



China's Ethical Review System





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The Chinese Ethical Review System and its Compliance Mechanisms

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Executive Summary

The report introduces the structure of China's research ethical review system and thereby its ethics compliance mechanisms.

Taking the ethical review system in the life sciences and medical fields as an example, the report describes how the S&T-related ethical review system is functioning in China. It should be noted that whilst the ethical review system in life sciences is gradually taking shape, building the institutional capacity for S&T-related ethical issues in other fields is still slow and weak in China. To date, China has not yet established an ethics committee at the national level, and the administrative responsibilities for S&T-related ethical issues in specific areas still rest with the relevant departments of the government. Except for the Ministry of Health, no ministry or cabinet institution has a permanent ethics committee.

Introduction

The research and administration of science and technology-related ethical issues in China can be traced back to the 1980s. Back then, inspired by the strict access rules and ethics censorship system in certain countries when conducting international joint research programs on clinical drug tests, supportive reproductive technologies, embryonic stem cell research and organ transplant, some biological and medical research institutions in China started to set up ethics commissions. With the mushrooming of clinical trials of new drugs and vaccines, novel biotechnologies, and new medical devices in China since the 1980s, the number of both clinical research methods and human research participants has been steadily increasing, accompanied by increasingly prominent issues related to informed consent, risk-benefit ratios, and distributive justice, among others. According to preliminary estimates, every year in China more than 800 new drugs enter human trials, with approximately 500,000 human research participants participating in them, raising concern for the protection of the rights and interests of human research participants. How to maintain a dynamic balance between continuously promoting Research & Development (R&D) and the application of new technologies, and complying with internationally recognized ethical norms has become a major issue to science and technology (S&T) and social governance regulators in China.

Through many years of development, China has established a mature research and administration structure for medical ethics, manifested by the founding of the Chinese Society of Medical Ethics of the Chinese Medical Association in 1988, and the promulgation of the *Organizational Charter of Hospital Ethics Committees* in 1995; the opening of the Medical Ethics Expert Committee in the Ministry of Health and the release of the *Guidelines for Hospital Management Evaluation* (2008 Edition); as well as the establishment of hospital ethics committees in most of the large-scale AAA hospitals².

However, although the system of life science ethics management is gradually taking shape, the institutional development of research ethics in other fields is still slow and weak. To date,

² AAA hospital (*Sanjia Yiyuan*) is the highest grade hospital according to the current Chinese rules to be in charge of hospitals by grade.

China has not yet established an ethics committee at the national level, and the administrative responsibilities for S&T-related ethical issues in specific areas still rest with the relevant departments of the government. Except for the Ministry of Health, no ministry or cabinet institution has a permanent ethics committee. In general, compared with high-income countries, China still has a long way to go in building a research ethics administration system.

This report takes research ethics in the life sciences and medicine as an example, and examines the following key areas: 1) institutionalization of China's research ethics review; 2) design and mechanism of China's Research Ethics Committee; 3) attainment of the goals of system design in terms of formal examination, process supervision and operational guidance; 4) assurance of the authoritativeness of research ethics review; and 5) current status of research ethics education and training in China.

A Brief History of China's Research Ethics Review System

China's Regulatory Documents on Research Ethics Review

In the 1980s, clinical pharmacologists Li Jiatai and Sang Guowei et al., founders of clinical trials in China, introduced the concept of ethical review, but it was not until the 1990s that the institutionalization of research ethics review began in the country, marked by the establishment of research ethics committees at leading university-affiliated hospitals, represented by Xiangya Hospital (1994), and Peking Union Medical College Hospital (1996). In March 1997, Chen Minzhang, then Minister of Health, ordered the establishment of research ethics committees at medical research institutions. In 1999, the State Food and Drug Administration (SFDA) issued the *Norms on Quality Management of Drug Clinical Trials*, which stated explicitly that,

“To protect the rights and interests of human subjects of clinical trials and provide public assurance for them, all medical institutions that conduct clinical trials shall set up their research ethics committee”.

Since 2000, China has accelerated its institutionalization of ethical review and released a succession of regulations and measures relating to research ethics. In 2000, the Ministry of Health formed the first session of its Expert Committee on Medical Ethics, responsible for research on ethical issues in medical research and consulting on ethical education. In 2001, the Ministry of Health released the *Administrative Measures for Assisted Human Reproduction*. In 2003, the Ministry of Health and the Ministry of Science and Technology jointly formulated the *Ethical Principles of Research of Human Embryonic Stem Cells*. In 2003, the SFDA issued the revised *Norms on Quality Management of Drug Clinical Trials*, requiring all medical institutions conducting clinical trials to be certified for the qualification, and the establishment of independent research ethics committees filed with the SFDA to safeguard the rights and interests of all applicants for participation and participants in clinical trials.

To strengthen the protection of human research participants and the regulation of biomedical research activities, the Ministry of Health released *Measures for the Ethical Review of Biomedical Research Involving Humans (For Trial Implementation)* in 2007, which promoted the institutionalization and development of medical ethics committees at various levels across China. To reflect the progress of the country's efforts to put biomedical ethics review within a comprehensive regulatory framework, the National Health and Family Planning Commission officially issued *Measures for the Ethical Review of Biomedical Research Involving Humans* in 2016. This further clarified the responsibilities and tasks of medical ethics committees, substantiated the content regarding the principles, processes, standards and tracking of ethical review, specified the basic scope of informed consent, and defined the responsibilities and tasks of medical ethics committees at medical institutions, as well as those at the national and provincial levels.

Table 1: China's Main Regulatory Documents on Research Ethics Review Issued Since 2000

Document	Issuance	Issuer
<i>Norms on Quality Management of Drug Clinical Trials</i>	2003	State Food and Drug Administration
<i>Ethical Principles of Research of Human Embryonic Stem Cells</i>	2003	Ministry of Science and Technology, Ministry of Health
<i>Measures for the Ethical Review of Biomedical Research Involving Humans (For Trial Implementation)</i>	2007	Ministry of Health
<i>Norms on Ethical Review of TCM Clinical Research</i>	2010	State Administration of Traditional Chinese Medicine
<i>Guiding Principles of Ethical Review of Drug Clinical Trials</i>	2010	State Food and Drug Administration
<i>Guiding Principles of Quality Management of Vaccine Clinical Trials (For Trial Implementation)</i>	2013	State Food and Drug Administration
<i>Administrative Measures for Clinical Research of Stem Cells (For Trial Implementation)</i>	2015	State Food and Drug Administration
<i>Norms on Quality Management for the Clinical Trials of Medical Devices</i>	2016	State Food and Drug Administration
<i>Measures for the Ethical Review of Biomedical Research Involving Humans</i>	2016	National Health and Family Planning Commission

These regulatory documents issued by China's relevant authorities have directly promoted the institutionalization of research ethics review in the country. Since 2000 China has

gradually put in place a comprehensive research ethics review system, where research ethics committees comprised of interdisciplinary experts have assumed the main responsibility for ethical review of research activities involving human research participants, working to maintain the balance between S&T development and ethical compliance, and to ensure full respect for and effective protection of human research participants' lawful rights and interests. The process of formation and development of China's medical ethics review system has been one of transition from discipline to self-discipline.³

China's Ethics Review System and Its Structure

As rapid progress is made in the development and creation of new drugs, with the implementation of key drug development programs during the 12th and 13th five-year plan periods, there have been increasing numbers of biomedical research activities involving human research participants. According to *Measures for the Ethical Review of Biomedical Research Involving Humans*, issued by the National Health and Family Planning Commission in 2016, research activities that fall within the scope of ethical review include:

- 1) research activities on human physiological and psychological behavior, pathological phenomena, causes of diseases and pathogenesis, and the prevention, diagnosis, treatment and rehabilitation of diseases using the techniques of modern physics, chemistry, biology, TCM, and psychology;
- 2) human experiments involving new medical techniques or products; and,
- 3) activities that collect, record, use, report or store specimens, medical records, and behavior of human research participants using the techniques of epidemiology, sociology, psychology and other related sciences.

It can be seen that with the expansion of the scope of ethical review, clinical research, basic clinical research and epidemiological surveys are also subject to ethical review, and that the health authorities and research ethics committees at various levels are assuming greater responsibilities.

Under China's current research ethics administration system, the National Health and Family Planning Commission is responsible for organizing inspection and supervision of the ethical review of biomedical research activities involving human research participants nationwide; the State Administration of Traditional Chinese Medicine is responsible for organizing inspection and supervision of the ethical review of TCM research activities nationwide. Nationwide, the health and family planning authorities above county level are tasked to strengthen the regular supervision and administration of the ethical review of biomedical research activities involving human participants within their purview. Medical and health institutions are tasked to strengthen regular management of their research ethics committees' ethical review of biomedical research activities involving human research participants by assessing their work quality on a regular basis, giving instructions or advice on improvement for identified issues, and making adjustments to their research ethics committees where necessary.

³ Miao Qing and Cao Yongfu, "Examination of the Nature of Medical Ethics Review", *Chinese Medical Ethics*, 2012, 5

The National Expert Committee on Medical Ethics is responsible for researching major ethical issues in biomedical research involving human participants, providing advice for policymakers, and directing, inspecting and evaluating the work of the expert committees on medical ethics at the provincial level. Founded in 2000, the committee underwent a composition adjustment in 2007 and formed its third session in 2015. The expert committees on medical ethics at the provincial level are responsible for inspecting and evaluating research ethics committees at medical and health institutions within their purview, with the evaluation being focused on committee composition, regulation system, compliance with review process in terms of independence, reliability of results and effectiveness of project management, and giving opinions or advice for improvement. So far, more than 10 provinces and provincial-level municipalities including Beijing, Shanghai and Guangzhou have established their expert committee on medical ethics, with other provinces making preparation for the formation of the said committee.

Medical and health institutions that conduct biomedical research activities involving human participants are responsible for ethical review of the activities, and are obliged to set up their research ethics committees and take effective measures to ensure that the committees will perform their ethical review work independently. As early as 2010, almost all tertiary hospitals in Beijing had established their research ethics committees, which have fulfilled their role in protecting the rights and interests of human research participants and instructing the implementation of research plans.⁴ *Measures for the Ethical Review of Biomedical Research Involving Humans* stipulates that medical and health institutions that do not have a research ethics committee may not conduct biomedical research activities involving human research participants. The research ethics committees are responsible for protecting the lawful rights and interests of human research participants and safeguarding their dignity, and ensuring the ethical compliance of biomedical research by performing ethical review of their institutions' biomedical research activities involving human research participants, including initial review, tracking review and re-examination, and organization of relevant ethical review training.

The Composition of Research Ethics Committees

The regulatory documents relating to ethical review issued in China since the onset of the 21st century have both similarities and differences in their provisions as to the number, gender and professional backgrounds of research ethics committee members, and the standing body and office conditions of the committees. The *Guiding Principles of Ethical Review of Drug Clinical Trials* includes requirements on the gender balance of members, and the *Norms on the Quality Management for the Clinical Trials of Medical Devices* also has requirements on gender, while other documents make no mention of gender. *Measures for the Ethical Review of Biomedical Research Involving Humans* (2016), has the most detailed provisions, stipulating that the research ethics committees of medical and health institutions at various levels shall have not less than seven members, selected from experts in related fields including

⁴ Wu Xiaorui, Li Yiting, Zhao Xuezhi and Luo Yanxia, "Investigation and Analysis of Functioning of Institutional Ethics Review Committees in Beijing", *Medicine & Philosophy: Humanistic & Social Medicine Edition*, 2010, 3

biomedicine, ethics, jurisprudence, and sociology, as well as members of the general public who are not employees of the institutions where the committees are established.

Table 2: Composition of research ethics committee provided for in State regulatory documents

Document	Issued	Members	Members' professional background and organization	Secretaryship
<i>Norms on Quality Management of Drug Clinical Trials</i>	2003	At least 5	Experts in medical and non-medical fields including jurisprudence, and personnel from other organizations	Not mentioned
<i>Ethical Principles of Research of Human Embryonic Stem Cells</i>	2003	Not mentioned	Experts in biology, medical science, jurisprudence or sociology	Not mentioned
<i>Measures for the Ethical Review of Biomedical Research Involving Humans (For Trial Implementation)</i>	2007	At least 5	Biomedicine, management, ethics, jurisprudence, sociology	Not mentioned
<i>Norms on Ethical Review of TCM Clinical Research</i>	2010	More than 5	Experts in medical (including TCM clinical research) and non-medical fields including jurisprudence, and personnel from other organizations	Not mentioned
<i>Guiding Principles of Ethical Review of Drug Clinical Trials</i>	2010	At least 5	Experts with diverse disciplinary backgrounds including medical and non-medical (including jurisprudence) fields, and personnel independent from the research / trial institution	The procedure for appointment of the secretary is expressly provided for in writing
<i>Guiding Principles of Quality Management of Vaccine Clinical</i>	2013	Not mentioned	Experts in medical and non-medical fields including jurisprudence, and personnel from other organizations, with a balance between members	Not mentioned

Trials (For Trial Implementation)

within and outside the institution

<i>Administrative Measures for Clinical Research of Stem Cells (For Trial Implementation)</i>	2015	At least 7	Specialists in medical science, ethics, jurisprudence, management science, sociology or related fields, and at least one non-specialist from the general public	Not mentioned
<i>Norms on Quality Management for the Clinical Trials of Medical Devices</i>	2016	At least 5	Specialists in medical and non-medical fields (including at least one in jurisprudence), and one member from outside the clinical trial institution	Not mentioned
<i>Measures for the Ethical Review of Biomedical Research Involving Humans</i>	2016	Not less than 7, with independent advisors as optional	Selected from specialists in biomedicine, ethics, jurisprudence, sociology or related fields, and members of the general public who are not employees of the institution	Staffed with full-time (part-time) personnel in a fixed workplace complete with related facilities

In fact, medical and health institutions, or research institutions of different types, vary remarkably in the composition of their research ethics committees. A survey of 23 research ethics committees affiliated to Huazhong University of Science and Technology finds that the number of members ranges from 8 to 19, with a significant difference in staffing. The number of committee members is closely related to a number of factors including workload, the types of ethical review involved, and the degree of engagement of members, and has to be analyzed individually rather than described in general terms. One could point out that extremes should be avoided, as too many members may affect the convening of committee meetings as scheduled, and too few members may create bias in conclusions. *Measures for the Ethical Review of Biomedical Research Involving Humans* stipulates that a research ethics committee may engage independent advisors where necessary, but they can only provide advice regarding specific issues under ethical review without participating in the voting procedure. A 2008 survey by Zhou Ping et al of the member composition of the research ethics committees of 33 public hospitals in Shanghai, found that their committee composition complied with relevant regulatory requirements, with quite a few hospitals having engaged independent advisors for their research ethics committees.⁵

⁵ Zhou Ping, Zhang Shike, Wu Rong et al, "Analysis of the Composition of Hospital-affiliated Ethics Review Committees in Shanghai", *Chinese Health Resources*, 2008, 11(6): 265-266

The *Guiding Principles of Ethical Review of Drug Clinical Trials* and *Measures for the Ethical Review of Biomedical Research Involving Humans* both have provisions regarding the setup of a full-time or part-time secretary of a research ethics committee, with the latter even providing for a workplace and facilities. The secretary of a research ethics committee serves as the focal point for communication with relevant parties and helps maintain the committee's normal functioning. A research ethics committee that is neither staffed by a full-time academic secretary nor has a fixed workplace or necessary facilities will have a difficult time classifying and archiving ethical review documents, thus undermining the quality of ethical review and the fulfillment of the ethical review function. Ethical review documents include administrative documents, member information, research plans, meeting records, adverse event reports, and the corresponding review and inspection documents.⁶

China's Ethics Review System: Current Status, Problems and Responses

Ethical Review Process and Key Points

According to *Measures for the Ethical Review of Biomedical Research Involving Humans*, upon receiving an application for ethical review, a research ethics committee shall organize the ethical review in a timely way, with the focus on 12 points, namely:

- 1) qualification, experience and technical competence of researchers;
- 2) scientific basis of the research plan, compliance with ethical principles and, for TCM projects, reflection of traditional practices and experience;
- 3) exposure of research participants to risks and expected benefits of research (risk-benefit ratio);
- 4) comprehensibility of information provided in the informed consent form, and appropriateness of the process of obtaining informed consent;
- 5) protection of confidentiality of research participants' personal and related information;
- 6) appropriateness and fairness of inclusion and exclusion of research participants;
- 7) informing research participants of their rights and interests, including withdrawal without reason, and protection from discrimination;
- 8) indemnification of reasonable expenses incurred by research participants, and reasonable and lawful compensation for any harm caused to research participants due to participation;
- 9) securing of informed consent by qualified or trained researchers, and readiness to answer questions regarding safety;
- 10) measures to prevent and respond to any risks that research participants may be exposed to;
- 11) conflict of interest; and,
- 12) public opinion.

⁶ Dong Pingping and Wang Liyu, "Exploration Regarding the Establishment of a Medical Ethics Review and Supervision System", *Medicine & Philosophy (A)*, 2012,4

Research ethics committee members are required to avoid any conflict of interest in relation to any research project under ethical review by the committee.

The requirements for research ethics committees at hospitals may relate to 4 aspects: committee composition; content subject to review; the openness, justice and transparency of the review process, and subsequent supervision after approval.⁷ The key factors that are considered by a research ethics committee in determining whether to approve a research project include:

- 1) adherence to bioethics;
- 2) scientific soundness of the research plan;
- 3) fair selection of research participants;
- 4) reasonable risk-benefit ratio;
- 5) signing of a proper informed consent form;
- 6) respect for research participants' rights; and
- 7) compliance with norms on research integrity.

A research ethics committee should perform ethical review in a timely way and take the corresponding measures to protect research participants' rights and interests including safety and health. A research ethics committee may be affiliated to an institution or operate independently, and in either case it should be free from influence from any institution and observe the principle of avoidance of conflict of interest. A research ethics committee should have its independence and be supported effectively in terms of its needs for personnel, funds and supplies.

Main Concerns in Ethical Review

In reality, some research ethics committees have not yet established their standard operation procedures (SOP), resulting in an excessive amount of discretion and arbitrariness, which may have a negative effect on the objectiveness and justice of ethical review. Some committees that have established their SOPs have not complied with the SOPs to the letter, leaving significant room for improvement in standardization and normalization of review at committee meetings.

According to a survey, research ethics committees at institutions conducting drug clinical trials have the following problems in their functioning: the SOP being not comprehensive; lack of familiarity with the SOP; lack of standardization of tracking review; poor management of documents of trial projects; and lack of necessary infrastructure.⁸ A 2012 survey by Xue Di et al of 13 hospital-affiliated research ethics committees found that while these committees had good functional positioning overall, they had relatively weak management and differed

⁷ Li Yongchang, Jiang Chunyan, Luo Bin et al, "On the Normalized Management of Medical Ethics Review at Hospitals", *Medicine & Society*, 2014, 2

⁸ Wu Min and Gao Jinglong, "Practices to Continuously Improve Quality Management of Drug Clinical Ethics Review", *Chinese Medical Ethics*, 2015(5): 769-771

significantly in functioning, with the committees affiliated to specialized hospitals being particularly ineffective.⁹

A survey by Luo Caiqin et al of AAA hospitals in Fujian found that, according to the 2877 ethics-related papers published by those hospitals, only 21.8% of projects passed ethical review¹⁰ A questionnaire survey of some of the research ethics committees in Heilongjiang found that they have generally functioned less than well, with the main problems including excessive variety of content for ethical review, lack of attention paid to systematic and consistent ethical review, and organizational issues.¹¹

The research ethics committee-based tracking review mechanism, which started rather late in China, is the weakest link of the ethics review system.¹² Common problems of research ethics committee meetings include lengthiness, low efficiency, and lack of specialization. These problems could be addressed by improving and standardizing the procedural rules, and focusing on the scientific basis and ethical implications of the research proposals under review, especially the scientific and ethical aspects related to risks and benefits, and research participants' rights and interests. These measures would not only increase the efficiency and effectiveness of research ethics committee meetings but also improve the ethics attainment of members and other attendees.¹³ An examination by Bai Hua et al of the 99 drug clinical trial projects reviewed and approved by their hospital's research ethics committee found that full board meeting-based review and expedited review take an average of 43.7 days and 40 days respectively, with projects whose ethical review was completed within 1 month accounting for only 40%. The lengthiest part is the interval between meeting commencement and approval, which takes up approximately 53.6% of the total time of a review, while initial review only takes 2.1–2.3 days. It can be seen that for a given ethical review, applicants and researchers spend significantly more time than the research ethics committee. Therefore, it is necessary for applicants, researchers and research ethics committees to strengthen communication while effectively performing their respective duties in order to increase the efficiency of ethical review.¹⁴ Further improvement is also needed in such aspects as top-down design of the tracking review mechanism, supervision, funds and length of duration of tracking review, capability-building of members, and methods of tracking review.

⁹ Xue Di, Xu Wen, Yang Weimin et al, "Analysis of the Organization and Management of 13 Hospital-affiliated Ethics Review Committees in Shanghai", *Medicine and Philosophy*, 2012, 33(17): 31-32

¹⁰ Luo Caiqin, Zhang Meifang, Zhang Zhijian et al, "Ethics Review of Hospitals' Research Projects as Informed by Published Papers", *Chinese Journal of Medical Science Research Management*, 2014, 27(4)

¹¹ Bi Zihao, Yin Mei, Zhang Xue and Zhou Jing, "Strategies to Strengthen Effectiveness of Research Ethics Committees — Based on a Survey of Research Ethics Committees in Heilongjiang", *Chinese Medical Ethics*, 2014, 5

¹² Zhang Xue, Yin Mei, Sun Fuchuan et al, "Tracking Review Function of Research Ethics Review Committees in China: Challenge and Solution", *Medicine & Philosophy (A)*, 2013, 5

¹³ Zi Mingjie, Weng Weiliang, Gao Rui and Tang Xudong, "Tentative Analysis of Common Issues of Ethics Review Meetings", *Chinese Medical Ethics*, 2013, 26(5): 562-564

¹⁴ Bai Hua, Sun Yan, Song Yajing, Guan Shuxia and Wang Huanling, "Analysis of Factors Influencing the Speed of Ethics Review", *Chinese Medical Ethics*, 2016, 29(3): 465-468

Measures to Strengthen and Improve the Quality of Ethical Review

In recent years, Chinese authorities have taken various measures to increase the ethical awareness of researchers and regulate the ethical review process. For example, for research projects involving human research participants, the National Natural Science Foundation of China requires applicants for grants to subject their projects to preliminary ethical review before applying. After their applications for grants are approved, applicants need to apply for official ethical review of their projects; for research projects involving animal experiments, applicants are required to complete official ethical review before submitting their applications. To publish papers involving human research participants, many journals require the author to provide materials and certificates verified by ethical review organizations to ensure that the principle of informed consent is properly implemented in the research. Chinese authorities have required further normalization of the ethical review process. Selection of research ethics committee members should fully consider candidates' expertise, review capability and sense of responsibility. Routines including member training and archive management should be in strict compliance with established standards.

Measures for the Ethical Review of Biomedical Research Involving Humans has the following explicit provisions: Medical and health institutions shall require their research ethics committees to implement measures for improvement put forward by health and family planning authorities at the county level or above; where a research ethics committee fails or refuses to rectify problems within the specified time limit, or the violation is serious, or a serious consequence results, the medical and health institution to which the committee is affiliated shall remove the chair of the committee and hold relevant personnel accountable. The main contents of supervisory inspection include:

- 1) whether the medical and health institution has established its research ethics committee and filed it with the competent authority as required;
- 2) whether the research ethics committee has established its ethical review system;
- 3) whether the research projects ethically reviewed have been registered in the China Medical Research Registry and Management System;
- 4) whether the results of ethical review have been complied with;
- 5) how ethical review records have been maintained;
- 6) training of research ethics committee members; and
- 7) implementation of requirements or advice for improvement given by national and provincial expert committees on medical ethics.

For high-risk research projects it is required that a research ethics committee convenes plenary sessions for review, and the frequency at which researchers submit their research progress reports should be increased to, for example, once every 3 months or on a case-by-case basis. For research projects with minimal risks, the expedited review mechanism may apply, and the frequency at which researchers submit their research progress reports may be decreased, to once a year, for example. Those research projects that have extremely low risks or almost no risk may be exempted from ethical review, and researchers are not required to submit reports for tracking review, in order to reduce the intensity or workload of ethical review, and the workload of the researchers.

Research Ethics Education and Training in China

Biomedical research activities involving human research participants involve many tricky ethical issues. Since the 1980s, especially with the publication of *Bioethics* by Mr. Qiu Renzong in 1987, rapid progress has been achieved in bioethical research and teaching, and international academic exchanges in bioethics in China. Since 2000, more academic offshoots of bioethics have emerged, including genetic ethics, assisted reproductive technology (ART) ethics, public health ethics, nursing ethics, research ethics and clinical ethics. Major research ethics scandals in history, including Nazi experiments on humans, Unit 731 Japanese human medical experiments, and the Tuskegee Syphilis Experiment (1932-1972) in the U.S.A., have appeared in medical ethics textbooks, and have been discussed in the classrooms of medical students in China, where there have been more than 20 research ethics textbooks, including *Introduction to Bioethics* (Zhai Xiaomei, Qiu Renzong, 2005), and *Medical Ethics*. With the publication of *Life's Wisdom Tempered* by Zhang Xinqing (2007), and *Clinical Practice Cases: An Ethical Analysis*, and *Analysis of Cases of Ethical Review of Clinical Research* by Li Hongying, Li Zhenliang and Chen Min et al, Chinese scholars have begun developing their own medical ethics teaching cases.

Medical ethics cases are frequently used in research ethics education and training. With the exposure in the media in recent years of various domestic and foreign research scandals, including quasi-scientific stem cell therapies, the “Golden Rice” incident in China¹⁵, and the cloning scandal of Hwang Woo-Suk in Korea, there has been profound reflection on ethics education, with increased awareness of human subject protection and ethical compliance. The National Conference on Bioethics, which has been held for 8 consecutive years, has had in-depth discussions of research ethics and promoted the dissemination of related knowledge. For example, the “Golden Rice” incident mentioned above has brought about a positive change in China’s research regulatory stance. In recent years, China CDC has imposed ethical review of all human experiments, and implemented a strict one-vote veto system. China CDC also arranges regular research ethics trainings of researchers and research management personnel within its system every year.

Research ethics committees at various levels have also provided tailored research ethics training for their members, researchers and research management personnel. These research ethics education and training activities generally highlight prominent issues commonly found in ethical review and are geared to familiarizing trainees with ethical norms that should be observed in biomedical research, and improving their analysis and decision-making capabilities, with the key being correct understanding and flexible application of ethical norms. The main ethical norms in ethical review include the following four aspects:

- 1) informed consent, i.e. respect and safeguard the research participants’ free will as to participation, strictly perform the informed consent process, prevent the use of any improper means such as deception, inducement or coercion to obtain the research

¹⁵ In 2012, a paper about “Golden Rice” jointly published by authors from Tufts University, Hunan Provincial Center for Disease Prevention and Control, Chinese Center for Disease Control and Prevention (China CDC), and Zhejiang Academy of Medical Sciences in *The American Journal of Clinical Nutrition* sparked a lot of ethical controversy. It is found that the researchers did not obey the rule of “informed consent” when conducting human experiments during their study on the effect of GMO rice.

participants' consent, and allow the research participants to withdraw without reason;

- 2) acceptable risk-benefit ratio, i.e. put the research participants' safety and health in a prioritized position, ensure a reasonable risk-benefit ratio, and protect the research participants from possible harms;
- 3) privacy protection, i.e. protect the research participants' privacy, truthfully inform the research participants of information about the storage, use and protection of their personal information, and not make any unauthorized disclosure of the research participants' personal information to any third party; and,
- 4) justice, i.e. select research participants in a fair and reasonable way, provide special protection for vulnerable groups including children, pregnant women and people with mental health issues, not charge any fee to the research participants, indemnify the research participants from any reasonable expenses incurred by participation, and provide them with free timely treatment of injuries caused during participation, as well as compensation as granted under applicable laws and regulations or agreed upon between the parties.

Obviously, maintaining the smooth progression of research while complying with these ethical norms is a key link between research activities and ethical review, and this can be addressed to a significant extent by education and training.

Research ethics committees in medical and health institutions at various levels across China vary significantly in terms of composition and members' qualifications and, as a result, in their ethical awareness and review capability. Prominent issues include the following: ethical review focuses on initial review without paying necessary attention to changes or revisions of research plans and changes to informed consent processes, and tracking review is often omitted. Some researchers lack knowledge and understanding of ethical issues relating to e.g. the use of placebo, protection of vulnerable groups, privacy protection and genetic information, and fail to clearly distinguish their role as doctor (in diagnosis and treatment activities) from researcher (in clinical research activities), thus inducing therapeutic misconceptions on the part of the research participants. On the whole, members of research ethics review committees are relatively weak in medical science-related knowledge and review competence.

One contributing factor is the lack of research ethics education and training, especially systematic ethics training. Research ethics committee members that have received systematic training are limited, and some research ethics committees have not yet established their education and training system and do not provide regular training; those training activities they do provide are confined to limited areas or training methods and are therefore not effective in improving the review capability of members. A survey of 401 medical workers from 9 public hospitals in Shanghai that maintain biobanks found that although the workers have a basic knowledge of bioethics, they do not have sufficient understanding of specific ethical issues related to biobanks, especially around informed consent.¹⁶ To improve matters, health authorities and hospitals should formulate rules on

¹⁶ Zhang Kan, Cai Meiyu, Xu Yiping et al, "Analysis of Biobank-related Ethics Awareness of Medical Workers at Public Hospitals in Shanghai", *Chinese Medical Ethics*, 2016, 29(3): 469-472

ethical management of biobanks, and research ethics committees at the hospitals should strengthen the biobank-related ethical training of medical workers.

The percentage of research ethics committees whose members have an academic background in ethics is not high in China. For example, of the 23 research ethics committees affiliated to Huazhong University of Science and Technology, only 6 have members with an ethics background. While members with a background in medical science all received training in good clinical practice (GCP), they generally do not possess enough knowledge in ethics and jurisprudence. A survey by Lu Xu et al of the research ethics committees at 15 public hospitals in Guangzhou showed that the committees' member compositions are basically compliant with relevant regulatory requirements, but the distribution of members in fields of expertise is not reasonable, with an excessive presence of administrative personnel. Efforts are still needed to increase training of research ethics committee members and improve their ethical review capability.¹⁷

To sum up, China should put in place a comprehensive training system for research ethics committees in order to ensure that committee members receive regular training in biomedical research ethics and related laws and regulations, and have the required knowledge and skills to perform their duty of ethical review. In this regard, committee members need to receive continued education and knowledge update services on a regular basis, including by attending domestic academic symposiums and medical ethics workshops in order to be informed of domestic and international frontier issues in ethical review and to improve their ethical review capability. Efforts are also needed to strengthen training of researchers, research management personnel, and clinical trial and drug management personnel, in order to familiarize them with GCP knowledge and the procedural and key aspects of ethical review, and to instil in them a strong awareness of the protection of research participants' rights and interests. Research ethics committee members should be enabled to attend relevant ethical review classes to improve their ethical review capability. Health authorities and medical journals should issue written documents to include medical ethical review as part of the review of submissions. Activities including lectures, training classes, and collaboration can be organized to improve the knowledge and capability of ethical review of medical journals' editors.¹⁸ The scope of training should include the principles and norms of ethics and related laws and regulations and activities, geared to improving trainees' ability to identify, analyze and resolve ethical issues. The methods of training should be diverse, to include discussion, case analysis, and ethics workshops, among others. Committee members should be assessed as to their ethical knowledge and skills on a regular or irregular basis.

¹⁷ Lu Xu, Lin Jieru and Li Zhicheng, "Survey and Analysis of Composition of Hospital-affiliated Research Ethics Committees in Guangzhou", *China Health Care & Nutrition*, 2013(11)

¹⁸ Dang Jingping, Li Enchang, Ji Pengcheng and Li Meng, "Role of Journals in Medical Ethics Review: Problems and Strategies", *Acta Editologica*, 2011, 6