the possibility that the diagnostic significance may alter according to the progress of the research, the implications of diseases with a genetic predisposition, and susceptibility to the harmful side-effects of drugs; the possibilities of the prevention, diagnosis and treatment of such diseases or susceptibilities; the possibility that his/her blood relatives may contract the same disease; and the availability of social and psychological support, such as genetic counselling. If, moreover, a disease is preventable or treatable at that time, the participant may be urged to understand that knowing his/her genetic information and the disease linked with it will be important for his/her own health. In such a case, the explanation should be given so that the participant can him/herself appreciate the importance of understanding the results of the research for his/her own health, and so make his/her own free choice about whether or not s/he wishes to be informed of the genetic information obtained from the research and the implications of any associated diseases. However, care should be taken that participants do not feel pressured during such explanations.

A participant may be informed of the results of the research and the implications of the related disease only when s/he chooses to be told them as a result of the aforementioned explanations. Moreover, a participant should not be informed of any results of the research whenever s/he expresses, despite all these explanations, that s/he does not wish to know them.

A participant may be given information that was not expected when s/he gave informed consent if a new factor arises that may have a significant effect on the participant's health; for example, when a targeted genetic factor is deemed very important for its diagnostic potential as a consequence of the research, or when a new genetic factor or its implicated functions are discovered, aside from the originally targeted factors, and the former leads to an effective diagnosis. The Ethics Committee should judge whether the result corresponds to the said case and what a kind of procedure should be taken to inform the participant. When the Ethics Committee has approved the explanation and disclosure of such new aspects arising from the research, if the participant, after having had explained to them the general outline of the results involving these new aspects, wishes to be informed further, the genetic information including the new aspects directly related to the participant, and any implications regarding the disease based on it, should be disclosed. Participants should not be informed of any such results of the research should they not wish it.

Research institutions should arrange appropriate social and psychological support, such as genetic counselling, for participants being informed about genetic information obtained from the research, and the implications of related diseases.

The interpretation of the results of research described in the present explanatory notes should be regulated by separate guidelines on genetic diagnosis and treatment, because it may be beyond the limit of the “research” that the present Fundamental Principle deals with but fall within the scope of “diagnosis” or “medical treatment.” The issues and criteria that the Ethics Committee takes into account in order to make a decision on this subject should be stipulated in the “guidelines” on the application and enforcement of the present Fundamental Principles.

If a participant does not have the capacity to give their informed consent, it is desirable that the researchers make every effort to explain the aforementioned information to his/her representative and to obtain consent for the results and their implications to be disclosed to the representative. In this case, the representative should decide whether or not to consent after consideration of the highest interests of the participant s/he represents.

Principle 15 Disclosure of information to blood relatives

1. *In principle, blood relatives or families of participants may be informed of the genetic information of the participant only when a participant gives his/her own permission. Personal information pertaining to a participant may not be disclosed to his/her blood relatives or family against his/her will.*
2. *Notwithstanding the principle described in the preceding paragraph, if the genetic information obtained from the research leads to the conclusion that a portion of the genetic characteristics of the participant is or may be connected to the aetiology of a disease, this conclusion may be disclosed to his/her blood relatives following authorization by the Ethics Committee, and only if preventive measures or treatment have already been established for the disease in question.*

Genetic information is not information pertaining to only a single individual; it has similarities with that of his/her blood relatives. Elucidation of the information of a participant implies that a portion of the genetic information of his/her blood relatives may be inferred. If the participant contracts some genetic disorder, there is a possibility that his/her blood relatives carry the same genetic factor that caused the disorder. This aspect of genetic information should be made clear to participants prior to obtaining their informed consent.

Consequently, when genetic information obtained from research indicates that a portion of the genetic characteristics of the participant is or may be a predisposing factor to a disease or to the susceptibility to a drug, in other words when the participant has already contracted a disease with a genetic predisposition or carries such predisposition, it may be desirable that the blood relatives of

participant be informed of the genetic information and its implications, while respecting the right of the participant not to be informed, if preventive measures or treatment for the disease, or anticipation of harmful side-effects, have been established.

When such a situation is predicted from the objectives or particulars of a study, the researchers should inform the participant, at the time of obtaining their informed consent, of all factors related to the research in question, as follows: the significance of the genome analysis; the possibility that genetic factors that are not initially anticipated may be found and analysed; the possibility that the diagnostic significance of the targeted gene may alter with progress of the research; the implication of diseases with a genetic predisposition, and the prediction of susceptibility to the harmful side-effects of drugs; the possibility of prevention, diagnosis and treatment of such diseases or susceptibilities; the possibility that his/her blood relatives may contract the same disease; and the availability of social and psychological support, such as genetic counselling.

If the participant still declares that s/he does not want his/her genetic information to be disclosed to any other persons other than him/herself, his/her blood relatives should not be informed solely on the judgement of the researchers concerned. In such a case, whether or not to inform blood relatives should be left to the judgement of the Ethics Committee. It is not the entire genetic information of the participant that would be disclosed to a blood relative of the participant, but only those results concerning the genetic disease or drug susceptibility relevant to the blood relative. Since the participant and his/her blood relatives share a portion of their genetic information, there is a conflict between the right of the participant to keep the information private and the right of the blood relatives to know about their own health, and some avenue should be left open to give priority to the latter.

In the situation above, the blood relatives also have both the right to be informed and the right not to be informed, as described in Principle 14. It is required that each blood relative concerned be asked to certify whether s/he consents to being informed of those results concerning the genetic disease or drug susceptibility that is indicated by the genetic information of the participant. Such an inquiry should be made prudently, so that a relative who chooses not to be informed will not become aware the results. After this confirmation of consent, the relevant results should be disclosed only to those relatives who have consented to be informed. They should not be disclosed to any blood relative who has refused his consent.

Since the entire genetic information of a participant is not disclosed when the blood relatives are informed, the latter may undergo genetic examination or analysis of their own genetic information if the situation requires it. Research institutions should be prepared to provide social and psychological support, including genetic counselling, for the blood relatives.

Since the scope for informing blood relatives varies depending on the nature of the genetic disease or drug susceptibility, the Ethics Committee should make a judgement on each individual case.

The conclusions concerning diseases described in the present explanatory notes are to be regulated by separate guidelines on genetic diagnosis and treatment, because they are beyond the limit of the “research” that the present Fundamental Principles are concerned with, but may fall within the scope of “diagnosis” or “medical treatment.” The issues and criteria that the Ethics Committee takes into account in order to make a decision on this subject should be stipulated in the “guidelines” on the application and enforcement of the present Fundamental Principles.

If a participant does not have the capacity to give their informed consent, it is desirable that the researchers make every effort to give the aforementioned information to his/her representative and to obtain consent for the results and their implications to be disclosed to the representative. In this case, the representative should decide whether or not to consent after consideration of the highest interests of the participant s/he represents.

Principle 16 Prohibition of discrimination

The genetic information of a participant forms the basis of his/her diversity as a member of humanity. The participant should not be subjected to any discrimination on account of any genetic characteristic in his/her genetic information that is obtained from the research.

This Principle describes the prohibition of discrimination as the right of participants. Discrimination may take place on various occasions such as employment, application for insurance, marriage, *et cetera*. Concerning employment and application for insurance in particular, discriminatory treatment should be prohibited and eliminated under law and should be regulated in the future by appropriate institutional measures, including the enactment of new laws. In light of the spirit of the present Fundamental Principles, all blood relatives and families of participants should likewise not be subjected to any form of discrimination.

Section 3 Other rights and interests

Principle 17 Gratuitousness and related principles

- 1. All research samples should be provided gratuitously.*
- 2. In the event that an outcome obtained as a consequence of a research project becomes the subject of intellectual property rights or other rights, these property rights are not attributed to the participant.*

The provision of a research sample is an act of a participant in good faith and in voluntary cooperation with the research, and it should be done, in principle, gratuitously. Unnecessary burden, however, should not be placed on participants who cooperate with the research, and it is desirable that the

participants should be refunded for any expense related to that provision, such as for travel or in compensation for time taken off work. The provision of a research sample should not be prompted by unreasonable distribution of benefit, such as bounty, that merely aims at the facilitation of the provision.

Researchers or research institutions can claim intellectual property rights such as patent rights based on the results of their research. A participant who simply provides a research sample cannot claim intellectual property rights relating to the sample, since the value of the subject of those intellectual property rights is brought about by scientific actions of the researchers, or by the ingenuity of those persons who make use of the outcomes of that research, and is not attributable to the provided sample or to the genetic information contained in it. It is desirable that it be made clear to participants, at the time that their informed consent is obtained, that they cannot automatically claim the intellectual property rights.

Protocols concerned with intellectual property rights should conform to existing laws.

Principle 18 Reparation for damages

A participant has the right to receive compensation or indemnity if s/he incurs damages during the course of any research on the human genome that involves the use of a sample provided by that participant, or in relation to that research.

Conditions, protocols, persons responsible, and other subjects concerned with compensation or indemnity are subject to existing law. This includes cases in which a participant incurs damages, discrimination for instance, due to the leakage of the identifiable genetic information of that individual. Concerning damages incurred during the course of research on the human genome, the responsibility of the injured participant to prove causality should be lessened in view of recent trends in judicial precedents.

Principle 19 Social and psychological support

On providing a research sample, or on knowing or being informed of the results of the research, a participant, and his/her blood relatives and family, must have access to all pertinent social and psychological support, including genetic counselling.

Research institutions should take appropriate measures so that participants, and their blood relatives and family, can receive pertinent social and psychological support, including genetic counselling, when providing research samples or being informed of genetic information obtained from research and conclusions (or diagnoses) concerning related diseases. Appropriate countermeasures, as well as genetic counselling, are specially required, as described in Principles 13 to 15, when a participant (or his/her

representative) or his/her blood relatives are informed of conclusions (diagnoses) concerning genetic predisposition to a disease, or the possibility of it, that are derived from the results of the research.

The systems of social and psychological support, and especially that of genetic counselling, currently remain in an unsatisfactory condition and require swift establishment and consolidation. The consolidation of the system itself underlies the understanding of the public on the human genome and the proper and effective implementation of research on the human genome. Therefore research institutions concerned should prepare supportive measures such as genetic counselling. It is desirable that those institutions that have not yet organized internal measures for support, should be prepared to use the facilities of other institutions. Genetic counselling should be granted a firm position as part of the present medical system.

Chapter 3 Fundamental requisites of research on the human genome

In this chapter, the principles that researchers and research institutions should observe are described.

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| <p><i>Principle 20 Human dignity and freedom of research</i></p> <ol style="list-style-type: none"><i>1. Research that violates human dignity should not be undertaken.</i><i>2. Freedom of scientific research should be respected.</i><i>3. Research on the human genome and its applications should be conducted with full respect for human dignity and human rights.</i> |
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As described in the “Basic Ideas,” science is one of the intellectual activities of humanity and underpins the development of human society. It is, however, confined within the sphere of human society, and research that violates “human dignity,” which is a fundamental value of society, should not be accepted under any circumstance.

Common standards should be drawn up, in light of the future progress of research, to judge what research offends against human dignity, and the Ethics Committee concerned is responsible for judging whether to adopt or reject proposed research projects. In the “*Universal Declaration on the Human Genome and Human Rights*” of UNESCO, reproductive cloning of human beings is described as an act that violates human dignity, and germ-line intervention is described as an act that could violate human dignity, and it is proposed that the International Bioethics Committee of UNESCO should make a judgement on other issues.

Freedom of scientific research should be respected since, as a part of the freedom of thought, it is one of the fundamental rights of researchers. Freedom of research is of the utmost importance for the progress of science and is the fundamental prerequisite for scientific enquiry.

However, “freedom of scientific research” is valid only within the social framework of respect for “human dignity and human rights,” and any research, which in its execution neglects or violates human dignity or human rights, does not merit the freedom of research described above as a fundamental human right, and should not be granted support or patronage. The applications of the outcomes of research should also not neglect or violate human dignity or human rights.

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| <p>Principle 21 <i>Requisites of research and establishment of research plans</i></p> <ol style="list-style-type: none">1. <i>Research on the human genome should be designed so that useful and beneficial outcomes can be expected in the fields of biology, genetics and medicine.</i>2. <i>Research on the human genome should be conducted on the basis of a clear and detailed plan of research.</i> |
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Research viewing the human genome as its subject should not be permitted to proceed merely in the interests of science. Even if the research is started from the point of view of pure scientific interest, it should be expected to produce results that contribute to human life, health and welfare, and, to this end, pertinent plans should be made, because in research dealing with the human genome, samples are provided from human subjects and the genetic information of individuals is determined. The results of research should therefore be expected to be useful from the viewpoint of basic life science, even if they do not directly contribute to the prevention or treatment of human disease. It is the Ethics Committee that should judge the usefulness of a proposed study.

Although the outcomes of research on the human genome are expected to make contributions in various fields besides biology, genetics, and medicine, pharmacology for instance, it is not necessary to specify them all. Genetics was referred to in particular because research on the human genome is a part of the field of genetics.

All researchers who plan research on the human genome should prepare research proposals, in which they clearly describe the objectives and methods of their research, their protocols for obtaining research samples, expected results, the procedures for ensuring the protection of personal information, issues mentioned in the present Fundamental Principles and the explanatory notes, and other necessary issues, and submit their proposals to their research institutions. The research proposals should undergo review by the Ethics Committee concerned.

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| <ol style="list-style-type: none">3. <i>Information regarding DNA sequence data should be released into the public domain.</i> |
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DNA sequences from the human genome cannot themselves be regarded as “inventions” that are subject to intellectual property rights, and information concerning DNA sequences obtained from research should not be considered subject to intellectual property rights. In the Human Genome Project,

the disclosure of DNA sequences has been agreed. In the joint statement of Mr. Clinton, the President of the United States of America, and Mr. Blair, the Prime Minister of the United Kingdom, in March 2000, following the speech of Mr. Chirac, the President of France, in February 2000, and in the statement of Mr. Nakasone, the Director General of the Japanese Science and Technology Agency, in April of the same year, it was confirmed that “free access should be secured to information on DNA sequences of the intact human genome.” UNESCO, as well as the International Bioethics Committee, expressed its support for the subject in the statement of Mr. Matsuura Koichiro, the Director General, in May 2000. It is admitted, in both of these statements, that some genetic information obtained beyond simple DNA sequences could be subject to intellectual property rights.

Material, methods, or information that are subject to property rights should be, in principle, disclosed to the public. However, such disclosure does not imply a loss of patentability; nor does publication of the results of research remove the possibility of their being patented. The system of intellectual property rights generally requires “disclosure” of the subject, and whoever wishes to can use the disclosed material, methods or information on payment of a set fee. Researchers, participants and the public need to have an adequate understanding of intellectual property rights.

Principle 22 Establishment and observance of protocols for conducting research

Research on the human genome is diverse depending on the objectives and subjects of each project. Adequate research protocols regarding the specific conditions detailed in the research plan should be established while respecting the present “Fundamental Principles of Research on the Human Genome.” All researchers and personnel involved in the implementation of the research should observe the said protocol.

It is important for the progress of research on the human genome that the most rational and effective strategy for each research project be taken, because the research is of itself highly diverse, covering areas from basic studies on human life to applied studies on genes implicated in diseases, and, in particular, it deals with a large variety of subjects for studies on polymorphism.

Protocols concerning the implementation of research should be agreed upon so that the most rational and effective methods can be taken. The conditions governing the implementation of research, which are defined in the present Fundamental Principles, should be embodied as practical protocols in appropriate forms, with attention paid to the following: the possibility that identification of the genetic information of individuals may give rise to ethical, legal and social issues; whether, given the objectives and particulars of the research, the said research is expected to contribute significantly to human health and the prevention and treatment of disease; and the principle that participants should be subjected to no more than the minimum disadvantages.

Principle 23 **Ethics Committee**

1. *On undertaking any research on the human genome, its research plan should undergo prior review by an independent, multidisciplinary and pluralist Ethics Committee.*
2. *The Ethics Committee should examine a submitted research plan on the human genome from ethical, legal and social points of view, in addition to its scientific merit, and comprehensively evaluate whether the implementation of the project should be approved or not.*
3. *The Ethics Committee should guarantee its transparency in its organization and reviewing deliberations.*

This Principle is concerned with the Ethics Committee. The review and judgement of the Committee play crucial roles with respect to research on the human genome. The Committee holds the important duties, and the authority to execute those duties, of judging each research project from an ethical point of view, deciding whether or not to approve the implementation of the project, and making judgements on various ethical, legal and social issues as the occasion demands, in accordance with the present Fundamental Principles and the separate “guidelines” on research on the human genome, which are secondary to the present Fundamental Principles. Correspondingly, each research institution and researcher should conduct their research with a full understanding of the importance of the ethical norms and their observance. The Ethics Committee should clarify its organization, protocols for reviewing, and criteria for review, and strive for fairness and transparency in their reviewing. In view of this Principle, the existing system of Ethics Committees in Japan is not deemed to be adequate to preside over the implementation of research on the human genome. Each research institution concerned requires the swift establishment and consolidation of a Bioethics Committee in accordance with the present Fundamental Principle and the separate guidelines.

The organization of the Committee described in the first point should be neutral and objective. It is important for the reviewing process, from an ethical viewpoint, to involve members from various fields including certain members from external institutions. Thus, in addition to specialists, the Committee should involve members of the general public and representatives from related organizations, e.g. those representing patients.

A subcommittee for scientific evaluation could be set up within the Ethics Committee in order to review research plans solely from a scientific point of view.

The organization of the Committee, the regulation of protocols, and the results of reviews should, in principle, be disclosed, although attention should also be paid to the protection of privacy of individuals and respect given for the originality of research, and transparency should be maintained by the Committee throughout all stages of the reviewing process, e.g. details of discussions and conclusions, lest the fairness and neutrality of the reviewing process be impaired. The review and judgement of the

Committee is valid only in so far as transparency is maintained and society can inspect that review and judgement.

The term “Ethics Committee” covers generically all committees that conduct reviewing and judging functions, regardless of the diverse names that the existing committees at different institutions actually hold.

Chapter 4 Relationship with society

In this Chapter, the way in which research on the human genome should be considered in relation to society is discussed. Research on the human genome in particular requires interaction with society.

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| <p>Principle 24 Understanding and support by society and accountability</p> <ol style="list-style-type: none"><i>1. Research on the human genome makes a significant contribution to the life and health of humanity and of each individual, and to the welfare of society.</i><i>2. Public support for the advancement of research on the human genome, with recognition of the role played by the said research in society now and in the future, is desirable. This support should be underpinned by a sound understanding of the present “Fundamental Principles of Research on the Human Genome” (especially the significance of the human genome outlined in Principles 1 to 3).</i><i>3. All people involved in research on the human genome have a general accountability to society on all aspects of the research in order to improve the understanding and recognition of the public as described above.</i> |
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When the principles of bioethics as set down in the present Fundamental Principles are actually applied, it is of absolute necessity that society recognizes the significance of research on the human genome. As described in the “Basic Ideas,” people who actually participate in the research, their blood relatives, their families and the general public are required to fully understand the significance of the human genome and the opinion of the present Fundamental Principles, although the ethical principles that researchers should follow comprise the main part of the present Fundamental Principles.

At the same time, in order to promote effectively the approval of society for the research, it is important to educate the public sufficiently about the research. This requires “accountability” concerning research on the human genome. Indeed it is the fulfilment of this accountability, and the sufficient recognition in society of the significance of the research, that underlies the progress of research on the human genome.

Principle 25 **Public disclosure of outcomes of the research and return of benefits to society**

1. *All beneficial outcomes in the fields of biology, genetics and medicine obtained from research on the human genome should be returned to society. In principle, they should be disclosed to the public.*

As described in the “Basic Ideas” and Principle 1, results of research on the human genome should be disclosed, because the human genome is a factor in the elucidation of what it is that constitutes human life and contributes to the improvement of the health and welfare of humanity and of each human being. “Disclosure” here does not imply disclosing the information of particular individuals, nor does it aim at restricting intellectual property rights. The disclosure considered in the scope of intellectual property rights has as its objective the promotion of industry, and is not contrary to that referred to here. While research is ongoing, it is not unreasonable to maintain secrecy for that period, whether or not it is concerned with intellectual property rights.

2. *All outcomes of research on the human genome should be employed for the development of science, the elimination of human suffering, the prevention and cure of diseases, and the improvement of health.*

This Principle is written in view of the fact that the applications of results obtained from research on the human genome will make large contributions, especially in the fields of medicine and pharmacology, although it is not necessary to mention that the research is conducted also as basic science.

Principle 26 **Appropriate measures**

Appropriate measures should be taken so that research on the human genome can be adequately and effectively promoted in accordance with the “Fundamental Principles of Research on the Human Genome.” In addition, general, adequate and prompt decisions and countermeasures should be taken regarding the various ethical, legal and social issues that may arise from research on the human genome and its outcomes.

The appropriate measures mentioned here could be the application of existing law, the drawing up of new laws, the discussion and laying down of national guidelines, and other administrative measures. As for social supports, various measures, legal or financial, should be taken to ensure the prompt consolidation of the genetic counselling system.

Principle 27 ***Dissemination of education and provision of information***

Bearing in mind that research on the human genome will have a serious impact on life, living and the future of humanity and of each individual, education on the human genome and its research, including bioethics, should be widely promoted. Endeavours should be made to spread information concerning research on the human genome and its applications.

Scientific education, and not only that concerning the human genome, is a primary requirement for the development of future generations. The sciences will not advance in an efficient and beneficial way unless society universally understands these pioneering fields. Therefore, a comprehensive scientific policy, including covering the education system, should be promoted.

It is important that not only researchers and participants but also the general public fully understand bioethics, in order to enhance the beneficial aspects of research in the biosciences and not to increase unnecessarily their disadvantageous aspects. The promotion of education on bioethics is therefore vital. This needs to include education on genetic medicine and the training of specialists in the field of bioethics.

Supplementary provision

These “Fundamental Principles of Research on the Human Genome” should be revised as appropriate in the light of the future progress of research on the human genome and the understanding of such research by the public and social trends in this regard.

The present Fundamental Principles should be revised as appropriate in the light of actual circumstances since research on the human genome is progressing rapidly and society is expected to show more understanding of research on the human genome and its clinical implications. Even without a particular change in circumstances, a re-examination of these Principles should be made every 3 to 5 years.

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Terminology

The terminology used in the Fundamental Principles is defined below.

[Genetic information]

Genetic information refers to the information that is passed down from one generation of living organism to another through deoxyribonucleic acid (DNA), which is located within the nucleus and mitochondria of a cell. Genetic information does not include information that is acquired through actions, such as learning.

[Gene]

A gene refers to the part of the genetic information that takes on the various functions required to sustain life through transcription to ribonucleic acid (RNA) and translation into protein.

[Genome]

The genome refers to all genetic information, including genes. It includes not only the entire DNA base sequence, but also the chromosome structure and information not contained in genes, such as repeating sequences. Genetic information is a term based on the more abstract concept of “information.” When talking about more specific information, the genome is a more concrete entity and it refers to everything including DNA.

[Polymorphism]

Among living organisms of a particular species there is great similarity between their individual genetic information, and 99% or more of their DNA base sequence is shared in common. However, a portion of this DNA differs slightly between individuals. This phenomenon is referred to as polymorphism, and as a result of polymorphism, while all humans belong to the same species, a wide range of different genetic traits is found throughout a population.

[Genome analysis research]

Genome analysis research refers to the research that involves the analysis of genetic information such as gene sequences, functions, regulatory mechanisms, the manifestation of traits, amino acid sequences in protein, and research analysing polymorphism as well as the research based on information obtained from these activities.

[Genetic diagnosis]

Genetic diagnosis refers to the process of examining the genetic information of an individual in order to analyse genetic traits. Genetic diagnosis is conducted with the objective of identifying the cause

of diseases, predicting diseases that might appear in the future, and assessing the potential effects and adverse reactions of drugs.

[Genetic factors in disease]

A disease can be caused by genetic factors that are governed both by the genome and by environmental factors, which are themselves governed by the living environment. There are diseases with an extremely strong genetic component such as haemophilia and familial adenomatous polyposis (FAP), and lifestyle diseases and cancer, to which the environment contributes greatly but which still have a multifactorial genetic component. It is thought at present that many diseases have a genetic component, and that genetic diagnosis, described above, will take on an increasingly important role in medical care.

[Drug responsiveness]

The degree of efficacy of a drug and any adverse reactions to it vary between individuals based on differences in *in vivo* absorption, distribution, metabolism and excretion, and differences in sensitivity to that drug, even when exactly the same dose of the drug is administered. In addition, unforeseen abnormal reactions may occur, depending on the individual. Drug responsiveness refers to those individual differences in reactions when drugs are administered. The reasons for these differences have yet to be fully elucidated, but it has been demonstrated that the genetic component is a contributing factor. Genetic diversity is thought to result in differences in how a gene works in each individual. Consequently, research on the use of “individually tailored” drugs is progressing based on the notion of using individual genetic information.

[Reproductive system cells]

Reproductive system cells refers to reproductive cells, such as the sperm and ovum, and those cells that will become reproductive cells in the future (fertilized ova, undifferentiated early stage embryos, primordial germ cells, spermatogonia, oogonia, spermatocytes and oocytes).

[Genetic counselling]

Genetic counselling refers to the provision of appropriate information to the patient (referred to here as the sample donor), and his/her blood relatives and family, using knowledge of medical genetics and counselling skills. Genetic counselling increases the patient’s (sample donor’s) understanding of genome research and diseases that have a genetic component, and allows him/her, and his/her blood relatives and family, to make their own life decisions. Genetic counselling also encompasses those medical care activities that support this process. It is not a part of the explanation provided during the obtaining of informed consent.

[Human Genome Project]

The Human Genome Project is a project that was proposed in the United States at the end of the 1980s, the aim of which is to unravel all human genetic information. Japan and some European countries, specifically England, France and Germany, joined the project in the 1990s, and a tripartite framework designed to promote international cooperation was formed. The objective of the project is not just to determine the genetic information within the base sequence, but also to conduct analyses including analysis of gene function. The project is ongoing at universities and national research institutes in each of these countries, including Japan.

[Nuremberg Code]

The Nuremberg Code is Control Council Law No. 10 entitled “*Permissible Medical Experiments*,” and is part of the judgment rendered at the Nuremberg Trial held in 1947 covering those human experiments that were conducted by Nazi Germany on Jewish subjects during the Second World War. The Nuremberg Code sets down the ethical standards for medical research using human subjects. It later served as the foundation for the Declaration of Helsinki.

[Declaration of Helsinki]

The Declaration of Helsinki refers to the ethical principles that were expressed in the “*Recommendations guiding physicians in biomedical research involving human subjects*,” which were adopted at the 18th World Medical Assembly held in Helsinki, Finland, in June 1964. The Declaration was substantially amended to its current form with additions on areas such as informed consent at the 29th World Medical Assembly, held in Tokyo, Japan, in October 1975.

[Universal Declaration on the Human Genome and Human Rights]

An International Bioethics Committee was established within the United Nations Educational, Scientific and Cultural Organization (UNESCO) in 1993 to look into the ethical, legal and social problems that were arising through the rapid development of the life sciences, including human genome research. The Committee drafted the Declaration, which was adopted at the General Conference of UNESCO in November 1997. The Declaration contains provisions banning actions that violate the dignity of humans, such as the creation of a human clone, and describing “informed consent.” The Declaration proclaims that human dignity and human rights will be protected in the course of dealing with problems that arise during human genome research.

[HUGO]

HUGO refers to the Human Genome Organisation. It is an international scientific body, established in 1989 by researchers participating in the Human Genome Project, with the objective of

promoting cooperation in the Human Genome Project. For example, it serves as a forum for the exchange of data, sharing of technology and provision of information and advice on the Human Genome Project as well as promoting study on a wide range of topics such as ethical, legal and social problems and intellectual property rights. The organization has released several declarations based on the results of studies into social problems surrounding the Human Genome Project.

Members of Human Genome Research Subcommittee

(Chairman)

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| Fumimaro Takaku | President, Jichi Medical School Internal Medicine |
| Ryuichi Ida | Professor, Graduate School of Law, Kyoto University International Law, Bioethics |
| Hideki Okuda | Chairman, Research and Development Committee The Japan Pharmaceutical Manufacturers Association (JPMA) Pharmaceutics |
| Junko Obata | Professor of Law, Sophia University Administrative Law |
| Takashi Gojobori | Director and Professor of the Center for Information Biology at the National Institute of Genetics Bioinformatics, Population genetics, Molecular evolution |
| Mariko Tamai | Associate Professor, Department of Psychology, School of Allied Medical Sciences, Shinshu University Psychology, Bioethics |
| Masaaki Terada | President, National Cancer Center Molecular Oncology |
| Kumao Toyoshima | Director, Sumitomo Hospital Oncology |

Yusuke Nakamura Professor, The Institute of Medical Science,
The University of Tokyo
Medical Genetics

Tomoh Masaki Director General
National Cardiovascular Center Research Institute
Pharmacology

Saku Machino Professor of Law, Sophia University
Criminal Law, Medical Law

Members of Bioethics Committee

(Chairman)

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|-------------------|---|
| Hiroo Imura | Member of Council for Science and Technology (Regular) |
| Tadao Ishikawa | Professor Emeritus of Keio University |
| Mitsugu Ishizuka | Member, Council for Science and Technology (Regular) |
| Ryuichi Ida | Professor, Graduate School of Law, Kyoto University |
| Yoshio Okada | President of SENRI Life Science Foundation |
| Nobuaki Kumagai | Member of Council for Science and Technology (Professor Emeritus of Osaka University) |
| Yoko Sano | Member of Council for Science and Technology (Professor, Tokyo International University) |
| Susumu Shimazono | Professor, Graduate School of Humanities and Sociology, The University of Tokyo |
| Ayako Sono | Novelist, Writer Chairperson, The Nippon Foundation |
| Fumimaro Takaku | President, Jichi Medical School |
| Shigeaki Tanaka | Professor, Graduate School of Law, Kyoto University |
| Yoshitaka Nagai | President, Mitsubishi Kasei Institute of Life Sciences |
| Norio Fujisawa | Professor Emeritus, Kyoto University |
| Katsunosuke Maeda | Member of Council for Science and Technology (Chairman of the Board, Toray Industries, Inc.) |

Saku Machino Professor of Law, Sophia University

Yasuhiko Morioka Director, Japanese Red Cross Medical Center

Hiroyuki Yoshikawa Member, Council for Science and Technology
(President, Science Council of Japan)