Kyushu University
Institutional Review Board (Observational / Intervention) Standard Operating Procedure

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Chapter 1 Overview

No. 1 Purpose of Manual

The purpose of this manual is to complement the "Kyushu University Regulations for Medical and Biological Research Involving Human Subjects" (2021 Kyushu University Regulations No. 48), "Kyushu University Institutional Review Board for Clinical Trials Regulations," and "Kyushu University Institutional Review Board for Clinical Research Regulations" and, of the ethical review boards established among Kyushu University's Medical Institutions, prescribe the operating procedures for those ethical review boards stipulated in No. 3 (hereafter, "ethical review boards").

No. 2 Scope of Manual

The ethical review boards shall review the following.

Research which falls under the scope of application of the "Ethical Guidelines for Medical and Biological Research Involving Human Subjects (2021 Ministry of Education, Culture, Sports, Science and Technology; Ministry of Health, Labour and Welfare; and Ministry of Economy, Trade and Industry Notification No. 1)."

However, this excludes research which falls under the scope of application of the "Guidelines on the Distribution and Use of Human Embryonic Stem Cells (2014 Ministry of Education, Culture, Sports, Science and Technology Notification No. 174)," "Guidelines for Gene Therapy Clinical Research (2002 Ministry of Education, Culture, Sports, Science and Technology and Ministry of Health, Labour and Welfare Notification No. 1)," "Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Act No. 145 of August 10, 1960)," "Act on Ensuring the Safety of Regenerative Medicine (Act No. 85 of 2013)" and "Clinical Trials Act (Act No. 16 of April 14, 2017)."

Chapter 2 Activities of Ethical Review Boards

No. 3 Categorization of Ethical Review Boards

The following ethical review bodies are covered by this manual.

<table>
<tr><th>Category</th><th>Board name</th><th>Target institution for review</th><th>Object of review</th><th>Guidelines</th></tr>
<tr><td rowspan="2">Research ethics</td><td>Kyushu University Medical Institutions Institutional Review Board for Clinical Research</td><td rowspan="2">Faculty of Medical Sciences, Faculty of Dental Science, Faculty of Pharmaceutical Sciences, Medical Institute of Bioregulation and Kyushu University Hospital</td><td>Review of research plans for observational studies</td><td rowspan="2">Ethical Guidelines for Medical and Biological Research Involving Human Subjects</td></tr>
<tr><td>Kyushu University Hospital Institutional Review Board for Clinical Trials</td><td>Review of research plans for intervention studies</td></tr>
</table>

No. 4 Requirements for Ethical Review Board Establishment

Ethical review boards must satisfy the following requirements.

1. Establish an administrative processing section for the handling of review requests from principal investigators and make the contact information for this section clearly known. (The following are the administrative processing sections for the ethical review boards covered by this manual.)

Ethical review board	Administrative processing section
Kyushu University Institutional Review Board for Clinical Research	Administrative Office Academic Research Cooperation Division, Bioethics Section TEL: 092-642-6772 Ext.: 6772 FAX: 092-642-6776
Kyushu University Institutional Review Board for Clinical Trials	University Hospital Administration Department Research Support Division, Section of IRB & Ethics Committee Administration TEL: 092-642-5082 Ext.: 5082 FAX: 092-642-6024

2. Secure enough administrative personnel to ensure the ongoing operation of the ethical review board, and have enough of a financial base to enable regular meetings of the ethical review board over the long term.

3. Ensure members of the ethical review board are independent of the research they are reviewing, and accurately publicize the ethical review board as per the provisions of No. 5-3.

No. 5 Obligations of Those Establishing Ethical Review Boards

1. The heads of the Medical Institutions comprising the "Medical Ethics Council" shall, in line with Article 8 of the "Kyushu University Regulations for Medical and Biological Research Involving Human Subjects," jointly establish ethical review boards and assign the duties that members of the ethical review boards and the boards' administrative staff will perform.

2. A principal investigator shall submit application forms to the relevant ethical review board and shall request its opinion. The principal investigator shall, after receiving the opinion of the ethical review board, submit these results, along with all documents submitted to the ethical review board and all documents requested by the head of the institution conducting the research (hereafter, "research director"), to the research director in order to seek permission to conduct the relevant research. The same process shall be followed even in the case of multi-institutional joint research when the review is entrusted to an ethical review board in another institution.

   In cases of multi-institutional joint research, the term "research representative" is used as an equivalent term for "principal investigator."

3. The heads of the Medical Institutions, when starting operation of an ethical review board, must publicize the ethical review board's structure and operational regulations, as well as list of board members, on the ethical review board reporting system. Also, at least once per year, those establishing an ethical review board must publicize the status of the board's meetings and a summary of its reviews on the ethical review board reporting system. However, this shall not apply to information contained in review summaries which the ethical review board deems must not be publicly disclosed so as to protect the human rights of research subjects and related parties, as well as other relevant parties, and to protect the rights and interests of researchers and related parties, as well as of other relevant parties.

4. The heads of the Medical Institutions must take all necessary measures to ensure that the ethical review board members and administrative staff receive training and education related to reviewing and other associated duties.

5. The heads of the Medical Institutions must cooperate with investigations conducted by government ministers and officials with regard to ethical review board compliance with the Guidelines in the context of board structure and operation.

No. 6 Roles and Responsibilities of Ethical Review Boards

1. When a principal investigator seeks the opinion of an ethical review board about the propriety of conducting research, the board shall conduct a fair and impartial review, from an ethical and scientific standpoint and in accordance with relevant guidelines, of all pertinent information, including information pertaining to conflicts of interest for the research institutions and researchers and related parties connected with the research, and shall then deliver its opinion in writing or via an electromagnetic method. In conducting the review, the written opinion of the Conflict of Interest Management Committee shall, when necessary, accompany the review documents of the ethical review board.

2. With regard to research reviewed as per the stipulations of Paragraph 1, when it is necessary to investigate what considerations are being made towards protecting the human rights and welfare of research subjects, or whether there are factors which could change the overall assessment of expected benefits and risks for research subjects, an ethical review board may carry out an investigation for that clearly defined purpose and deliver its opinion to the principal investigator on any changes that need to be made to the research plan,

whether the research should be discontinued, etc.

3. With regard to research reviewed as per the stipulations of Paragraph 1, when it is necessary to investigate whether there are fabrications or falsifications in the research content, an ethical review board may carry out an investigation for that clearly defined purpose and deliver its opinion to the principal investigator on any changes that need to be made to the research plan, whether the research should be discontinued, etc.

4. In the event of a situation, such as an unintentional and/or improper leak of information related to research reviewed as per the stipulations of Paragraph 1, which raises serious concerns from the standpoint of respecting research subjects' and related parties' human rights, of research implementation, and/or of ensuring the impartiality or fairness of the review, ethical review board members and those tasked with carrying out board administrative duties must promptly report this to the research director.

5. Prior to performing reviews and related administrative tasks, ethical review board members and those tasked with carrying out board administrative duties must receive education and training in the ethical guidelines and various research-related rules to follow which will equip them with the knowledge required to carry out reviews, such those intended to determine the propriety of research implementation. Subsequent education and training must also be undertaken on an ongoing, as-needed basis. This education and training need not be limited to workshops given within the research institution of the ethical review board in question but can also encompass workshops at external organizations, e-learning, etc.

No. 7 Undertaking Ethical Review for Another Institution

1. When requested by a principal investigator at another institution, an ethical review board may perform a review of research to be conducted at that institution. In such cases, the review must be carried out in consideration of the research administration system at the institution and of other systems deemed necessary for research implementation.

2. In the case stipulated in the preceding paragraph, if the principal investigator of the institution continues to request reviews related to the research, these must be carried out and opinions offered.

No. 8 Entrusting Ethical Review to Another Institution

1. Requests for reviews by ethical review boards at other institutions can be made to ethical review boards established at one of the following institutions.
   1) Clinical Research Core Hospitals
   2) Boards recognized by the Ministry of Health, Labour and Welfare Ethical Review Board Certification Project
   3) The 6 National Research Center for Advanced and Specialized Medical Care
   4) Other institutions approved by the research director

2. The principal investigator, following the procedures stipulated in No. 5, and based on the results of institutional review stipulated in the preceding paragraph, shall submit an "Implementation Authorization Request to Conduct Medical and Biological Research Involving Human Subjects" to the research director, and the relevant authorization to perform research must be provided in writing.

No. 9 Ethical Review Board Composition and Meeting Requirements

1. The composition of ethical review boards must satisfy each of the following requirements so that they can appropriately carry out their duties, such as reviewing research plans, and 1) through 3) cannot be satisfied by any one person concurrently. The requirements shall be the same for holding meetings.
   1) Must include an expert in the natural sciences, such as a medical or healthcare professional.
   2) Must include an expert in the humanities and social sciences, such as an ethics or legal professional.
   3) Must include someone capable of giving an opinion from a general perspective, including that of

the research subject.

4) Must include multiple people who do not belong to the same institution as the person(s) establishing the ethical review board.

5) Must comprise male and female members.

6) Must have at least five members.

2. The researchers and related parties involved in conducting the research under review must not be present while the ethical review board is deliberating and deciding its opinion. However, they may attend meetings at the request of the ethical review board in order to provide research-related explanations.

3. The principal investigator who requested the review must not be present while the ethical review board is deliberating and deciding its opinion. However, he or she may attend meetings with the board's permission when the board needs to explain the content of the review to him/her.

4. Ethical review boards may, when deemed necessary by the chairperson in light of the subject, content, etc., of review, request the attendance of non-members in order to provide an explanation or opinion from a specialist's standpoint.

5. When reviewing and giving an opinion about research plans which involve research subjects requiring special consideration, ethical review boards must, when necessary, seek the opinions of those with insight into said research subjects.

No. 10 Chairperson and Vice-Chairperson

1. Each ethical review board shall have a chairperson and vice-chairperson who are chosen by mutual election among board members.
2. The chairperson shall convene the ethical review board, preside over meetings and exercise general control over the board's business.
3. The vice-chairperson shall assist the chairperson and, when other commitments, illness or accident prevent the chairperson from attending to his or her duties as chairperson, the vice-chairperson shall serve as acting chairperson.

No. 11 Confidentiality Obligations of Board Members and Board Administrative Staff

Board members and those who perform review-related administrative duties must not leak, or allow to leak, to anyone outside of the ethical review board any information acquired during the review process. The same shall apply after the completion of said board-related duties.

No. 12 Ethical Review Board Meetings

As a rule, the chairperson shall convene a meeting of the ethical review board once per month. However, meetings can be convened whenever necessary to accommodate a request from the research director for an urgent opinion.

No. 13 Attendance by the Research Director

The research director may attend meetings of the ethical review board to provide his/her opinion; however, he/she may not be present while the board is deliberating and deciding its opinion.

No. 14 Board Members Related to Research

Board members who are part of the implementation structure for research which is the subject of board review may not be part of the review process for said research. However, they may attend as part of the applicants to provide their opinion.

No. 15 Object of Review

Ethical review boards will investigate, deliberate and vote on the following matters and will create accompanying records.

1) Matters relating to the ethical and scientific appropriateness of research to be conducted
2) Matters for investigation/deliberation when continuing or concluding research
3) Other matters deemed essential by the board

No. 16 Most Current Review Materials

Ethical review boards shall perform reviews using the most current materials submitted by applicants. Review materials encompass any of the following.

1) Application
2) Research implementation plan
3) Explanatory documents and consent forms
4) Information disclosure documentation for research subjects
5) Conflict of interest update form
6) Copy of clinical research insurance contract or estimate
7) Copy of the review board notification of approval for the main research institution
8) Table of research alterations
9) Other essential materials

No. 17 Explanation to Ethical Review Boards

When conducting a review, an ethical board may, as a rule, have the researchers and related parties involved with the implementation of the research under review attend the review board meeting to provide the members with an explanation about the research.

No. 18 Board Deliberation

As a rule, board members who do not participate in deliberations may not participate in voting. However, the deliberation format shall include deliberation in absentia using written documents.

No. 19 Ethical Review Board Vote Approval

As a rule, approval of a decision must be made by a unanimous vote of all board members. However, if there is difficulty in achieving unanimity, the chairperson may, when necessary, allow approval by a majority vote of those members present. However, even in such situations, the chairperson shall endeavor to ensure that the minority opinion is respected as much as possible in the vote.

No. 20 Ethical Review Board Decisions

Ethical review board deliberation result decisions shall encompass any of the following.

1) Approval
2) Qualified approval
3) Changes recommended
4) Put on hold (conduct re-review)
5) Disapproval
6) Not applicable
7) Revocation of approval

No. 21 Qualified Approval and Changes Recommended

When the board's decision regarding the research is "qualified approval" or "changes recommended," the ethical review board chairperson shall confirm and approve revisions received from the applicant. In such cases, the chairperson may, when necessary, seek the opinion of other members.

No. 22 Reporting of Deliberation Results

The ethical review board chairperson shall report the deliberation results to the principal investigator in a "Deliberation Results Report" or similar format. The ethical review board chairperson shall entrust report creation and reporting duties to the relevant section according to the categories stipulated in No. 4-1.

No. 23 Research Implementation Status Report

Ethical review boards shall review the content of research implementation status reports and either give the principal investigator approval to continue or shall make necessary recommendations.

No. 24 Expedited Review

1. Ethical review boards may perform expedited reviews of the following matters.
    1) Reviews of research conducted jointly with another research institution and already subject to an overall review by an ethical review board at the joint research institution, with said opinion being that the research is appropriate
    2) Reviews relating to minor alterations in research plans
    3) Reviews relating to research involving no invasive procedures and no interventions
    4) Reviews relating to research involving minimally invasive procedures and no interventions

2. The ethical review board chairperson will report the results of expedited reviews to the ethical review board. The members of the board who receive the expedited review results report may, with reason, ask the chairperson to have the matter in question reviewed again by the board. If the chairperson agrees that there is sufficient reason, he/she must promptly convene a meeting of the board to review the relevant matter.

3. The procedures for expedited review by the different ethical review boards shall be carried according to category, as stipulated in No. 25 and No. 26.

No. 25 Expedited Review by the Kyushu University Institutional Review Board for Clinical Research

1. When conducting expedited reviews, the Kyushu University Institutional Review Board for Clinical Research may entrust said reviews to a document reviewer, as per Article 7 of the separately established "Kyushu University Institutional Review Board for Clinical Research Regulations." In such cases, it shall be handled in line with the categorization used in the attached table.

2. In the case of expedited reviews of already approved research content which contain any of the following small alterations only, the review can be handled by the chairperson.
    1) A one year or longer extension of the research period from its starting date
    2) Change of principal investigator and changes accompanying this, such as a change in location of where research is conducted
    3) Change of joint research institution and party to which duties are outsourced
    4) Change in the number of target cases and research subject target period
    5) Change in research items which do not increase the degree of invasiveness
    6) Other matters as determined by the chairperson

However, if the chairperson is the applicant or a member of the research team, this decision shall be made by the vice-chairperson. Further, if both the chairperson and the vice-chairperson are the applicant or members of the research team, this decision shall be made by a member of the board nominated by the chairperson.

3. In the case of expedited reviews of already approved research content which contain any of the following alterations only, the board shall receive a report from the principal investigator of the changes made, and only these changes then need to be checked.
   1) Extension of the research period by less than one year
   2) Change of research team members conducting research under the principal investigator and changes accompanying this, such as a change in location of where research is conducted
   3) Change of institution which is only providing samples/information
   4) Other changes as approved by the Board

No. 26 Expedited Review by the Kyushu University Institutional Review Board for Clinical Trials

Expedited reviews conducted by the Kyushu University Institutional Review Board for Clinical Trials shall be handled in accordance with Article 16 (Simplified Review Handling by the Secretariat) of the separately established "Standard Operating Procedures for the Secretariat of the Kyushu University Certified Institutional Review Board for Clinical Trials."

No. 27 Public Release of This Manual

The regulations and manuals relating to the operation of ethical review boards, as well as the names of ethical review board members shall be made public. This shall be accomplished by publishing these materials on the Internet, e.g. on the Kyushu University Hospital homepage.

No. 28 Public Release of Meeting Minutes

With due consideration given to protecting intellectual property rights and to protecting the personal information and privacy of trial subjects, the minutes of ethical review board meetings shall be made publicly available on the ethical review board reporting system of the Ministry of Health, Labour and Welfare.

No. 29 Operation of Ethical Review Boards

The research directors shall assign the administrative tasks involved in the running of ethical review boards to the relevant section according to the categories stipulated in No. 4-1.

No. 30 Records Relating to Ethical Review Boards

Documents (including electromagnetic records and other media) to be preserved which relate to ethical review boards shall be kept for ten years by the relevant section according to the categories stipulated in No. 4-1. The principal record keeper for said records shall be the head of the relevant section. In all cases, the separately established "Kyushu University Document Management Regulations" and "Kyushu University Information Disclosure Handling Regulations" shall be followed and, in the case of document preservation in hospitals for the Institutional Review Board for Clinical Trials, said documents shall also be properly managed in line with the "Kyushu University Hospital Personal Information Protection Regulations" and the "Internal Regulations for Handling Kyushu University Hospital Operational Data."

Supplementary Provisions

1. All revisions to this manual must be approved by the Kyushu University Medical Ethics Council.
2. This manual shall come into effect from June 30, 2021.