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An overview of ethical review committees in Japan: examining the certification applications of ethical review committees

Yoshihiko Iijima[1], Kazuyoshi Ogasawara[1], Soichiro Toda[2], and Tadao Takano[2]

[1]*Medical Research and Clinical Promotion Office, Nagoya University Hospital, Nagoya, Japan*
[2]*Clinical Research Innovation and Education Center, Tohoku University Hospital, Sendai, Japan*

ABSTRACT

The survey involves examining the applications from 142 institutions that have consented to make available all certification applications from 2015 and 2016 to a research project for building a certification system for an ethics committee run by the Agency for Medical Research and Development. The number of certified institutions is 20 (14.1%). In the applications from uncertified institutions, there are cases in which requirements of ethics guidelines are unmet, and there is insufficient information provided on regulation and procedure.

An analysis of the committee members who can contribute as members of the general public (general public committee members) has indicated that the number of committee members who do not belong to an institution in which an ethics committee is instituted (external committee members) is 41 (95.7%) among the certified institutions and 224 (84.5%) among the uncertified institutions. The proportion of general public committee members drawn internally from institutions tends to be higher among uncertified institutions.

While a separate committee examined conflicts of interest in research in 19 certified institutions (95.0%), such conflicts were found in 41 uncertified institutions (33.9%) by the ethics committee.

The survey confirms that the challenge lies in increasing the number of external committee members and in further improving the system to manage conflicts of interest, and the education and training regime.

Keywords: research ethics, research ethics committee, certification of ethical review committees, quality of research reviews

Abbreviations:
AMED: Agency for Medical Research and Development
ERCs: ethical review committees

INTRODUCTION

As of April 2017, approximately 1,700 ethical review committees (ERCs) were registered in the Ethical Review Committee Reporting System of the Japan Agency for Medical Research and

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Corresponding Author: Yoshihiko Iijima, MD, PhD
Medical Research and Clinical Promotion Office, Nagoya University Hospital, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8560, Japan
Tel: +81-52-744-2973, Fax: +81-52-744-2973, E-mail: iijima@med.nagoya-u.ac.jp

Development.[1] Furthermore, as of November 2017, approximately 1,269 ERCs that review clinical trials, which collect findings pertaining to the use of medications to obtain state approval, were registered.[2] Thus, it can be estimated that there are approximately as many as 3,000 committees reviewing clinical trials in Japan, if we count only those that are registered in the public system.

Meanwhile, even though clinical research has become more sophisticated and complex, when it comes to the ethical review of clinical research, the review criteria and focal points still remain unclear. There are indications of inconsistencies in the quality of the committees' work.[3]

Under these circumstances, in 2014, the Ministry of Health, Labour and Welfare launched the Project for the Certification of Ethical Review Committees, which evaluated the ethicality, safety, and scientific validity of clinical research (the project was delegated to the Agency for Medical Research and Development (AMED) in fiscal year 2015). The project aims to improve the quality of reviews conducted by ERCs.[4] When certifying ERCs, after reviewing application documents submitted by each institution regarding the implementation system, the situation concerning research reviews, etc., based on pre-established certification requirements,[5] a field survey is conducted to investigate whether everything is actually done as described in the application documents. We analyzed the application data of 142 institutions who applied for certification to the "Project for the Certification of Ethical Review Committees" between fiscal years 2015 and 2016, thereby attempting to clarify the current situation of ERCs in Japan and the issues they face.

OVERVIEW OF INSTITUTIONS SURVEYED

Of the institutions that applied for certification to the "Project for the Certification of Ethical Review Committees" between fiscal years 2015 and 2016, we studied the application data of 142 institutions who had granted their consent for the use of the documents in this study. The total number of application data is not publicly disclosed. However, this survey may not be subject to selection bias, because the 142 institutions includes most leading institutions in Japan. Of the 142 institutions, there were 48 universities (33.8%); 61 hospitals, including university hospitals (43%); 13 other research institutions (9.2%); and 20 other institutions (14.1%). The number of ERCs established by the institutions is as follows: 121 institutions (85.2%) have established 1 committee each, 14 institutions (9.9%) 2 committees each, 2 institutions 3–4 committees each, and 5 institutions (3.5%) over 5 committees each. In total, the institutions that submitted applications for certification have established 164 ERCs.

RESULTS

Certification rate

Of the 142 institutions, 20 were certified (14.1% certification rate). Furthermore, on examining the certification rate of ERCs by parent bodies, we find that: ERCs established by 11 out of the 48 universities (22.9%) were certified, ERCs established by 5 out of the 61 hospitals (including university hospitals) (8.2%) were certified, ERCs established by 3 out of the 13 (23.1%) other research institutions were certified, and ERCs established by 1 out of the 20 other institutions (5%) were certified (Fig. 1).

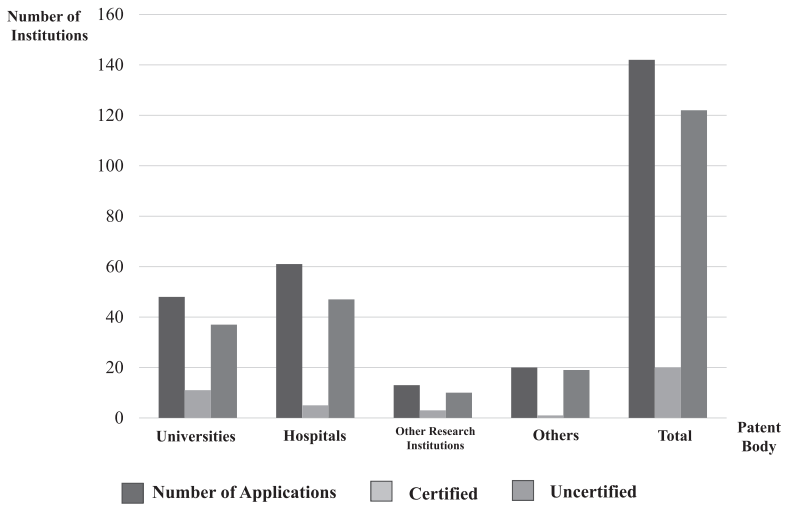

Fig. 1 Ethical Review Committee Certification System: Certification rate

Composition of ERCs

The average number of members in ERCs (n=164) was 13.6. The average number of the so-called external committee members per committee was 4.4. There were 139 (97.8%) institutions that had established committees with 2 or more external committee members, but committees established by 2 organizations did not include external committee members.

Furthermore, the average number of female members per committee was 3.5. ERCs consisting of both sexes were established by 141 of the institutions, whereas one of the institutions established a committee consisting of only male members.

If we focus on those who can express their opinions from a general standpoint (hereinafter referred to as "members who can provide opinions of the general public including viewpoints of research subjects") (n=362), 94 committee members belonged to an institution (26%), whereas 265 (73.2%) did not. In the committees established by certified institutions, there were 4 such members who belonged to an institution and 41 who did not (n=45), whereas in the committees established by uncertified institutions, there were 90 such members who belonged to an institution and 224 who did not (n=314) (Fig. 2). Their occupations were quite diverse. Mainly, there were 83 office workers who worked for the institutions, 43 general citizens, 38 people affiliated with nonprofit organizations (NPOs), 28 university faculty members, and 20 corporate officers, office workers, Rotary Club members, etc. (Table 1).

Conflicts of interest screening systems pertaining to the research topic

Conflict of interest screening systems varied among the institutions. In 83 institutions, "separate committees specializing in conflicts of interest conduct screening and submit the results to ERCs." In 42 institutions, "separate committees conduct screening, after which the secretariat confirms the results," and in one of the institutions "no screening is conducted."

Secretariat

A total of 139 institutions have secretariats, while one institution (uncertified) does not. Furthermore, 133 institutions have help desks. The average number of secretarial employees was 3.4, 1.9 of which were full-time employees. Of the 132 heads of secretariats, 26 were

"doctors," 4 nurses, 26 pharmacists, and 76 clerical workers. The screening results were shared as "documents" (137 institutions), through "email" (81 institutions) and "phone" (32 institutions: 3 certified, 29 uncertified) and on "website" (multiple answers).

Managing the conflicts of interest pertaining to the committee members

While 75 institutions required that the members of the committees they have established submitted a declaration of conflicts of interest, 67 institutions did not have any such requirements. While committees of 131 institutions checked their members' conflicts of interest with respect to research topics prior to conducting a review, committees of 11 institutions did not.

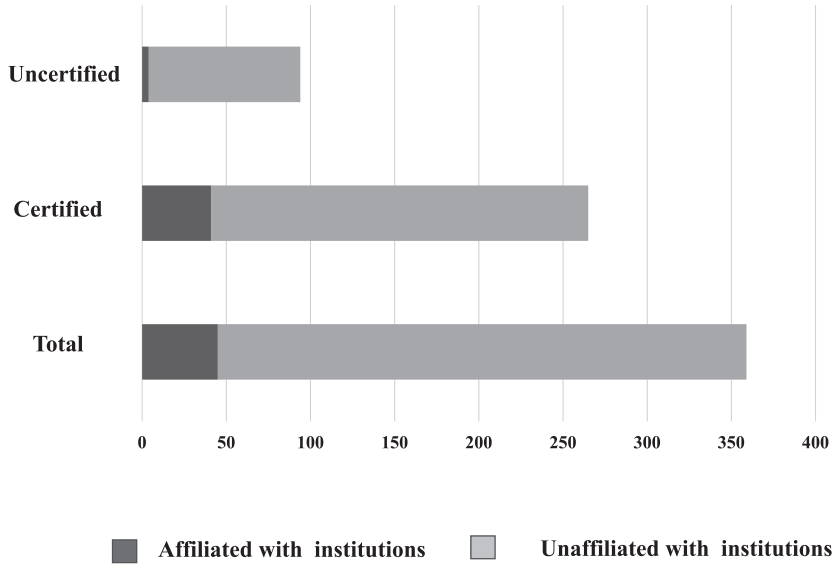

Fig. 2 Members who can provide opinions of the general public including views on research subjects

Table 1 Members who can provide opinions of the general public including views on research subjects

Detailed Occupational Description	No of people
Intraorganizational secretarial employees (department head, section chief, chief clerk)	83
General citizens	43
NPOs and Associations (Foundations)	38
University faculty members/Research institute staff (including the University President)	28
Corporate officers, office workers, and Rotary Club members	20
Teachers (headmaster, teacher, educational committee members, etc.)	16
Patients Association (including association of victims of medical accidents, etc.)	13
Secretarial employees (external), including auditors	11
Healthcare professionals, nurses, childcare workers, counsellors, etc.	11
School advisors, social welfare corporation employees, preschool principals, etc.	9
Members of the press	9
Volunteers	9
Administrative officials (mayor, government official, etc.)	8
Religious workers (head priest, etc.)	8
Welfare workers	6
Housewives (househusbands)	6
Mediation Committee Members, etc.	5
Lawyers (including certified social insurance and labor consultant) and Accountants	5
Members of the Diet	3
Academic experts	3
Consumer organization employees	2
Consultants	2
Freelance writers	2
Cultural class organizers	1
Part-time workers	1
Labor union staff members	1
Unemployed	1
Unspecified	14
Total	362

State of education and training provided to committee members

While 123 institutions provided induction training to newly appointed committee members, 19 institutions did not. While 127 institutions provided continuous training to committee members, 15 institutions did not. Those institutions that did not provide continuous training were all uncertified.

Various methods of training were used. While 113 institutions held training seminars, 27 institutions did not. As for the annual frequency of workshops: 69 institutions (48.6%) held 1 workshop per year, 39 institutions (27.5%) 2 workshops per year, 12 institutions (8.5%) 3 workshops per year, 18 institutions (12.7%) 4–6 workshops per year, 14 institutions (9.9%) 7–9

workshops per year, and 6 institutions (4.2%) over 10 workshops per year. With regard to E-learning, 100 institutions introduced it, whereas 42 institutions did not. Although 113 institutions provided opportunities to participate in external training sessions, 20 institutions did not offer such opportunities.

Management of ERCs

Regulations pertaining to committee organization and management were introduced by most of the institutions with the exception of one uncertified institution. Methods of adopting a resolution were stipulated by 138 institutions, whereas 1 uncertified institution did not stipulate any such methods. Methods of adopting a resolution when a unanimous vote is problematic were stipulated by 112 institutions. Further, 27 institutions required a "unanimous vote," whereas 2 uncertified institutions did not introduce any stipulations regarding this matter.

With regard to the time required for a committee meeting, 19 institutions answered "less than 1 hour," 76 institutions answered "1–2 hours," 32 institutions answered "2–3 hours," and 14 institutions answered "over 3 hours."

Entrustment of ethical reviews

A total of 119 institutions, including all 20 certified institutions, were entrusted with ethical reviews by other institutions. On the other hand, 22 institutions (all uncertified) did not have a system in place to encourage other institutions to entrust them with ethical reviews. In 2016, 9 out of 14 certified institutions were entrusted with conducting ethical reviews, whereas 34 out of 47 uncertified institutions were not.

DISCUSSION

Many of the ERCs surveyed in this study seem to be driven to seek assurance of the quality of ethical reviews and establish systems to appropriately assess ethicality and scientific validity. However, the overall certification rate remained low at 14.1%. Some of the committees did not comply with Japan's "Ethical Guidelines for Medical Research Involving Human Subjects (Public Notice of the Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labour and Welfare No. 3 of 2014)." For example, there was one committee that did not include members of both sexes, and there were two committees that did not include multiple external committee members. Furthermore, education and training for committee members was not provided in approximately 14% of the institutions. A survey of 378 ERCs conducted in 2013 reported that 12.4% of the institutions did not include external committee members, and 6.2% did not have female members. Some of the institutions reportedly did not comply with the guidelines. The following can be suggested as countermeasures: ensuring registration with the "Ethical Review Committee Reporting System,"[1] and ERCs' guideline compliance checks conducted by government agencies.[7] Furthermore, since public disclosure of legal compliance with "Ethical Guidelines for Medical Research Involving Human Subjects" is required in the system, it is necessary that ERCs that have not disclosed legal compliance are considered out of compliance with the guidelines.

Similar problems were observed among ERCs in the USA. The U.S. Federal policy requires that an IRB have at least five members of varying backgrounds including a chair person, a scientific member, a non-scientific member, a representative of the community not affiliated with the institution, and a member of the institution. The diversity of members' backgrounds is important for taking into consideration their advice and counsel in safeguarding the rights and welfare of

human subjects. Federal regulations also state that ERCs should be sufficiently qualified through the experience and expertise of its members.[8] However, the data from a survey of university ERCs in the USA show that ERCs were predominantly white and male. Thirty-six percent of ERCs were all white, while one in ten had less than 10 percent female membership. Also, most ERCs offered minimal (less than four hours) training, and 25% offered no training at all.[9]

Our analysis and examination of the application documents indicated that the majority of the institutions have been making improvements with regard to the items in the application form. Nevertheless, the certification rate was a low 14.1%. There are administrative inadequacies that cannot be revealed by screening the application data, and it can be surmised that the discovery of inadequacies by conducting field surveys was one of the reasons for the low certification rate. Since this is a limitation of the study, please consider including suggestions to overcome this limitation in future studies. However, as the passing rate pertaining to application screening and the results of field surveys are not publicly disclosed, the actual indications of field surveys are unclear, which is a limitation of this study.

In this study, the biggest differences between ERCs of certified and uncertified institutions were related to general standpoint committee members, secretariat, and the entrustment of ethical reviews by other institutions.

Reviewing a total of 362 general standpoint committee members revealed the following considerable difference between certified and uncertified institutions: 91.1% of the general standpoint committee members of certified institutions were external committee members, whereas 71.3% of the general standpoint committee members of uncertified institutions were external committee members. Moreover, in some of the uncertified institutions, the administrators of the institutions, such as secretariat heads or department heads, were committee members. For someone in an administrative position at an institution, it may not be possible to express their opinions freely from a general standpoint, which leaves room for improvement. Furthermore, general standpoint members come from diverse occupations. According to the survey of 362 ERC members (171 healthcare professionals; 191 non-healthcare professionals), there were several educational staff members and civil servants among the 46 general standpoint committee members, namely, 18 "retired" university faculty members, educational staff members, civil servants, 8 civil servants, 6 corporate officers, 4 educational staff members, 3 people involved with patient's associations, 3 housewives, 2 office workers and 2 self-employed people.[10] The fact that there were healthcare professionals as well as specialists in law and religion among general standpoint committee members in this study complicates compliance with ethical guidelines, which clearly distinguish general standpoint committee members from committee members specializing in the field of humanities and social sciences. However, it is not clear as to what kind of qualities general standpoint members are required to have. Therefore, further consideration of the required qualities for general standpoint committee members is necessary.

In the USA, the new National Institutes of Health (NIH) Policy on the use of central ERCs for multi-site research was adopted primarily to simplify and accelerate the review of complex multisite clinical trials.[11] However, accelerating a review requires overcoming a number of obstacles. Perhaps the most substantial obstacle is the time and effort needed to develop reliance agreements among the participating sites.[12]

A trend toward the spread of central ERCs has taken place in Japan too. With regard to entrustment of ethical review by other institutions, 81% of the institutions had a system in place to promote it. However, only 42.6% of the institutions have actually been entrusted with conducting ethical reviews by other institutions. Under the guidelines that are in place in Japan, entrustment of ethical reviews is permitted systematically, but it is not widely practiced yet. Under these circumstances, AMED launched the Project for Development of Central Institutional Review

Board in 2016. This project aims to reinforce the system under which centralized ethical reviews are conducted and improve its management. Furthermore, it targets qualitative homogenization of the reviews of multicenter collaborative research, consolidation of ERCs, and improvement of the efficiency and speed of the reviews.[13] Since the enactment of the Clinical Research Act in April 2016, the clinical research ERCs newly certified by the Ministry of Health, Labour and Welfare (MHLW) must be entrusted by other institutions to conduct ethical reviews of "specific clinical research." Hence, central ethical reviews are promoted systematically.[14]

Secretariats of ERCs were established in most of the institutions, and the average number of employees at a secretariat was 3.4. However, since duties other than conducting reviews may be included, the number of people in charge of ERC-specific office work may be lower. Making necessary provisions for the secretariats that manage ERCs is indispensable for conducting high-quality ethical reviews. As the application forms that are subjected to screening must have been provided to conduct a thorough review, the secretariat must check the application data. It can be argued that the secretariats support ethical reviews by managing ERCs, checking and documenting application data, and by having full-time faculty members conduct preliminary reviews depending on circumstances.[15] In some of the institutions, full-time faculty members examine the content of the research, point out issues and provide guidance, and it becomes necessary to share responsibilities with the so-called academic research organizations (ARO) that provide support for clinical research. Although there is concern that the review will be reduced to a formality if the content of the research is examined and adequate improvements are made at the preliminary stage, it may allow ERCs to focus on the ethical issues inherent in the research plan.

This study examines application data submitted to the Project for Certification of Ethical Review Committees and aims to clarify the current state and issues of ERCs established in institutions seeking to conduct high-quality ethical reviews. This study investigates fundamental issues in conducting high-quality ethical reviews, and also suggests measures to deal with those issues. However, this study has some limitations as well. As the passing rate pertaining to application screening and the results of field surveys have not been clarified, it is a mere examination of application data self-reported by the institutions. Therefore, it is unclear whether ERCs actually operate as described in the application documents. Furthermore, as the systems of reviewing various clinical research studies are diverse, there are reservations as to whether the summary made in this study accurately represent actual ethical review systems.

CONCLUSION

Among the application data submitted to AMED's Project for Certification of Ethical Review Committees between the fiscal years 2015 and 2016, we analyzed the application data of 142 institutions, who had granted their informed consent, to examine the current state and issues pertaining to the ethical review of research. Of the 142 institutions, only 20 (14.1%) were certified. Some of the institutions that were not certified did not meet the requirements specified in ethical guidelines.

Issues elucidated in this study included the fact that a considerable number of administrators within the institutions were appointed as general standpoint members and the fact that the practice of centralized ethical reviews was not spreading. The authors of this paper believe that it is necessary to increase the number of external committee members to offset the influence of the administrators of institutions, promote centralized ethical review and increase researchers' ethical literacy by further improving training systems.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest directly relevant to the content of this manuscript.

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