6.4 Getting ethical approval for your research

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6.4.1 Learning objectives

To understand the following in relation to applying for ethical approval for a research study in health emergency disaster risk management (Health EDRM), with a focus on WHO guidance:

1. The general processes involved in ethical approval of research projects.
2. The types of document that are usually needed for an ethics application.

6.4.2 Introduction

Research is an essential component in public health – it is the gateway to evidence on the effects of interventions, disease trends, health system structures and processes. In the context of Health EDRM, research is especially important for investigating the effectiveness of emergency prevention, preparedness, response and recovery, and providing an evidence base for decision making. Research that involves living human participants require ethics approval in order to ensure that the people who participate in research are treated ethically, not taken advantage of, and that the research procedure is carried out to high ethical standards; this is discussed in depth in Chapter 3.4, with particular issues for at-risk groups described in Chapter 2.5. Researchers have a duty to promote and ensure respect for all human subjects and protect their health and rights *(1)*. Specific morals that need to be upheld include respect for persons, non-maleficence, beneficence, justice and utility. According to WHO *(2),* best practice is that all research involving human beings should be reviewed by an ethics committee, except for studies which only access publicly available data and do not involve human participants. Ethics approval should be obtained before the study begins from a recognized ethics committee – this chapter introduces the procedure and basic components required for obtaining ethics approval.

6.4.3 Where to request and obtain ethics approval

A research ethics committee (REC) has the responsibility to ensure the ethical safety and scientific merit of the research. It has the authority to reject, approve or cease the research and to require modification to the research protocol. The main responsibility of the REC is to protect the safety of potential research subjects and to evaluate the risks and benefits brought to subjects and the community. In general, RECs evaluate research proposals with reference to established ethical documents *(3-4)*. Each REC may have its own standard. For example, the WHO ethics committee *(5)* is guided by the World Medical Association Declaration of Helsinki *(1)* and the International Ethical Guidelines for Biomedical Research Involving Human Subjects *(6)* . Hence, researchers should check with the REC they intend to approach (in their academic institution, region or country, for example) to identify the documents that will need to be submitted with their application.

RECs are usually based in regional or national public facilities or individual academic institutions. They usually consist of scientific members (with related research expertise) and non-scientific members (with diverse backgrounds) in order to provide for a comprehensive and quality ethical evaluation.

Individual institutions may have their own committees as an internal regulatory process, such as an institutional review board (IRB) or University Human Research Ethics Committee (UHREC). These have the advantage of being able to evaluate the research protocol with local and familiar perspectives and to monitor the study more closely. For example, the community ethics committee of the Center for Bioethics of the Harvard Medical School *(7)* has members from the Greater Boston area, which makes the ethics review a better fit with the local culture and needs. However, financial interests within the studies may present challenges for a local REC such as this to refuse an application or to request significant changes to the research protocol. For that reason, regional or national committees might provide a stronger legitimacy and consistency when reviewing research conducted by the public and research community. For example, the National Health Service (NHS) in the United Kingdom has a Health Research Authority, which is responsible for the management and conduct of national-level research, including the REC process *(8)*.

6.4.4 Research approval for studies that will take place beyond local regions

For studies that will be conducted outside the researchers' local region, the researchers should ensure that the proposed procedure is locally acceptable. The study design should take local culture and tradition into account, and there should ideally be input from local researchers *(9)*. Furthermore, researchers may be required to obtain approval from the relevant foreign authorities, as well as from their host institution. This may require a request to a REC close to the target community, to ensure the evaluation of the research procedures for cultural and legal appropriateness. As Wright, Parker and the Nuffield Council on Bioethics Working Group *(9)* argue, the decision-making of funders, research institutions, RECs and many others should be centred on the priorities and needs of the local community they try to support.

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When applying to the researcher's host institution, the application should indicate that the study will be an international study and that approval from a local REC will be obtained after approval by the host institution. Likewise, the application to a foreign institution should indicate that approval has been obtained from the host institution. When preparing these applications, it is important to remember that the different RECs may follow different processes and require different documents.

6.4.5 What if no REC is available in the affected area?

If no REC is available in the affected region during a health emergency or disaster, such as the 2014 Ebola outbreaks in West Africa, less orthodox actions may be needed to obtain ethics approval *(10-11)*. There is no consensus guideline for this type of situation, but some possible courses of action and their limitations are shown in Table 6.4.1.

Table 6.4.1 Obtaining ethics approval if a local REC is not available: Some possible actions and their limitations

Action	Limitation
Ask the relevant local authorities (such as village elder or community leader) for approval.	Approval might be biased to one or a small number of local authorities.
Ask the relevant local authorities (for example, village elder or hospital director) to organize a review committee.	It takes time to organize a committee and the members might not have the necessary experience for review and decision.
Obtain ethics approval from an international organization (such as WHO).	Approval might not have considered local context.
Obtain approval from an established special review board.	It takes time to organize the committee and must be organized by a trusted organization.

6.4.6 Types of ethics review

Different levels of ethical review may be required depending on the invasiveness of the procedure, urgency and the design of the research. Furthermore, review levels vary across different institutions. The researcher should check the requirements of the target institutions before submitting an application. WHO suggests five common types of ethics review for proposals *(5)*, which are outlined below.

Full committee review of proposals
Research proposals that present more than minimal risk to human subjects are reviewed by two REC members who present the proposal to the full committee, which then has a general discussion before reaching a consensus decision (see Section 6.4.7). Researchers responsible for the proposal under review are subsequently invited to respond to queries raised and to provide clarifications or justifications.

Expedited review of proposals

The proposal is circulated for expedited review when the research procedures present no more than a risk of minimal harm to the research participants or communities. In this case, the proposal is sent to two REC members who are required to provide their feedback to the secretariat within ten working days. The proposal is then either approved or returned to the researcher for further action.

Exemption from REC review

Proposals are exempt from REC review when there is no possibility of harm arising from the conduct of the research or when information being collected is available from a public domain.

Accelerated review

In a public health emergency, such as the investigation of a disease outbreak or a disaster relief operation, an application may be submitted for accelerated review. This is discussed further below.

Continuing review

Since ethics approvals are valid for a limited time period, the REC reviews the progress of the study at periodic intervals. In order to renew the approval, the researchers should submit the necessary documentation to the REC before their approval expires.

6.4.7   Definition of minimal risk

In some decisions around ethics approval, the REC may consider the concept of "minimal risk". There is no global consensus on minimal risk, but similar definitions are used by many organizations and countries. For instance, Australia, Canada, South Africa, USA, and the Council for International Organizations (CIOMS) have a standard for minimal risk which revolves around comparisons and interpretations of 'everyday risks', 'routine examinations' and 'best interest' of the studied population. These standards need to be adjusted for vulnerable research participants such as prisoners, incapacitated adults and children *(12)*. Researchers should check the minimal risk definition of the REC they are applying to before submitting their application for ethics approval.

6.4.8   The need for accelerated review: Limitations of the non-emergency ethics review process during emergencies

Although most of the ethical issues in emergency-related research are not unique to emergencies, in an emergency the perceptions of potential harm, benefit, and trust (including the patient-provider relationship) differ, and this should be considered in the ethics review, as discussed in Chapter 3.4 *(13)*. Furthermore, research during an ongoing emergency or disaster is likely to require a faster approval decision. Accelerated reviews are designated for this purpose, but some existing ethics review system cannot accommodate these. In considering this, Kayano and colleagues *(14)* emphasized the importance of ethics review systems evolving constantly; this is discussed in Case Study 6.4.1.

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Many existing ethics review systems are established to operate in non-emergency situations. However, for emergency research, the complexity of the emergency setting may make it difficult to address practical ethical issues. In such contexts, ethics governance may need to consider non-ideal ethical and methodological approaches rather than insisting on the ideal situation in humanitarian research *(15)*. Decision making will require striking a balance between speed and ethics, with the addition of the voice of the affected communities.

For example, during the Ebola outbreak in 2014-2016, WHO *(16)* was responsible for reviewing and discussing ethics for various interventional and observational studies to control the outbreak. The WHO REC established a subcommittee to conduct accelerated reviews to facilitate this process. This was the first time that the accelerated review was put into practice. The subcommittee reviewed 24 new and 22 amended applications, with an average reviewing time of 6 working days.

6.4.9 The research protocol: what to include when preparing an ethics application

This section lists the documents commonly required as part of an ethics application. However, researchers should always check and understand the specific requirements of the REC they are applying to before submitting their application.

Research Protocol

This is the core document of the application. It describes why the study is needed and how it will be conducted. The WHO recommended format for a research protocol is that it should have the following components *(17):*

- **Project summary:** This summary should include the rationale, objectives, methods, participants, time frame and expected outcomes.

- **General information:** This should include the protocol title (identifying number and date), investigators, sponsors and the locations and institutions where the research will be done.

- **Rationale and background information:** This should describe current knowledge about the research topic and intervention, and the need for the research to be conducted in a disaster, rather than a non-disaster, setting. The proposal should provide basic information about the target population, and the potential benefits and harms of the intervention to them. It should also explain the expected benefits from the research and how these outweigh any potential harms of the study.

- **Study goal and objective:** This should include the intended outcomes and aims for the research, and should be considered alongside the research question (Chapter 3.5).

- **Study design:** This should include the type of study (as discussed in Section 4 of this book) *(18)*, target population, the recruitment procedure, research or diagnostic tools and duration of the study. Information on the study's inclusion and exclusion criteria and any criteria for withdrawal should also be mentioned.

– **Methodology:** This should provide detailed information about the research procedure. This would include information on how the following will be conducted: interventions, measurements, observations, laboratory investigations, and procedures. How participant confidentiality will be ensured should also be included. Standardized and clearly defined procedures will be required for any sites where special protocols are needed. For studies in disaster settings, providing participants with sufficient information about the study and the freedom for participants to choose whether or not to participate are especially important (see Chapter 3.4) and should be clearly stated in the protocol. If the study involves an intervention, the standardized and documented procedure (for example, the frequency of study visit, intervention procedure) should be clearly described and evidence supporting the interventions should be provided (see Chapter 3.3). The procedure for receiving questions and feedback from participants should be clearly defined. If the study is a randomized trial, additional information on randomization, blinding or masking and any stopping criteria for ending the research prematurely will be needed (Chapter 4.1).

– **Safety consideration:** This should describe the safety of the research procedure and how adverse events will be reported. WHO requirements are that this should be compliant with the Declaration of Helsinki and the International Ethical Guidelines for Biomedical Research Involving Human Subjects *(2)*. Investigators should also check whether the REC they are applying to has any special requirements for this.

– **Follow-up:** This should describe what follow-up activities will be provided to the research participants and the duration of this follow-up – for example, follow-up activities relating to data collection or monitoring of adverse events.

– **Data-management and statistical analysis:** This should describe how the data collected will be processed, stored and analysed. Physical and electronic data may have different management protocols and information should be provided about which personnel will have access to the data, and how the confidentiality of participants will be protected.

– **Quality assurance:** This should describe the quality control and quality assurance system for the research.

– **Expected outcome of the study:** This should discuss how the study results might contribute to the advancement of knowledge, how the findings will be made available, and how it may impact on the health services, systems and policies.

– **Dissemination of results and publication policy:** The dissemination process for the findings of a study should include information on the method, policy and responsible personnel, target audience (relevant policy makers, scientific media, the community and participants, for example).

– **Duration:** A detailed timeline of the project should be provided, ideally in months and beginning from the point that ethics approval is received.

- **Anticipated challenges:** This should include the foreseeable problems and possible solutions for the study.

- **Project management:** This should describe the roles and responsibilities of each member of the research team.

- **Ethics:** This should describe the ethical consideration, including issues such as the right to withdraw and power coercion during disaster situations that are particularly relevant to the study. Any procedures that might raise specific ethical issues should be discussed. This section should also describe how informed consent will be taken during recruitment and the relevant documents should probably be included in the application, as discussed below.

- **Conflict of interest:** The researchers should declare any interests that any of them have which are related to the study or its results and might be regarded as a conflict. WHO provides guidance for this online in Guidelines for Declaration of Interests *(19)*.

- **Budget and other financial support:** Some RECs require details on the study's budget and funding source. Researchers should check whether the REC they are applying to requires this.

- **References:** A list of the cited references should be provided to support the content of the protocol.

Informed consent form

An informed consent form is a document used for recruiting potential participants to the research study and obtaining their agreement before they enter it, receive the intervention or have data collected. The form should show study information, and the contact details of the responsible investigators, the ethic committee and of the research institution. It also needs to have space for the name and signature of the researcher (or their representative), the participant and, if necessary, a witness. Procedures should be in place for non-written consent if, for example, potential participants are visually impaired or illiterate *(1)*; obtaining their consent is likely to require the presence of an independent witness and a note (written, audio or video) indicating the person's willingness to join the study.

Patient information leaflet (if available)

The patient information leaflet is a document providing more detailed information on the study, which would be given to potential participants and those who are recruited to the study.

Any associated study instruments

These include questionnaires, interview guides, focus group discussion guides or other documents related to the research intervention. They may be required to be in English and the native language of the participants. The collection procedure should give an explanation and reason for the data collected, especially if any of this is sensitive data.

Final approval document by the scientific/technical review committee, or peer reviewers

If the research intervention involves novel technology or instrument, its implementation should have been already reviewed and approved by peer reviewers or the scientific/technical review committee. The approval document should be provided with the application.

Principal investigator's response to previous review (if the protocol has been submitted before)

If a resubmission is being made to the REC, perhaps following "conditional approval" (which is described below), the researcher should indicate any changes made in the revised protocol in response to the previous review.

Comments made by the other scientific peer review groups (if the protocol has been reviewed by another REC or other committee)

In international studies, approvals from multiple REC may be required. In such cases, any other submissions or approvals should be mentioned, including proof of these.

Information and curriculum vitae (CV) of the researcher(s)

Information, including a curriculum vitae (CV) for each member of the research team may be required by the REC and researchers committee should check the requirements for this with the REC that they will apply to.

Data collection forms, case report forms, patient diaries, and so on (if the study will use these)

Some RECs require these data collection documents to be submitted. The format of each will depend on how the research has been designed, and how the data will be collected and stored.

Recruitment material (if available)

Recruitment material refers to, for example, any advertising tools that will be used to recruit participants to the study. These might be pamphlets, posters or other media. The materials should be compliant with the local culture and language, and should contain sufficient contact information for the researcher and their organization.

6.4.10 Providing potential participants with information on the study

As noted above, the patient information leaflet and informed consent form provide essential background information on the study to potential participants, in lay language. Several components are recommended for both documents. Firstly, they should provide the background and reasons for the study in the target community and explain why the person is being invited to participate. Secondly, they should describe the selection criteria. Thirdly, there should be a clear explanation of the research procedure (including number of visits and estimated research duration), potential safety concerns, rights of participants, data confidentiality, where and how participants can ask questions or raise concerns, procedures and reason for the collection of any sensitive data and the right of the participant to withdraw from the study. Fourthly, contact information of the responsible researcher, the REC and detail of the research institution should be provided.

WHO encourages the use of English and the native language of the participants for these documents. In some cases, the native language version might be prepared after ethics approval *(17)* but the REC should usually be provided with the translated document. Furthermore, if the study will involve multiple distinctive groups, tailored consent might be needed for each of them.

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6.4.11 Approval status

After reviewing an application, the REC will usually make a decision that the application is approved, needs modification or is rejected. RECs usually use four classifications to indicate the status of an application after they have processed it (Table 6.4.2).

Table 6.4.2. The description of each different approval responses of ethics application

Status	Description
Approved as submitted	The proposal is approved and no modifications are required.
Approved conditionally; requires amendments or clarifications	The REC requires clarification or amendment about the application, which the researcher is required to provide before it can move forward. The proposal would be re-evaluated after re-submission.
Not approved; requires additional information or rewriting	The REC considered that the proposal was not acceptable but is willing to consider a revision of the protocol if this is submitted in a new application.
Rejected	The REC considered that the proposal was not acceptable and did not advise re-submission.

6.4.12 Responses to questions from the REC

After the research protocol has been submitted, the REC may have comments or questions for the researcher about it. Researchers are typically required to respond to these queries and the requested amendments by preparing a note which includes a point-by-point response to all queries and to submit a revised protocol which shows the changes they have made.

6.4.13 Other communications with the REC

This section describes a variety of situations which need to be reported to the REC, according to WHO *(20)*.

Progress report
For non-cross-sectional studies, a progress report might be required by the REC on an annual basis. This would cover the status of the study, number of participants (recruited, withdrawn and completed), a summary of any major changes to study procedures, serious adverse events, participants' complaints, and significant updated information or deviation from approved activities which are related to safety or participation.

Application for continuing review (if needed)
If a study needs continuing review, the researchers may need to submit a renewal application including information justifying the renewal and a progress report of the ongoing study, a report from their study's Data and Safety Monitoring Board (if available), and any amended or new documents.

Application for Amendment

If the originally submitted documents and study protocol are amended after approval or the research has started, the researchers should notify the REC about these amendments. Revised documents include an explanation of the amendment and an amended protocol (highlighting the changes) should be submitted. If the amendment involves significant changes in the study design, additional justification should be provided.

Project closure

When the study is successfully completed or terminates early, the researchers should inform the REC and provide a completed set of documents. This should include the final report with a summary of the study's findings, the latest progress report and any Data and Safety Monitoring Board reports, and any other documents required by the REC.

Adverse events

According to the WHO, an adverse event is any untoward medical occurrence that presents during treatment with medicine, but which does not necessarily have a causal relationship with the treatment *(21)*. In addition to these, some REC also include non-medical occurrences as adverse events. Researchers should check the specific requirements of their REC and ensure that adverse events are reported according to these requirements.

Serious adverse events

WHO defines a serious adverse event as an untoward medical occurrence which is life-threatening, requires inpatient hospitalization, results in persisting and significant disability to the subject or causes congenital anomalies or birth defects *(21)*. These should be reported promptly to the REC. As with adverse events more generally, some REC also include serious nonmedical occurrences as serious adverse events and researchers should check the specific requirements of their REC to ensure that they report serious adverse events appropriately.

6.4.14 Conclusions

Research ethics applications and approvals are necessary before research involving human subjects, except for those studies that will be limited to publicly available, anonymous data. This chapter provides a general overview of different types of ethics review, procedures, documents required and other important points, which are part of the WHO guidelines for ethics approval. However, the variety of national and institutional policies around ethical approval mean that there is no single, globally-agreed standard or requirement that applies to all research ethics systems or RECs *(14)*. Researchers should therefore always check the specific requirements of the REC they are applying to before submitting their application.

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6.4.15 Key messages

o   **The approval of a research ethics application is necessary before research involving human subjects, unless the study will be limited to publicly available anonymous data.**

o   **Research should be conducted in ways that protect the safety and confidentiality of the participants, both physically and mentally (in protocol and document) and be carried out in accordance with the principles underpinning the Declaration of Helsinki.**

o   **The type of ethics review required will depend on the nature and the urgency of the study.**

o   **Current ethics review procedures might not be fully applicable to the challenges encountered in the Health EDRM context, especially during rapid onset emergencies and disasters because of the relatively long lead time of non-emergency ethics review processes. Changes in the ethics review procedure are needed to accommodate the special needs for emergency researches.**

o   **Ethics application requirements vary across REC. Researchers should check the requirements of the REC they plan to submit their application to.**

6.4.16 Further reading

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