

Informed Consent in the Protection of Human Genetic Resources: Evolutionary Change in Chinese Legislation

İnsan Genetik Kaynaklarının Korunmasında Bilgilendirilmiş Onam: Çin Mevzuatındaki Evrimsel Değişimler

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ABSTRACT Objective: The human genetic resources are the base of innovative research in the field of life science and technology nowadays. The concrete practice of informed consent is of great significance in reasonable protection of human genetic resources. The aim of this study was to compare the common ground and difference of informed consent between the collection, preservation and utilization of human genetic resources for the purpose of scientific research and such activities in clinical care and clinical trial, and discusses how to reflect and provide for informed consent in the legislation of human genetic resources. **Material and Methods:** The relevant Chinese laws and regulations since 1993 and Regulations on the Administration of Human Genetic Resources (Submission for Review) was collected and compared. And the practical dilemma of informed consent was analyzed from the perspective of ethics, law and social implications. **Results:** Informed consent in the human genetic resources collection, preservation and research and development activities has demonstrated different characteristics on the aspects of the subject of informed consent, informed contents and re-consent etc., which are also the very dilemma confronted by the practice of informed consent in the human genetic resources protection. **Conclusion:** The reasonable provision in human genetic resources-related legislation on informed consent should take into account both the human dignity and Self-Determination and the particularity of human genetic resources and social and natural human attributes.

Key Words: Bioethics; informed consent; genetics, medical; China

ÖZET Amaç: İnsan genetik çalışmaları günümüzde yaşam bilimleri ve teknolojik alanlarda yenilikçi araştırmaların temelini oluşturmaktadır. Bilgilendirilmiş onamın somut uygulaması insan genetik kaynaklarının korunmasında çok önemlidir. Bu çalışmanın amacı bilimsel araştırmalarda, klinikte tedavi görürken ve klinik araştırmalarda insan genetik kaynaklarının korunmasında ve kullanılmasında bilgilendirilmiş onamın nasıl sağlandığını araştırmak ve aradaki farkları karşılaştırmak, ve insan genetik kaynaklarının yasallaştırılmasında bunların nasıl yansıtılacağını ve sağlanacağını tartışmaktır. **Gereç ve Yöntemler:** 1993'ten beri uygulanan Çin yasa ve yönetmelikleri ile İnsan Genetik Çalışmaları hakkındaki düzenlemeler bulundu, ve karşılaştırıldı. Etik, yasalar ve sosyal çıkarımlar açısından bilgilendirilmiş onamın pratikteki çelişkileri de analiz edildi. **Bulgular:** İnsan genetik kaynaklarının toplanması, saklanması ve araştırma ve geliştirme faaliyetlerindeki bilgilendirilmiş onam, bilgilendirilmiş onam alınan denek ve bilgilendirilmiş onamlar ve tekrar onam alma gibi konular yönünden farklı özellikler göstermektedir ki, bunlar zaten insan genetik kaynaklarının korunması anlamında bilgilendirilmiş onam alınması pratiğinde karşılaşılan çıkmazlardır. **Sonuç:** Bilgilendirilmiş onamlar hakkında insan genetik kaynakları ile ilişkili yasaların makul hükümleri hem insan itibarını ve kendi hakkında karar verme hakkını, ve hem de özellikle insan genetik kaynaklarını ve insanın sosyal ve doğal niteliklerini dikkate almalıdır.

Anahtar Kelimeler: Biyoetik; bilgilendirilmiş onam; genetik, tıbbi; Çin

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The life science and technology initiated from Human Genome Project (HGP) is more and more deeply revealing and interpreting life code, and having significant impact upon the prediction, prevention and individualized medical treatment of human diseases. Since life science research is strongly dependent upon the human genetic resources which has become the basis for innovative research in the field of life science and technology nowadays. Under the research mode of mega science, large project and big data, in order to promote the flow and allocation of such strategic human genetic resources and the release of innovative energy generated possibly from them, and meet the demand of research activities for human genetic resources, more and more countries and regions have established biobanks to collect and preserve human genetic resources based on population group.

With the growth of life science and technology, we come to realize gradually that the genetic information carried with the human biological samples is likely to both contain something sensitive and be lifelong correlative, and may have an effect upon both the individual sample donors and their families or even a wider range of communities. Due to the long-term nature and hereditary of human genetic resources, the human genetic research has to be confronted with a large number of concerns in terms of ELSI (ethics, law and social implications). Informed consent, as relate to respect for human dignity, has aroused much wider and deeper deliberation. In the era of post-genomes, facing the large number of biobanks and the large-scaled research project on functional genomes, proteome and Pharmacogenomes, the practice of informed consent is exposed to greater challenge.

On this occasion that *Interim Measures for the Administration of Human Genetic Resources* is proposed to be upgraded to *Regulations on the Administration of Human Genetic Resources*, this paper will discuss the practical dilemma possibly confronted by informed consent in human genetic resources collection, preservation and research and development (R&D) activities, and the emphasis which should be duly considered in case of mak-

ing proper and reasonable regulations on informed consent in the legislation of human genetic resources around the Chinese legislation in force and the provision under *Regulations on the Administration of Human Genetic Resources (Submission for Review)* on informed consent.

CHINA'S LEGISLATION PROCESS AND ANALYSIS ON THE CAUSE

The modern life science and technology has been increasingly revealing implausible potential. For the strategic dominating elevation, countries all over the world attach more and more importance to the strategic position of human genetic resources. How to promote the utilization of human genetic resources in scientific research activities with innovative legal institutional arrangement and balance, the demands of different subjects for protection of their respective rights and interests has become the difficulty confronted by the legislation of human genetic resources. This chapter introduces human genetic resources-related legislation process in China, and the backgrounds of *Regulations on the Administration of human genetic resources (Submission for Review)*.

LEGISLATION PROCESS

Until 1998, China made no special provisions on any R&D activities concerning human genetic resources, but mainly normalized the collection, preservation and utilization of human genetic resources for any purpose other than scientific research such as clinical diagnosis and treatment or blood (or plasma) collection and supply. For example, *Blood Collection and Supply Institutions and Blood Administrative Measures (expired)*, *Regulations on the Administration of Medical Institutions (1994)*, *Detailed Rules for the Implementation of the Regulation on the Administration of Medical Institutions (1994)*, *Regulations on Administration of Blood Products (1996)*, *Blood Donation Law (1997)* and similar regulations have regulated activities of collecting and testing such human genetic resources as blood in a medical institution's conventional clinic diagnosis and treatment or blood (or plasma) collection and supply service.

With the development of life science and technology, the research value and commercial value of human genetic resources are increasingly manifested. The human genetic resources in China, characterized by widespread complexity of disease pedigree and pureness of ethnic and family genetic resources, have become valuable research resources. China's human genetic resources, being increasingly used in international scientific and technological cooperation, once had lost seriously. In order to strengthen the effective protection and reasonable utilization of China's human genetic resources, and facilitate human genome research and international scientific and technological cooperation, on 10 June 1998, Chinese Ministry of Science and Technology and Ministry of Health enacted *Interim Measures for the Administration of Human Genetic Resources*, which was the first specification in China on the administration of human genetic resources, emphasizing regulation on approval of international cooperation project involving human genetic resources, principle for managing intellectual property right in R&D results and approval of human genetic resources export, and giving positive effect to the protection of China's human genetic resources. On this stage, the specification on collection, preservation and utilization of human genetic resources for any purpose other than scientific research is mainly reflected in *Measures for the Administration of Blood Stations (Effective)*, *Guiding Principle on Planning of Blood Collection and Supply Institutional Setting (Expired)* and the like regulations.

However, *Interim Measures for the Administration of Human Genetic Resources* has gradually fallen behind the rapid progress of life science and technology, which is in particular reflected in that the effectiveness level is not as high as expected and administrative measures on collection, preservation, research and utilization of human genetic resources are absent. Since 2006, in accordance with the State Council's plan on legislation, the Ministry of Science and Technology, in collaboration with the Ministry of Health and other competent authorities, has conducted the drafting work of the regulations on administration of human genetic resources, and developed *Regulations on the*

Administration of Human Genetic Resources (Submission for Review). On 31 October 2012, Chinese State Council Legislative Affairs Office released the full text and instructions of *Regulation on the Administration of Human Genetic Resources (Submission for Review)* for public consultation. It is known through *the Ordinance concerning the Procedures for the Formulation of Administrative Regulations* and *the Notification of the Chinese State Council Legislative Affairs Office on Public Consultation for Regulations on the Administration of Human Genetic Resources (Submission for Review)* that such Submission for Review is still under review. The Chinese State Council Legislative Affairs Office will modify *Regulations on the Administration of Human Genetic Resources (Submission for Review)* upon comprehensive study on opinions from all walks of life and through consultation with the drafters to form the draft and its instruction which shall be submitted to the executive meeting of the State Council for review.

THE CAUSE OF LEGISLATION CHANGE

Regulations on the Administration of Human Genetic Resources (Submission for Review), in comparison with *Interim Measures for the Administration of Human Genetic Resources*, has changed substantially not only in terms of legal effectiveness level, but in specific aspects of management system, management measures and legal liabilities. These changes are mainly due to the demand on human genetic resources protection in the context of developing life science and technology.

THE INFLUENCE OF INTERNATIONAL DECLARATION AND PROCLAMATION

In the field of life science and technology, notwithstanding the difference among countries in the development level of science and technology and the stage of industrial development, technological development trend and demand of industrial growth are identical with each other and the research activities would also be confronted with some common ethical issues. Since the end of 20th century, international community has focused more and more attention on the effect of R&D in life science

and technology upon human dignity, freedom and right. The General Conference of UNESCO adopted *Universal Declaration on the Human Genome and Human Rights*, *International Declaration on Human Genetic Data* and other such international proclamations, and Human Genome Organization (HUGO) issued *Statement on the Principled Conduct of Genetics Research and Statement on DNA Sampling: Control and Access*, being committed to making the conduct of research on human genomes and their application ethical, and respecting for the human right, basic freedom and human dignity of individuals and associated communities. The basic ethical principle which should be followed in the activities of research on human genomes and their application as emphasized in these declarations and proclamations is intended to reflect human rationality in common. China has acknowledged such basic principle and rules set forth under these declarations or proclamations in drafting *Regulations on Administration of Human Genetic Resources (Submission for Review)*.¹

INTERNAL DEMAND OF HUMAN GENETIC RESOURCES PROTECTION

China has rich human genetic resources. In face of the great change of contemporary life, science and technology system, and the international pattern of economic globalization, reasonable protection and utilization of human genetic resources have played an increasingly important role in promoting national development of biotechnology and elevating technological innovation capability. In addition, the national strategy designer, policy-maker and legislator are attaching more and more importance to the strategic position of human genetic resources and understanding the essential goal of human genetic resources protection from the perspective of maintaining national security, promoting technological development, elevating national capability of R&D in biological and pharmaceutical science and technology, and protecting human body health, etc. For example, in June 2011, the Ministry of Science and Technology, Ministry of Health, and National Commission of Population and Family Planning co-issued *the Notice on Pro-*

moting human genetic resources Protection and Management. The Biotechnology Development Program under "12th-Five-Year Plan" released by the Ministry of Science and Technology in November 2011 made "building national bio-information scientific and technological infrastructure, National Bio-Information Center, including national biotechnology management information base, bio-information base of genome, proteome and metabolome, large-sized biological sample, specimen, case resource and human genetic resources bank and shared service system" as one of the important measures for enhancing capability building in biotechnological innovation. In 2009, China's Action Plan of Intellectual Property Protection explicitly proposed to expedite the study and drafting work of *Regulations on the Administration of Human Genetic Resources*, perfecting the protection, development and utilization of China's human genetic resources by operation of law, and building a reasonable system of genetic resources acquisition and interest sharing.

Furthermore, in comparison with the historical background under which *Interim Measures for the Administration of Human Genetic Resources* was enacted, life science research and application have made an unprecedented leap, and a large number of new problems have also been found in over one decade's legal practice of such *Interim Procedures* and should be responded legally.

INFORMED CONSENT: FOCUS IN HUMAN GENETIC RESOURCES PROTECTION

From HGP to the HapMap Project, and then to the international 1000 genomes project, bioscience, as an ancient discipline, is increasingly bursting with youthful energy. With rapid progress of life science and technology, the issue of informed consent has received more and more attention. As an important principle of bioethics, from *the Nuremberg Code* to *Declaration of Helsinki*, informed consent has gradually developed from an abstract and simple ethical principle to a specific and ample ethical norm. Nevertheless, exploration to the issue of informed consent has never been receded in the least for this reason. On one hand, the boundary be-

tween biomedical and behavioral research and generally accepted conventional healthcare as well as the nature and definition of informed consent or similar issues have received close attention all the time. As indicated in *Belmont Report*, “*The distinction between research and practice is blurred partly because both often occur together (as in research designed to evaluate a therapy) and partly because notable departures from standard practice are often called ‘experimental’ when the terms ‘experimental’ and ‘research’ are not carefully defined.*” “*.....if there is any element of research in an activity, that activity should undergo review for the protection of human subjects.*” On the other hand, as influenced by human genome research, informed consent and proxy consent, personal consent and group or community consent as well as informed consent and re-consent or issues like that will become a challenge that the principle of informed consent should be facing in practical.

As a bioethical norm, informed consent is also facing the demand of being rendered into a statutory principle or rules, i.e. this ethical code of informed consent will be expressed in the form of legal norm by virtue of legislative procedures, specific path of which shall include being rendered into legal principle or statutory rule, or permeation of ethical concept into rule of law. Of course, in the field of life science and technology, bioethics and law is neither replaceable with each other nor mutually exclusive, regulating on informed consent in legislation should be maintained a tensile force with bioethics and should be reasonably made on the legal dimension.

With regard to biological sample donors, execution of informed consent principle should be not only limited to his/her decision on whether to donor, but manifested on that whether the donor has made the aforesaid decision on his/her own will on the basis of fully understanding the intended use and scope of application of his/her biological sample, potential risk or any other details. Such donor’s own discretion is not simply to express his/her consent or dissent, such simple decision of one or the other, but specifically embodied in giving consent or dissent under some certain circumstance. There-

fore, from the perspective of social implications, overall communication and risk prompt are key connotations of informed consent.

It is thus clear that how to achieve informed consent in the process of human genetic resources collection, preservation, R&D, and to which extent that legislative stipulation in human genetic resources should be made have been the focus of attention by lawmakers, scientists, physicians, socialists, public policy makers and even the entire social public all the time.

INFORMED CONSENT: THE DIFFERENCE BETWEEN THE INTERIM PROCEDURES AND DRAFT (SUBMISSION FOR REVIEW)

The normative difference of informed consent between *Interim Measures for the Administration of Human Genetic Resources* and *Regulations on the Administration of Human Genetic Resources (Submission for Review)* is mainly embodied on the aspect of the subject of informed consent, the informed contents, the re-consent, and the legal liability for breach of the principle of informed consent, etc. (Table 1). In general, in contrast to *Interim Measures for the Administration of Human Genetic Resources*, provisions under *Regulations on the Administration of Human Genetic Resources (Submission for Review)* on informed consent are more comprehensive and specific in content.

INFORMED CONSENT: COMPARISON AMONG DIFFERENT CONTEXTS

With regard to informed consent, there are some common problems presented and may be certain difference existed in the medical practice of healthcare, clinical trial and the human genetic resources collection, preservation and R&D (Table 2). Comparison and analysis on these common grounds and differences are of great necessity for the principle of informed consent to be reasonably reflected and stipulated in the legislation. In the prevailing legislation of China, regulations on informed consent are mainly reflected in such laws and regulations as *Tort Law* (2009), *Measures for the Ethical Re-*

TABLE 1: Comparison between Provisions under *Interim Measures for the Administration of Human Genetic Resources and Regulations on the Administration of Human Genetic Resources (Submission for Review)* on Informed Consent.

	Interim Measures for the Administration of Human Genetic Resources	Regulations on the Administration of Human Genetic Resources (Submission for Review)
The subject of informed consent	The donor of a biological sample and his/her Relatives	a) The donor of a biological sample b) If the donors are persons with no capacity or with limited capacity, then the informed consent is given by their statutory proxies
The informed contents	No provision	The form of informed consent is comprised of the purpose of collection, use, the potential hazard to health, the benefit sharing measures, the personal privacy protection, the voluntary opt-in and the right of unconditional opt-out from time to time
Circumstance under which informed consent must be obtained	International cooperation project involving China's human genetic resources	The collection, preservation and utilization of biological samples should follow the principle of voluntary and informed consent
Circumstance under which informed consent is exempted	No Provision	No Provision
Re-consent	No Provision	a) The unit being approved to collect and preserve human genetic resources should use the resources for the purpose consented by the donor b) The unit collecting and preserving human genetic resources can furnish the resource to others to be used in the R&D activities consented by the donor c) For utilization of their genetic resources beyond the purpose consented by the donor, re-consent by him/her should be acquired
The legal liability for breach of the principle of informed consent	No Provision	The unit being approved to be engaged in collection, preservation, R&D and exit or entry of human genetic resources, in case of infringing the principle of informed consent in the process of human genetic resources collection, preservation and utilization, shall be instructed to correct by the competent administrative authorities in charge of science and technology under provincial government, and in case of gross violation, shall be imposed a fine more than RMB 50,000 but less than RMB 200,000

R&D: Research and development; RMB: Renminbi.

view on Biomedical Research involving human subject (for trial implementation) (2007), Provisions for Clinical Trials of Medical Devices (2004), Code of Quality Management on Pharmaceuticals' Clinical Trial (2003), Law on Practicing Doctors (amended in 2009), *Interim Measures for the Administration of Human Genetic Resources (1998)* and *Regulations on the Administration of Medical Institutions (1994)*, etc.. The following comparison is based on specific provisions in these laws and regulations and it should be noted in particular that if human genetic resources collection, preservation and R&D activities are involved, then provisions

under *Interim Measures for the Administration of Human Genetic Resources* and *Regulations on the Administration of Human Genetic Resources (Submission for Review)* are covered.

THE SUBJECT OF INFORMED CONSENT

Healthcare is a medical intervention for the purpose of improving a patient's personal health by providing him/her with effective means of disease prevention, diagnosis and treatment. In the healthcare activities, the subject of informed consent include patients and their family members. Clinical trial on human body means experimental applica-

TABLE 2: Manifestation of informed consent in healthcare, clinical trial and human genetic resources collection, preservation and R&D activities.

	Health Care Activities	Clinical Trial	Human Genetic Resources Collection, Preservation and R&D Activities
The Subject of Informed consent	The patient or his/her relatives	<p>a) The Testee or his/her statutory proxy</p> <p>b) For incapacitated testees, if the ethics committee has approved in principle and the researchers consider such testees' participation to be in their own interest, their consent shall be given by their statutory guardians</p> <p>c) For children testees, informed consent from their statutory guardians shall be obtained and they shall sign the informed consent; if the children are capable of making decision on consent to be involved in the research, their own consent must be obtained</p>	the donor of a biological sample and his/her relatives
Informed contents	Condition of illness and medical measures	<p>a) Voluntary opt-in and opt-out at any time</p> <p>b) research project including trial purpose, trial process and duration, inspection, possible benefit and risk , and he/she is likely to be assigned to different groups of trial</p> <p>c) Rights and benefits which testee have</p>	No Provision
Circumstance under which Informed Consent must be obtained	<p>a) In case that surgical operation, special examination and special treatment are needed, medical personnel should inform the patient timely of medical risk and alternative health care scheme, and obtain his/her written consent.</p> <p>b) Any information inadvisable to be known by the patient should be indicated to his/her near relatives and their written consent should be obtained</p>	<p>a) The testee's voluntary written informed consent must be obtained in advance</p> <p>b) If written informed consent is inaccessible, oral consent should be obtained in advance and evidentiary material of oral consent should be submitted</p> <p>c) For incapacitated testees or those who are unable to make his/her own decision, their guardians or proxies' written informed consent must be obtained</p>	International cooperation project involving China's human genetic resources
Circumstance under which informed consent is exempted	In case of emergency for rescue of the dying patient and it is impossible to consult him/her or his/her near relatives, corresponding medical measures can be taken immediately, with the approval of the principal or authorized representative of the medical institution	If informed consent of the patients' own and their legal proxies is unavailable in case of emergency, for instance, lack of therapeutic method being proven effective, while the investigational drug is expected to rescue their life, regain their health or relieve their pain, they can be incorporated into the trial, however, it is required to clearly describe the method of accepting them in the testing scheme and related documentations and obtain the approval of the ethics committee in advance	No Provision
Re-consent	No Provision	<p>a) If the procedures or conditions of biomedical research involving human subjects and related technical application have changed, re-consent from the testee shall be obtained; furthermore, ethical review application shall be submitted to the ethics committee</p> <p>b) In pharmaceutical clinical trial, if the latest important data related to pharmaceutical trial is found, re-consent from the testee shall be obtained ,and the informed consent shall be modified in writing and submitted to the ethics committee</p>	No Provision

[Source: systemized from such laws and regulations as Tort Liability Law, Practicing Physician Law, Medical Institution Management Ordinance, Code of Quality Management on Pharmaceutical Clinical Trial, Regulations on Medical Devices' Clinical Trial and Interim Measures for the Administration of Human Genetic Resources]

tion of healthcare technologies or products developed through biomedical research on human body. For clinical trial of pharmaceutical or medical device, informed consent shall be given by the testee in person or his/her statutory proxy. Clause 15 of *Code of Quality Management on Pharmaceuticals' Clinical Trial* has special provisions on incapacitated testees and children testees. For incapacitated testees, if the ethics committee has approved in principle and the researchers consider such testees' participation to be in their own interest, the consent shall be given by their statutory guardians. For children testees, informed consent from their statutory guardians shall be obtained, and they shall sign the informed consent; if the children are capable of making decision on consent to be involved in the research, their own consent must be obtained. In the human genetic resources collection, preservation and R&D activities, as set forth in Table 1, *Interim Measures for the Administration of Human Genetic Resources* has defined the biological sample donors and his/her relatives as the subject of informed consent. While *Regulation on the Administration of Human Genetic Resources (Submission for Review)* has stipulated that the subject of informed consent shall be the biological sample donors; if the biological sample donors are persons with no capacity or with limited capacity, then their statutory proxies can give the informed consent.

INFORMED CONTENTS

In the healthcare activities, physicians delivering diagnosis and treatment to a patient shall provide him/her with information on his/her physical condition, informing him/her of the role, risk and possible negative consequence of clinical test and therapeutic regimen, and he/she decide whether to be treated under such regimen on his/her own discretion under the condition of having full knowledge on the state of his/her illness and the therapeutic regimen. Therefore, in clinical care, mainly the state of illness and medical care measures shall be informed. In human clinical trials, the testee could suffer damage or even die due to participation in clinical trial, therefore, when con-

ducting a clinical trial of pharmaceutical or medical device, the person in charge of such clinical trial or his/her proxy shall inform the testee of particulars concerning clinical trial, including his/her voluntary opt-in, the right to opt-out on any stage of the clinical trial, that his/her participation and personal information in the trial shall be maintained confidential, testing program, and that he/she can be medically treated and accordingly compensated in case of injury suffered in connection with the trial. In human genetic resources collection, preservation and R&D activities, the detailed information that the collection, preservation and R&D institutions should give to the biological sample donor is not explicitly stipulated in *Interim Measures for the Administration of Human Genetic Resources*. However, *Regulations on the Administration of Human Genetic Resources (Submission for Review)* has required to inform the donor of the objective and use of the biological samples and related information, potential hazard to health, benefit sharing measures, personal privacy protection, voluntary opt-in, right of unconditional opt-out at any time and so on; the biological sample donor shall decide whether to provide the biological sample and related information on his/her own discretion.

THE CIRCUMSTANCES REQUIRED TO OBTAIN INFORMED CONSENT

In the healthcare activities, in case that surgical operation, special examination and special treatment are needed, medical personnel should inform the patient timely of medical risk and alternative healthcare scheme, and obtain his/her written consent. Any information inadvisable to be known by the patient should be indicated to his/her near relatives and their written consent should be obtained. For the clinical trial of pharmaceutical or medical device, the written informed consent from the testee or his/her statutory proxy must be obtained in advance. In comparison with *Interim Measures for the Administration of Human Genetic Resources*, provisions under *Regulations on the Administration of Human Genetic Resources (Submission for Review)* concerning the circum-

stance under which informed consent should be obtained in the human genetic resources collection, preservation and R&D activities have changed to a large extent. Specification under *Interim Measures for the Administration of Human Genetic Resources* on informed consent is only embodied in the procedures of submission for approval of international cooperation project in connection with China's human genetic resources, while *Regulations on the Administration of Human Genetic Resources (Submission for Review)* has specified the principle of informed consent, and set forth that informed consent shall be obtained in case of collection and preservation of the biological sample and related information, which shall be utilized for the purpose consented by the donor. However, at the beginning of biological sample collection and preservation, the future use of these biological samples could not be fully foreseen, whether broad consent is allowed or specific consent must be obtained has become one of the most controversial issues. Furthermore, it should be noted that many countries collect and preserve human genetic resources for life science research by establishing biobanks in the post-genome era. Then, collection and preservation of human genetic resources for the purpose of subsequent R&D are different from that for the purpose of conventional service of clinical diagnosis and treatment or blood (or plasma) collection and supply.

THE CIRCUMSTANCES UNDER WHICH INFORMED CONSENT IS EXEMPTED

During medical activities, in case of emergency for rescue of the dying patient, and when it is impossible to consult him/her or his/her near relatives, corresponding medical measures can be taken immediately, with the approval of the principal or authorized representative of the medical institution. For pharmaceutical clinical trial, if informed consent of the patients' own and their legal proxies is unavailable in case of emergency, for instance, lack of therapeutic method being proven effective, while the investigational drug is expected to rescue their lives, regain their health or relieve their pain, they can be incorporated into the trial. However, it

is required to clearly describe the method of accepting them in the testing scheme and related documentations and obtain the consent of the ethics committee in advance. For the human genetic resources collection, and preservation and R&D activities, China has made no special provisions on the circumstance under which informed consent is exempted till present.

CIRCUMSTANCE UNDER WHICH RE-CONSENT IS REQUIRED

In human clinical trial, if the latest important data related to pharmaceutical trial is found or the procedures or conditions of human subject research have changed, re-consent from the testee shall be obtained; re-examination and approval from the ethics committee shall be acquired. *Interim Measures for the Administration of Human Genetic Resources* has no provisions on re-consent. While *Regulations on the Administration of Human Genetic Resources (Submission for Review)* has specified that re-consent from the donor shall be obtained when his/her biological sample, and related information are used for any purpose other than those consented by him/her in the R&D activities.

It is known from the above comparison that in contrast with the clinical care and clinical trial, the informed consent in the human genetic resources collection, preservation and R&D activities has demonstrated different characteristics on the aspects of the subject of informed consent, informed contents and re-consent etc., which are also the very practical dilemma confronted by the practice of informed consent in the human genetic resources protection.

THE REALISTIC PERPLEX CONFRONTED BY INFORMED CONSENT

The ethical argument on informed consent in the human genetic resources collection, conservation and R&D activities has extended from whether informed consent is required to which form of informed consent is required. To be specific, perplexes confronted by informed consent in human genetic resources protection mainly include

whether proxy consent is allowed, or only self-consent is acceptable; whether only personal consent is needed or family consent and even group or community consent is still required; whether broad consent can be made or only specific consent is virtually effective informed consent.

SELF-CONSENT AND PROXY CONSENT

It is an important issue confronted by the biobanks and researchers that which subject's informed consent should be sought in the collection, preservation and R&D activities involving human genetic resources. In the process of collection and preservation, whether only the donor of a biological sample himself can make the effective decision of consent? Whether the proxy consent by a statutory proxy or other subject is allowable? If other subject can give proxy consent, whether the scope and sequence shall be limited? These issues, as a matter of fact, are concerned with the subject of informed consent and the capability of consent.

The Nuremberg Code limits the informed consent to self-consent, pursuant to Section I of such Code, "*The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision.*" *The Declaration of Helsinki* has specified the proxy consent. On legislation level, different countries have made different responses. For example, *Human Tissue Act (2004)* of U.K. has provided that it is lawful to removal, storage and use of human organs and other tissue for scheduled purpose with appropriate consent. In addition to personal consent, the informed consent shall also cover appropriate consent given by the person who has parental responsibility for the child, nominated representatives or the person who stood in a qualifying relationship to the donor at that time. The qualifying relationships should be ranked

in the following order: (a) spouse or partner; (b) parent or child; (c) brother or sister; (d) grandparent or grandchild; (e) child of a person falling within paragraph (c); (f) stepfather or stepmother; (g) half-brother or half-sister; (h) friend of longstanding (Article 27).

In fact, in the context of biobanks, the issue of proxy consent is far more complex than conceived. Firstly, in the collection, preservation and R&D activities, proxy consent is generally manifested as the consent given by the statutory proxy, instead of consent by an entrusted agent. In other words, if the donor of a biological sample has corresponding capacity of consent, his/her own consent shall be obtained. Only if the donor of a biological sample has no capacity of consent for the reason of age, intellectual impairment or behavior disorder, the statutory proxy can give proxy consent. Secondly, proxy consent has doubt in time validity. Taking a minor as an example, if his/her parent or other statutory proxy has given consent on his/her behalf to donor sample for a biobank, once such minor has come of age and had capacity of consent, whether the biobank must obtain his/her own consent?² Or the biobank is not required to obtain such consent but to acknowledge that such donor has the right to withdraw his/her previous proxy consent once having the capacity of consent? Thirdly, with regard to the specific content of such consent, whether broad proxy consent is allowable or only specific proxy consent is acceptable? In addition, although for these donors, collection of their biological samples such as human tissue tends to fall within the extent of de minimis, only at the time of collection they will feel discomfort such as pain, if the standard operating procedure is followed, there will be usually no other physical risk. Nevertheless, in case of proxy consent, the intention of biological sample donor who has no capacity of consent should also be considered and valued.

PERSONAL INFORMED CONSENT, FAMILY CONSENT AND GROUP CONSENT

Whether a person has decided on his/her own to be involved in a specific research based on being

informed and to donor biological sample, which risk and benefit exist for him/her arising from the aforesaid participation, which effect they will have upon him/her later on these are usually highlighted by in discussion of informed consent. However, this is still an individual-centered way of thinking, having ignored the right and interest of the subject concerned, and the possible impact from potential risk, and interest upon any third person in the present or prospective gene research, namely, if the biological sample and data are used for the purpose of scientific research, especially gene research on a specific group or community, the long residual action and heredity of human genetic research enable some genetic information to have non-exclusive particularity for the individual, the revelation of genetic information not only will have an effect upon the individual donor of biological sample but is likely to affect his/her family members or even a wider range of groups or communities, thus possibly prejudicing or discriminating some individual or even his/her community. For example, the research on biological sample and data in biobanks has indicated that some particular ethnic group has high incidence to a certain specific disease or genetic predisposition of some action, members in such group would be insulted and discriminated.³ The research on the biological samples of some ethnic group or religious group member such as human tissue will also be likely to impede other members of such ethnic group or religious group. Therefore, in collection of the biological sample and related information of the human genetic sample donor, not just personal consent, family consent and group or community consent should also be considered, can respect for human dignity be embodied.

BROAD CONSENT AND SPECIFIC CONSENT

The specifications and ethics on informed consent often require the participant to be fully informed of the research's nature and risk. However, in the context of biobanks, the path of the aforesaid specific consent has been challenged. The biobanks will collect human genetic resources from a large

number of people or even based on population group and their samples may be subject to repeated, long-term and prospective use. These prospective research programs could not be explicit in case of collection, then whether the biobanks is allowed to adopt broad consent in the process of collection?

The scholars objecting broad consent hold that informed consent should be given on the basis that the participant is informed of the research project as well as the benefit and risk arising from or in connection with the project are evaluated. The broader the consent is, the lower the degree of being informed is. The broad consent is a misleading use of informed consent, because such research is unforeseeable to him/her and has not been explicitly expressed in the research program.⁴ The reason why broad consent is objected also lies in that only specific consent can really show respect to the biological sample donors. The principle of informed consent requires free consent to donor biological sample for related research, this means consent to potential risk exposure from participation in these researches, thus in consideration of risk exposure, broad consent should be excluded.⁵ In addition, although adopting broader consent indeed can save cost for re-consent, however, the biological sample donor, since unable to foresee the risk which may be brought to him/her by the prospective research, is likely to reduce his/her expectation and confidence in privacy protection, thus influencing his/her will of donating biological samples.

The reason why broad consent is supported lies in that biobank-related research is of great significance in promoting human welfare, as long as the information is encoded and applied securely, the biological sample donors and their families can be protected from aggression, then there is no need to restrict their autonomy. Incorporating broad consent as an option of opt-in does not mean dishonoring autonomy. The biobanks conducting a large-scale prospective research is allowed to continuously update their research progress, and give the biological sample donor a choice to withdraw his/her consent, however, to a prudential participant, broad consent and specific consent are nearly

the same.⁶ For the use of samples in prospective research, as long as conditions on three aspects as follows are satisfied: confidentiality on personal data, the guaranteed right for the donor to withdraw his/her consent, and new research's being approved by the ethics committee, broad consent can protect his/her autonomy.⁷ Broad consent given on prospective research also does not constitute a waiver of informed consent; instead, under the safeguard mechanism of research project approval system and ethical review system, broad consent is also a form of consent.⁷

It can be seen from the hot debate between scholars that whether informed consent can be further expanded to allow the use of samples in the unforeseeable prospective research is a challenge of practice for informed consent in the era of post-genome. Broad consent is different from both blank consent and specific consent. When the biological sample donor is giving his/her broad consent, although not merely consent to his/her own biological sample's being used in a specific research project, whether the prospective purpose can be limited to a certain extent? For example, whether his/her own biological sample can be limited to one or more types of research? Whether the circumstance can be list explicitly under which the biological sample can not be used? All these still have to be furthered reflected from the perspective of ethics, law and social implications (ELSI).

INFORMED CONSENT AND RE-CONSENT

With the proceeding of human genetic resources from the process of collection and preservation to R&D, the subsequent main user, scope of use and way of application of human genetic resources tend to be materialized, and will have a substantial effect upon the biological sample donor. Usually, which purpose of research, and which project of research the collector, preserver, researcher or developer can use the biological sample and data of the donor for shall be subject to the informed consent signed by him/her. If such consent is a specific one, once beyond original scope of consent, re-consent from the donor shall be obtained, this is seemingly uncontroversial. However, what if such consent is a broad

one? Whether the donor's giving broad consent means no re-consent needed for subsequent use of their samples? Or re-consent is needed only when the ethics committee deems that the use of samples for the research project submitted for ethical review is of inconformity with the initial target of biobanks? In the context of biobanks, taking into account the operability of obtaining re-consent, and the possible effect upon the biological sample donors without prejudice to the driving effect of large population-based biobanks upon the R&D is a potential challenge confronted by re-consent in practice.

INFORMED CONSENT IN THE LEGISLATION CONCERNING HUMAN GENETIC RESOURCES

It is known from the above-mentioned analysis that practical dilemma between personal consent and proxy consent, personal consent and group or community consent, broad consent and specific consent as well as informed consent and re-consent may be confronted in the biological sample collection, preservation and R&D activities. However, in the progressive change of human genetic resources legislation in China, how the provision on informed consent should be optimized?

Firstly, attention should be focused on coordination of relationship between the subject of informed consent, and the individual, family, community or ethnic group on the aspect of "consent" to donor his/her own biological samples.

Interim Measures for the Administration of Human Genetic Resources has defined the subject of informed consent as "the donor of the biological samples and/or his (her) legal representatives", it is seen from the provisions therein that these interim measures focus on the possible effect upon the family members once the human genetic resources are used for R&D, and require that the donor's personal consent and family consent shall be obtained if China's human genetic resources are acquired for international cooperation project. While *Regulations on the Administration of Human Genetic Resources (Submission for Review)* has defined the subject of informed consent as the donor of a biological sample, and the statutory proxy of such

donor of incapacity or with limited capacity. As stipulated in such *Submission for Review*, personal consent or proxy consent should be obtained when the human genetic resources are collected and preserved. It can be found that neither *Interim Measures for the Administration of Human Genetic Resources* nor *Regulations on the Administration of Human Genetic Resources (Submission for Review)* focuses on the status of the community on the aspect of “consent” to provide the human genetic resources. With the development of biotechnology, more and more researches focus on the genetic resources of communities or ethnic groups. In comparison with the specific manner of consent adopted in traditional medical research specific to testees, in addition to the biological samples and information of specific individuals, those of communities or groups are studied in human genetic R&D activities. If the purpose and schedule of R&D activities are followed, due to the particularity of human genetic resources, the research result is likely have a significant effect upon the entire community or ethnic group. It is then the focus and of difficulty to cope with personal consent and group or community consent.

Secondly, in the era of biobanks, the controversy between broad consent and specific consent become fierce day by day. The reason why the institutions collecting and preserving human genetic resources expect the donor to give broad consent is that they could not foresee the prospective purpose and risk as well, furthermore, when the human genetic resources are collected and preserved via biobanks based on population group, obtaining specific re-consent once the specific research program is finalized will also be confronted with tremendous difficulty in practical operation. Nevertheless, the biological sample donor’s giving broad consent means neither signing of a blank consent nor such broad consent’s being applicable for all research types.

Neither broad consent nor specific consent is involved in *Interim Measures for the Administration of Human Genetic Resources*. With regard to the stipulations in *Regulations on the Administration of Human Genetic Resources (Submission for*

Review), i.e. “the institutions being approved to collect and preserve the human genetic resources should use them for the purpose consented by their donors”, where the “consent” is usually understood as specific consent. However, whether the “purpose” can be described much broadly or only concretely and clearly in the written informed consent is still unknown, such regulations only provide that the format text of written informed consent must be approved by the ethics committee of the collecting and preserving institutions.

It is thus clear that whether broad consent should be allowed, how to specify applicability of broad consent, and whether the foregoing is reflected in legislation are all subject to in-depth exploration.

Thirdly, with regard to informed consent and re-consent, as mentioned above, *Interim Measures for the Administration of Human Genetic Resources* only requires to submit the biological sample donor’s and their relatives’ written informed consents for the formalities of submission for approval of international cooperation project involving China’s human genetic resources, while the content of informing and re-consent are not dealt with therein. *Regulations on the Administration of Human Genetic Resources (Submission for Review)* has provisions on re-consent, i.e. “the re-consent from the biological sample donor shall be obtained when his/her biological sample are used for any purpose other than consented by him/her”.

In practice, the researcher, if having to obtain the donor’s re-consent, must contact him/her once again. In that case, the researcher may be confronted with the circumstance that the donor has died or become inaccessible according to original information or his human genetic resources has undergone irrevocable anonymization or his identity could not be determined. Under the circumstance that the donor has died or become inaccessible according to original information the R&D of genetic resources is still limited to the scope of original consent, rather than improperly expanded such scope through family consent.

CONCLUSIONS

The progress made by *Regulations on the Administration of Human Genetic Resources (Submission for Review)*, in comparison with *Interim Measures for the Administration of Human Genetic Resources*, is not only the elevation of legislative effect order and the expression design of legislative provisions, but in a substantial sense, the more sufficient respect to human subjectivity and the more comprehensive consideration to the complexity of relationship between the human subjects as well. In a certain sense, in comparison with other genetic resources (genetic resources of animal and plant), particularity of human genetic resources in ethical and legal norm may lie in the discretionary power of “human” as the subject and the complexity of social and natural attribute of “human and mankind”. This particularity is profoundly reflected in the scope of informed consent. In the human biological collection, preservation and R&D activities, informed consent is not purely procedurally required or an issue of control. When the discretionary power of “human” as the subject is confronted with the long residual action and hereditary of human genetic resources and the complexity of social and natural attribute of “human and mankind”, chal-

lenge in practice between personal consent and proxy consent, family consent and group or community consent, broad consent and specific consent as well as informed consent and re-consent is thus emerging. The reasonable provision in human genetic resources-related legislation on informed consent should take into account both the human dignity and discretionary power and the particularity of human genetic resources and human social and natural attribute.

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