CATALYZING ETHICAL RESEARCH IN EMERGENCIES

Ethics guidance, lessons learned from the COVID-19 pandemic, and pending agenda

SUMMARY

PAHO Pan American Health Organization
World Health Organization Americas

The publication *Catalyzing ethical research in emergencies. Ethics guidance, lessons learned from the COVID-19 pandemic, and pending agenda* offers a revised and integrated version of the ethics guidance documents for research in emergency situations previously developed by the Pan American Health Organization (PAHO). It supplements them with lessons learned in the Region during the COVID-19 pandemic. It also offers general recommendations that resulted from a series of regional dialogues held by PAHO, with the ultimate goal of catalyzing ethical research for health emergencies that may occur in the future.

This publication was developed by the Regional Program on Bioethics, which is part of PAHO's Department of Health Systems and Services, with the contribution of health authorities, research ethics committees (RECs), researchers and ethicists from the Region of the Americas that participated in the regional dialogues, and the financial support of the Wellcome Trust grant 220028/Z/19/Z.

It is urgent to learn from this experience to ensure that, in a future health emergency, research conducted in the Region has high social and scientific value and is capable of answering research questions quickly in order to guide the emergency response.

CONTENTS

Lessons learned from the Zika outbreak and challenges during the COVID-19 pandemic

(CHAPTER 1)

Learning from the Zika outbreak in the Region of the Americas led to important points of consensus about health emergencies:

- research is an essential component of the response;
- research conducted in emergencies must adhere to international ethical standards, including prior ethics approval by a REC; and
- ethics review processes must be modified to ensure rapid and rigorous review of research.

A subsequent regional reflection led to PAHO's Member States commitment to improve their ethics preparedness for future emergencies. For this purpose, PAHO's research ethics indicators included a specific one to measure the number of countries that have established procedures for thorough accelerated ethics review of research during emergencies.

To know more about PAHO's indicators for assessing national research ethics systems, visit: https://iris.paho.org/handle/10665.2/54869

When SARS-CoV-2 began to spread, the Region was better prepared than when the Zika outbreak occurred. However, detailed guidance on how these accelerated ethics review processes should be conducted was still needed. As soon as the pandemic started, PAHO published ethics guidance and worked closely with health authorities and RECs to catalyze ethical research conducted in response to the COVID-19 pandemic. Ten countries from Latin America rapidly issued guidance and regulations to accelerate the ethics review of COVID-19 research.

How can trust in research conducted in emergencies be strengthened? Transparency and public engagement

(CHAPTER 2)

Transparency is a key component of the ethical governance of research that, in health emergencies, is essential to promote public trust in research and the public health response. If society and all stakeholders know what research is being conducted and what mechanisms are in place to ensure that research is conducted ethically, they will be more willing to contribute to research efforts and trust in their results, and to demand that all aspects of the response be supported by scientific evidence.

Examples of actions to strengthen trust in research

- Make available to the public a list of the studies conducted in the country.
- Include a public engagement plan as part of research protocols.
- Share research results rapidly in order to guide decision-making.
- Inform the public about the purpose of RECs and their role during health emergencies.

How to ensure that the ethics review and monitoring of research conducted by research ethics committees are agile yet rigorous in emergencies

(CHAPTER 3 AND ANNEX 1)

To ensure research is conducted rapidly, RECs should accelerate review processes without compromising their rigor. It is therefore necessary to adapt and seek alternatives to ordinary processes of ethics oversight, which include the review and monitoring of research.

The relevant authorities should:

1st Define in advance the strategy (or combination of strategies) for organizing the ethics oversight of research that is best suited to their context, in order to avoid multiple and repetitive review processes by various RECs.

2nd Establish rapid and flexible standard operating procedures (SOPs) that ensure a rapid and rigorous review of research and an agile and adequate monitoring of ongoing studies.

SOPs should include topics such as:

- ☑ Submission of electronic documentation
- ☑ Flexibility in the submission requirements
- ☑ Virtual meetings
- ☑ Tight deadlines
- ☑ Reduced quorum
- ☑ Staggered decision-making
- ☑ Mechanisms for communication and coordination
- ☑ Digital registry and documentation archive

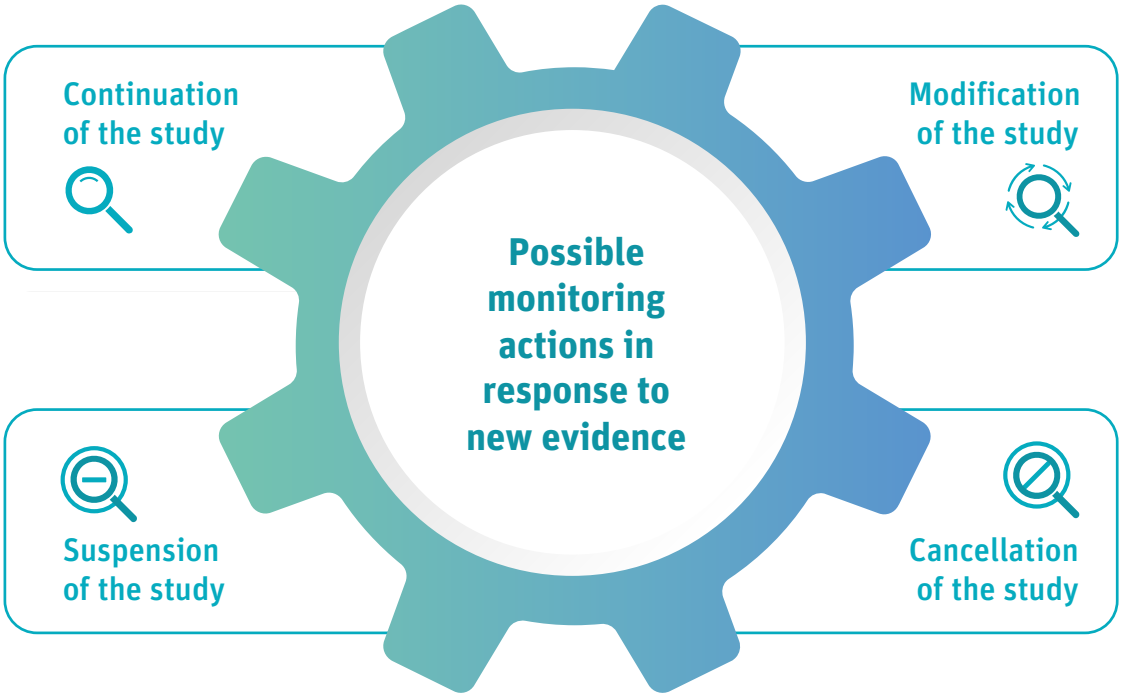
How can the ethical acceptability of research be ensured in response to emerging evidence?

(CHAPTER 4)

In emergency situations, evidence is produced quickly. Therefore, research protocols that were initially ethically acceptable may soon cease to be so: new scientific evidence can impact different aspects of the ethical acceptability of ongoing research.

> *A study can cease to have social value if the question it aims to answer has been answered by another study with high-quality evidence. A study can also cease to have a favorable risk/benefit ratio if the study intervention is found to be riskier than initially thought, or if an effective treatment has already been found for the condition being studied. A consent process could cease to be adequate because it does not inform potential participants about alternative treatments that are now available but were not available at the initiation of the study.*

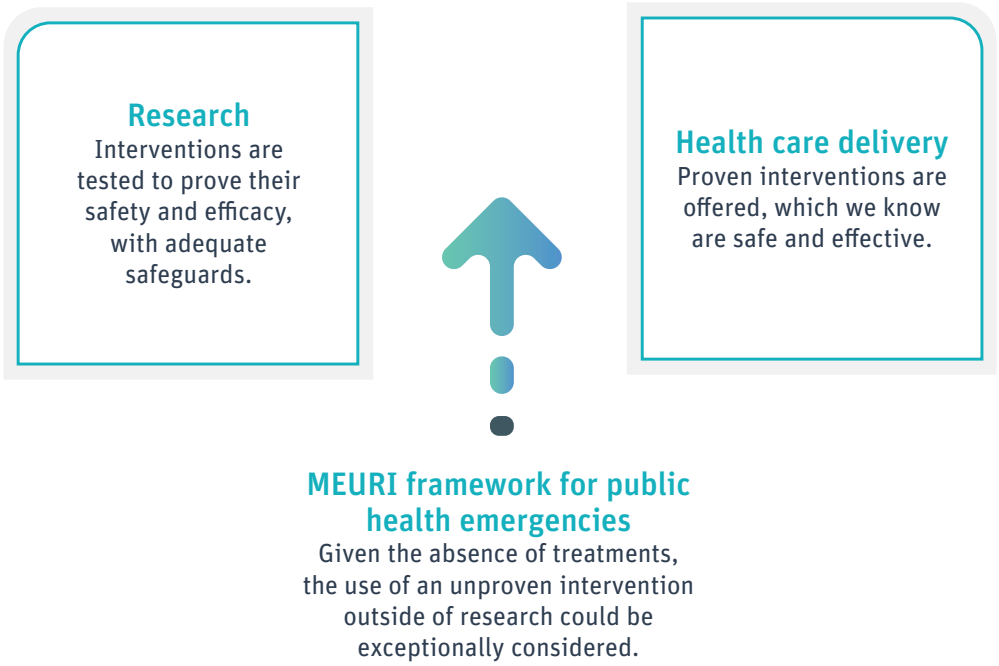
Researchers and RECs are responsible for ensuring that research continues to be ethically acceptable in light of the most up-to-date available evidence.



How can the ethical use of unproven interventions outside of research be ensured in health emergencies?

(CHAPTER 5 AND ANNEX 2)

Rigorous research, specifically randomized controlled clinical trials, are necessary to prove the safety and efficacy of health interventions. However, in health emergencies marked by an absence of safe and effective treatments, it *could* be ethically acceptable to exceptionally offer unproven interventions outside of research.



In these cases, the four criteria of what is known as the MEURI ethical framework must be met. MEURI, which stands for *Monitored emergency use of unregistered and experimental interventions*, aims at facilitating exceptional access to unproven interventions in view of their *possible* benefits, while ensuring that their use is monitored to protect patients and contribute data to the generation of evidence.

The four ethics criteria of the MEURI framework

1

Justification

If no proven effective treatment exists and it is not possible to initiate a clinical trial immediately, preliminary evidence must support the use of the intervention on the basis of its *potential* benefits in relation to its risks.

2

Ethical and regulatory oversight

Prior review and approval by a REC and the relevant health authority is needed. Both must monitor the use of the intervention to ensure its continuous adherence to the ethical criteria of the MEURI framework.

3

Informed consent process

People should voluntarily decide if they want to receive the unproven intervention after being informed that it might not benefit them and may even harm them.

4

Contribution to the generation of evidence

Data that provide information about the safety and efficacy of the intervention must be collected and shared with the scientific community and health authorities without delay.

How to ensure that data and samples are shared ethically for future research

(CHAPTER 6)

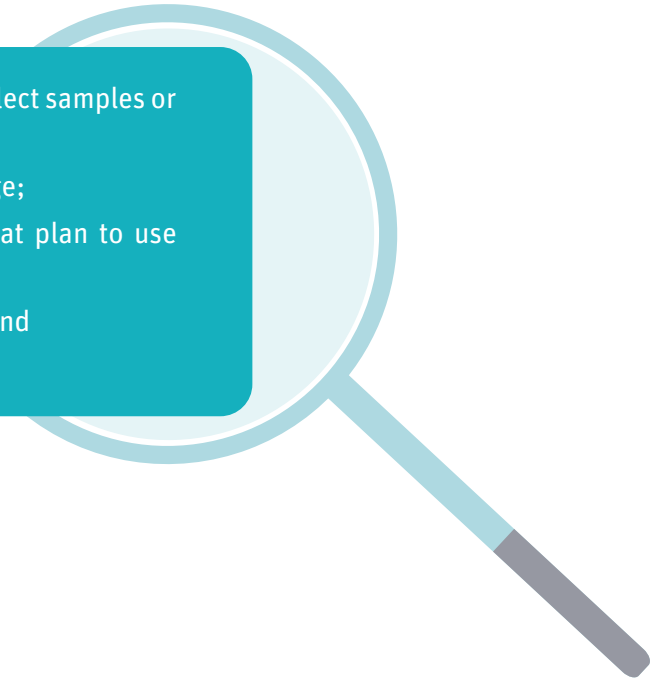
In health emergencies, samples and data should be collected with a view to their potential use in future research, i.e. studies that are not planned at the time of collection but that may be conducted in the short or long term by local or international researchers. Samples and data with research potential can be collected from research settings, public health surveillance and health care delivery.

> *Some samples and data are only available during an emergency, so if they are not properly collected and stored at that time, the necessary inputs for future socially valuable research will not be available.*

Ethical sharing of samples and data entails responsibilities at different points of the process: during the collection, storage, transfer, and future use of samples and data in research projects.

To ensure that samples and data are shared ethically for future research issues like the following should be considered:

- broad informed consent processes to collect samples or data for future research;
- governance mechanisms for their storage;
- RECs approval of research protocols that plan to use stored samples or data;
- Material or Data Transfer Agreements; and
- a fair return for research contributions.



Final recommendations

(CHAPTER 7)

The publication establishes recommendations for action and recommendations to conceptualize necessary actions. In both cases, the recommendations may be relevant only to health emergencies or may apply to both emergency and non-emergency situations.

Recommendations for action		
Responsible entity	**For health emergencies**	**For ordinary situations and health emergencies**
Health authorities	• Establish strategies for the oversight of research ethics in future health emergencies. • Entrust the relevant health authorities with responsibility for coordinating research efforts in emergencies. • Designate a person who serves as a contact point for research as part of the national incident response team that is established during every health emergency. • Establish processes for involvement in the research conducted in response to health emergencies to ensure that countries and their populations benefit from their potential results.	• Establish mechanisms to gather information about studies that were submitted for REC review and not approved, and share this information with other RECs as necessary. • Require all clinical trials to be registered in registries that feed WHO's International Clinical Trials Registry Platform (ICTRP) before they begin. • Establish a website that lists the studies with human participants that have been approved. • Continually inform the public about the research conducted. • Strengthen scientific journalism and spaces to disseminate scientific research in the media.
RECs		• Require that researchers submitting a proposal for review report prior reviews conducted by other RECs and to include a copy of their decisions. • Establish communication mechanisms to inform the public about the studies if it becomes necessary.
Institutions that conduct research		• Compensate REC members financially or through another appropriate formal mechanism for their time and dedication.

Recommendations for action		
Responsible entity	**For health emergencies**	**For ordinary situations and health emergencies**
Health authorities and RECs		• Review their procedures to incorporate virtual tools, and agile communication and coordination mechanisms. • Allow for different ways of carrying out informed consent processes. • Establish clear and agile procedures to determine which activities constitute research with human subjects and thus require REC review.
Health authorities and international organizations		• Advocate for expanding the scope of ICTRP so that it includes all research with human participants.
Health authorities, international organizations, and the scientific community	• Develop generic research protocols for potential health emergencies.	
Authorities, RECs, international organizations and the scientific community		• Strengthen capacities in research ethics.

Recommendations for conceptualization	
For health emergencies	**For ordinary situations and health emergencies**
• Design and implement mechanisms for effective coordination of research efforts initiated in emergencies. • Plan a strategy to generate collaborations within the Region to conduct research in emergencies. • Develop mechanisms for the ethics oversight of research at the (sub)regional level.	• Design and implement strategies that streamline the review and monitoring carried out by multiple RECs.

PAHO/HSS/BIO/COVID-19/22-0033

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