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Commentary

The new Good Clinical Practice-2020 in China: Views from ethical perspective

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1. Publication of Good Clinical Practice (GCP)-2020

The Drug Supervising and Regulatory Department of China has formally joined the International Council for Harmonization (ICH) of Technical Requirements for Pharmaceuticals for Human Use, and has become a member of the ICH council. ICH-GCP, known as E6 in the Efficacy E Series of ICH, is the international standard for ethical integrity and scientific quality for conducting trials involving the participation of human subjects [1,2]. However, due to rapid developments in drug research, and a consolidation of system reforms in drug examination and approval, a disparity between the GCP-2003 framework and more recent international codes now exists. An updated framework, GCP-2020 was officially published in April 2020 by the China National Medical Products Administration (NMPA) and the National Health Committee (NHC). GCP-2020 aligns with the basic requirements of the technical direction principles of the ICH [3].

2. Optimization of safety management

Safety report management in drug clinical trials is essential to the comprehensive and objective evaluation of a trial drug [4]. In comparison with GCP-2003, there has been a significant adjustment in safety report management in GCP-2020. As shown in Table 1, the standards and requirements of safety reports have been substantively modified.

3. Possible risks

Since the adoption of GCP-2020 on July 1st, 2020, the Ethics Committee of our center has performed its responsibilities towards safety management. However, in the practice of GCP-2020, we have found that GCP-2020 does not address all of the safety requirements of a clinical trial, and we have identified several potential risks:

(1) In accordance with GCP-2020, investigators should only report SAEs to sponsors in written form. SAE data from the investigational center will not be available to the Ethics Committees. As a consequence, it is not possible for an Ethics Committee to initiate a prompt ethical review of SAEs to protect injured subjects. According to the GCP-2020, sponsors should be liable for trial-related injuries involving the subject. However, because the investigators only report drug-related SAEs directly to the sponsor, if the sponsor determines that an SAE was not related to the test drug, the rights and interests of patients may not be protected.
(2) GCP-2020 only requires sponsors to promptly report SUSAR and to provide a DSUR to the Ethics Committee. However, a periodic report of out-of-hospital SAEs to Ethics Committees is not required. As a consequence, an Ethics Committee is unlikely to obtain the overall safety information concerning a trial drug in a timely manner. Moreover, the safety information eventually received may differ from the safety information presented in the brochure provided by the investigator. This constitutes a potential safety hazard.
(3) In drug clinical practice, sponsors are primarily responsible for managing potential risks. Investigators play a key role in clinical trial practice, as their ability to control experimental risks determines what risks the subjects will face [5]. According to

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Table 1
Differences between GCP-2003 and GCP-2020.

Type of report	GCP-2020 Responsibility of investigators	GCP-2020 Responsibility of sponsors	GCP-2020 Responsibility of the Ethics Committee	GCP-2003 Responsibility of investigators	GCP-2003 Responsibility of sponsors	GCP-2003 Responsibility of the Ethics Committee
SAE[a]	Report to sponsors	Sign off and analyze	No longer Sign off and review	Report to the CFDA[d], NHC, sponsors, and the Ethics Committee	Evaluate and report to the CFDA, NHC, and the Ethics Committee	Sign off and review
SUSAR[b]	Sign off and read	Evaluate and report to NMPA, health administrative department investigator, and the Ethics Committee	Sign off and review	Not mentioned	Not mentioned	Not mentioned
DSUR[c]	Sign off and read	Report to investigator, clinical trial facilities, and the Ethics Committee	Sign off and review	Not mentioned	Not mentioned	Not mentioned

[a] Serious Adverse Event;
[b] Suspected Unexpected Serious Adverse Event;
[c] Drug Development Safety Update Report;
[d] China Food and Drug Administration.

GCP-2020, after acquiring safety-related information from any resource, only sponsors can immediately analyze and evaluate the safety information and promptly report SUSAR to the Ethics Committee. There is a risk that this process may lead to omissions in the SUSAR report. For example, a test drug-related SAE that is evaluated as expected by sponsors but unexpected by investigators should also be reported to the Ethics Committee.

4. Suggestions on countermeasures

4.1. Establish a safety management information system

Ethics Committees should establish a safety management system to enable clinical trial investigators to conveniently and systematically manage SAEs and SUSARs on site. Investigators could then comprehensively analyze and evaluate the risks of subjects, produce a periodic risk evaluation report, and report to the Ethics Committee on a timely basis [6].

4.2. Propose periodic reporting requirements for security information

Reference safety information (RSI) in the investigators' brochure is the main source of information regarding an unexpected SAE [6]. However, as regulated in GCP-2020, sponsors need only update the investigators' brochure once a year during the clinical trial. This update frequency is too low. Therefore, sponsors should report out-of-hospital and inconsistent SAEs periodically (for example, every three months) to the Ethics Committee and update the investigators' brochure accordingly.

4.3. Conduct risk-based ethical reviews and ethical routine site visits

After receiving center-specific SUSAR submitted by sponsors, it is recommended that investigators compare RSI in the investigators' brochure with the SAE reports in their own center. Investigators should then report SAEs withdrawn from the brochure by sponsors and important differences in interpretations by investigators and sponsors to the Ethics Committee. The Ethics Committee should also carry out a risk-based ethical review and establish an ethical routine site visit system to verify whether clinical trial safety management complies with the ethics-related requirements, thus protecting the safety and rights of subjects [7–9].

Declaration of Competing Interest

No conflict of interest.

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