

# FINAL REPORT

## Regional workshop

Strengthening clinical trials to provide high-quality evidence on health interventions, and to improve research quality and coordination



Brasilia, October 4 and 5, 2023

## I. Background

On 27 May 2022, the 75th World Health Assembly adopted the resolution [WHA 75.8](#) on Strengthening clinical trials to provide high-quality evidence on health interventions and to improve research quality and coordination.

As part of the implementation of this resolution, the Pan American Health Organization (PAHO) held a workshop on October 4 and 5, 2023, in Brasilia, Brazil with more than 50 participants from different countries of the Region of the Americas, including researchers, national and regulatory authorities, and members of research ethics committees, as well as representatives of the government of Brazil, PAHO and the World Health Organization (WHO) (Annex 1). The objective was to identify, discuss, and propose concrete actions to strengthen the conduct of scientifically and ethically sound clinical trials in the Region of the Americas. The regional workshop was funded by WHO, PAHO and the Ministry of Health of Brazil. It was also funded in part by the second European & Developing Countries Clinical Trials Partnership programme (EDCTP2) supported by the European Union (grant number CSA2023WHO-3454-WHORCT) with funds from the UK National Institute for Health and Care Research (NIHR) using UK Aid from the UK government to support global health research.

The agenda was organized on the basis of discussion questions in four thematic areas that pose major challenges for the region:

1. The conduct of high-impact clinical trials.
2. Research capacities.
3. Clinical trial networks.
4. Ethical and regulatory efficiency.

The questions on the agenda were sent to participants in advance so they could be reflected on and concretely discussed in the workshop. The discussion was not limited to clinical trials on drugs and medical devices; it included clinical trials defined as any research study that prospectively assigns human participants to one or more health-related interventions to evaluate the effects on health outcomes, as mentioned in resolution WHA 75.8.

Prior to the workshop, WHO conducted the survey *Perspectives on Key Barriers and Areas of Focus Needed to Improve the Clinical Trials Ecosystem*<sup>1</sup>; its results were presented at the beginning of the workshop with a focus on the Region of the Americas (Box 1). These findings highlight many of the challenges that had already been identified throughout a series of regional dialogues led by PAHO in response to the experience of the COVID-19 pandemic (1). Indeed, the final recommendations from this reflection, contained in the PAHO publication [Catalyzing Ethical Research in Emergencies. Ethical guidance, lessons learned from the COVID-19 pandemic, and](#)

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<sup>1</sup> The survey aimed to understand the main barriers and areas we need to focus on to improve the clinical trial ecosystem. The survey was virtual, lasted 15 minutes and was available until September 10, 2023, in English, French, Spanish and Portuguese.

pending agenda, were an important input for the elaboration of the agenda for this workshop (Annex 2).

### **Box 1. WHO Survey to Improve the Clinical Trials Ecosystem: Results for the Region of the Americas**

<b>Participants</b> Participants from the Region of the Americas accounted for 21.1% of the total respondents (623/2953).
<ul style="list-style-type: none"><li>- Nearly half were from high-income countries, mainly the United States.</li><li>- Most were ethicists and regulators – not health care professionals, as was the case globally.</li><li>- Greater participation from the pharmaceutical industry sector and private hospitals.</li><li>- Greater participation of professionals with more than 10 years of experience, in contrast with the global trend of more participants who are relatively new to the field of clinical trials.</li><li>- Greater participation of people with experience in the areas of ethics oversight and health guideline or policy development than those with experience in the implementation of clinical trials and public engagement.</li></ul>
<b>Results</b> Respondents indicated that:
<ul style="list-style-type: none"><li>• The three most important barriers to the design and conduct of clinical trials in the region are (in order):<ol style="list-style-type: none"><li>1. Inadequate funding.</li><li>2. Timelines for review of medicines/health products under investigation by regulators.</li><li>3. Inadequate patient and community engagement mechanisms.</li></ol></li><li>• The three priorities to be addressed in the immediate future in the region are (in order):<ol style="list-style-type: none"><li>1. Greater integration of clinical trials into healthcare delivery.</li><li>2. Greater focus on research design that could answer key questions robustly and produce reliable evidence.<ol style="list-style-type: none"><li>1. Creation of large-scale national and international research networks for diseases and/or geographical areas where there are current knowledge gaps, with effective coordination mechanisms.</li></ol></li></ol></li><li>• The three best approaches for implementing best practices for clinical trials are (in order):<ol style="list-style-type: none"><li>1. Targeting research funding to align with key weaknesses, as identified locally.</li><li>2. Developing coordinated processes between regulator networks.</li><li>3. Expanding adaptive platform trials with associated protocols, moving to perpetual models for ongoing high priority trials to national, regional, and global priorities.</li></ol></li></ul>

## **II. Challenges and general reflections**

This section contains a summary of participants' reflection and discussion of the issues and challenges identified based on the workshop agenda questions. The views expressed in this report are those of the participants and not necessarily reflect the views or positions of any entities they represent or those of EDCTP, NIHR or the UK Department of Health and Social Care.

## 1. The conduct of high-impact clinical trials

Clinical trials are often small and repetitive, thus incapable of producing the high-quality evidence that is needed to address people's health needs. Although the registration of clinical trials is useful to know which trials are already underway, it is not enough to ensure that large-scale high-impact trials are conducted across the Region as opposed to multiple small trials.

Discussion questions:

1. How can this problem be solved? Whose job is it to ensure coordination among trials?
2. Is it necessary to set research priorities at the regional level to advance regional clinical trials?
3. What specifically is preventing the launch of large-scale regional trials? How can these hurdles (regulatory, logistical, organizational, etc.) be overcome?
4. Is the establishment of a regional clinical trial network necessary? What would this network look like? Who should be part of it?

The discussion began by referencing the clinical trials conducted in Latin America and the Caribbean in response to the COVID-19 pandemic. Although the regional response was rapid, many clinical trials were scientifically and ethically questionable because they were small and repetitive and were incapable of producing valuable and quality knowledge (2-3). Therefore, it is critical to implement the lessons of the COVID-19 pandemic to strengthen the clinical trial ecosystem.

Three axes of discussion were identified in relation to this problem. These are closely linked and overlap with the other agenda items: i) insufficient funding for the conduct of quality clinical trials, ii) gaps in capacities to conduct research, and iii) the need to create networks and work collaboratively.

The lack of sufficient resources (especially public resources) to conduct clinical trials in the region (and, more generally, for research) was a common concern among participants. Resources are a key factor in ensuring quality studies and strengthening local capacities. Countries' efforts must therefore be focused on funding quality clinical trials at the local level, for which sustainable public funding mechanisms must be created and guaranteed. These mechanisms should cover all aspects and stages of research development, not just the clinical trials that usually constitute the final stage of the research process.

The lack of resources for research also deepens gaps in capacities within and among countries in the region and precludes opportunities to build permanent and sustainable research teams and infrastructure at the local level. These range from basic and pre-clinical to clinical research and include the methodological and logistical aspects of research. Collaborative work – including the

public and private sectors, and the academia – is useful to overcome these barriers and key to promoting the design and implementation of high-impact clinical trials in the region. However, one of the difficulties in achieving these collaborations lies in the incentive system, which is focused on the individual researcher as opposed to the collective recognition of the research team. For this reason, a transformation of the incentive system is essential to promote collaborative research.

In this context, establishing a network of clinical trials at the regional level, with the support of PAHO, was considered an attractive initiative to respond to the problems discussed. A network would be a mechanism to identify capacities and areas of work of the stakeholders, helping create alliances to work collaboratively, based on what has been built and without duplicating efforts. In order for this network to benefit all the parties involved, it would be crucial to define in detail its composition, scope and objectives. Additionally, the operation of a network should include efficient coordination mechanisms, as well as ethical and regulatory reliance agreements, which should abide by international standards.

## 2. Research capacities

Research capacities are limited at the local level. Researchers from the region who obtain high-level training often establish themselves abroad.

Discussion questions:

1. How can we enhance the capacities to conduct robust, high-impact clinical trials? What skills and areas of specialization are needed for each role associated with the conduct of clinical trials? What has been successful in terms of bolstering individual skills, leadership, infrastructure, and available resources?
2. How can we augment capacities to secure funding, handle logistics, and ensure long-term viability?
3. How can we address the challenges of recruiting and retaining talent in the region?
4. Which incentives should be adopted to increase the number of local researchers? Which strategies have proven effective to attract local researchers who were trained abroad?
5. In order to enhance capacity to conduct clinical trials in all phases, is it necessary to develop capacities to conduct a prior type of research (e.g., basic research, animal research)? What strategies to transfer knowledge to local researchers are feasible and effective?
6. How can we ensure that clinical trial capacities are responsive to emergencies?

Research staff is not limited to researchers and it is crucial to have large, multidisciplinary teams with sufficient competencies to conduct quality clinical trials. Unfortunately, the absence of key personnel in research teams (e.g., monitors, coordinators, data managers, pharmacy or laboratory staff) is a common issue in the region. Likewise, the absence of lawyers with knowledge and experience in the governance of research who are also needed as part of the clinical trials teams, especially in the case of multi-country trials poses an important challenge.

Additionally, researchers do not have adequate logistical or regulatory support to conduct research in the region. Except in the case of research sponsored by the pharmaceutical industry (which is organized and has sufficient resources), researchers in the public or academic sector tend to perform functions unrelated to their role that hinder their work in the long run and discourage them from engaging in research.

This situation is further aggravated by the fact that there are no quality educational spaces dedicated to the training of professionals in different stages and activities of research and there is a lack of preparation and interest on the part of students, from an undergraduate level, to work in research. Moreover, most of the open access research courses and trainings are in English, which is a barrier for most research staff in Latin America.

For training opportunities to be truly valuable, they must be relevant to the role that staff will play in the clinical trial. It is not justified to require all clinical trial personnel to have the same training or degree of specialization (e.g., not everyone should receive IATA training). In addition, virtual tools should be leveraged, and mechanisms should be created to promote staff training (e.g., rotation and exchange systems, internships, public-private partnerships for graduate studies, and mentoring). It is also important to involve universities so they can offer more research-focused programs to their students.

Along with the education and training of human resources, achieving a culture of commitment and sustainability is also key. For this purpose, strategies to attract and retain human talent should not only consider economic aspects but also offer opportunities for personal and professional growth. Incentives that have been successfully used in countries of the region include scholarships that require trainees to return to their home country, and secured positions or promotions for trainees after they complete their studies.

### **3. Clinical Trial Networks**

The establishment of networks and collaboration could facilitate the conduct of larger, high-impact clinical trials, as well as increasing local research capacity.

Discussion Questions:

1. Are clinical trial networks needed to foster collaboration? If so, what would they look like? Who should be part of them? Should they be specific to a disease or type of treatment?
2. Which strategies are necessary to ensure sustainable regional networks?
3. What other strategies should be adopted to strengthen collaborative clinical trials? Who should lead them?
4. Which mechanisms should be devised to increase opportunities for collaboration among different stakeholders?

5. What role should funders play in encouraging collaboration? What role should PAHO play?
6. How can we address barriers to cooperation and collaboration among countries of the region?

The biggest obstacles to working as part of a network in the region revolve around financial and regulatory aspects. The absence of clear regulations in some countries and the need for greater coordination among authorities of the region complicate the collaborative conduct of clinical trials. In addition, the limited number of professionals with expertise in these topics (e.g., legal issues focused on clinical trials) makes collaborative research even more difficult. For this reason, participants called for convergence on regulatory issues at the regional level.

Lacking knowledge about which individuals or institutions with specific capacities related to clinical trials exist in the region (e.g., which reference laboratories exist in the region or which institutions are engaged in preclinical research in a country) is a challenge to the establishment of regional networks. It is therefore necessary to start identifying, country by country, investigators and their research areas or research centers authorized to conduct clinical trials, and to maintain an up-to-date registry at the regional level, such as the Clinical Trials Community platform of Africa ([Clinical Trials Community](#)).

Research institutions, for their part, must promote and ensure working as part of networks. To this end, they should provide regulatory support, as well as academic and scientific support to researchers in order to guarantee quality collaborative research.

Participants considered that PAHO should play an active role in establishing clinical trial networks on the basis of what has already been built at the regional level (e.g., by the Pan American Network for Drug Regulatory Harmonization ([PANDRH](#)) or MERCOSUR in relation to the regulation of clinical trials and good clinical practices) (4).

#### **4. Advancing ethical and regulatory efficiency**

In some cases, national regulatory authorities (NRAs) do not exist or have a limited scope of work. In others, their requirements and procedures for the authorization and control of clinical trials do not adhere to international standards and become practical obstacles. These hurdles are even more complex when a trial must comply with regulations of different NRAs at different maturity levels, and there are no adequate channels of communication and coordination between the NRA and the investigators, RECs, or other authorities involved in conducting clinical trials.

Several research ethics committees (RECs) must review the same trial. Numerous reviews by different RECs within the same jurisdiction (i.e., country, state) are often necessary, which

delays the processes to launch trials without necessarily strengthening them from an ethics perspective. Additional reviews are needed from different jurisdictions where trials are being conducted.

Discussion questions:

1. What is the best strategy to ensure rigorous yet efficient ethics review of clinical trials in the region, i.e., within specific jurisdictions and in Latin American and Caribbean countries?
2. A “single IRB” policy has been implemented recently in the US. Can a similar policy be developed for the needs of Latin American and Caribbean countries, and implemented successfully, considering the lessons learned in the US and prior experience centralizing ethics review processes in Latin America?
3. Are there other strategies that should be explored to avoid repetitive ethics review processes, e.g., adopting novel mechanisms for review that have been used in Argentina during COVID or establishing an extra-territorial ethics review committee, at least in certain jurisdictions like the Caribbean?

The region is still tasked with improving coordination between research stakeholders, reducing complexities (especially in the regulatory field) and accelerating the processes of ethics and regulatory oversight without sacrificing their rigor.

NRAs should articulate and develop requirements and procedures for the authorization and control of clinical trials in an efficient way. This is difficult due to the limited number of people with the necessary competence and experience in issues related to research governance. However, there is an urgent need for regulatory frameworks to be reviewed to ensure their compliance with the standards of the International Conference for the Harmonization of Technical Requirements for Pharmaceutical Products for Human Use (ICH), as well as other relevant standards.

In addition, other key aspects of clinical trial regulations, such as the core elements of clinical trial contracts or minimum clauses in insurance policies, need to be standardized at the regional level. Promoting and achieving regulatory convergence in the region was a topic present throughout the workshop. Also discussed was the need to establish adequate mechanisms for communication and coordination between the relevant research stakeholders (NRAs, RECs, research institutions, researchers and other authorities where appropriate).

The requirement of multiple reviews by different RECs of one research study (which is present in many regulations of the countries of the region), does not ensure greater protection of research participants and can bureaucratize the ethics review processes. RECs must be competent and efficient, and rigorously monitor research in accordance with international ethical standards. For this reason, it is important to approach the REC’s work from a more professional perspective in the institutions that establish them.

Improving the functioning of the RECs and strengthening their capacities are aspects that must be promoted during the accreditation processes, which is carried out by the corresponding



authorities. Standardizing these accreditation processes at the regional level is the first step to establishing mechanisms that will allow a REC to adopt the review carried out by another, without the need to repeat the review process (e.g., through previous reliance agreements). Although there is no one-size-fits-all formula for the latter, it is important to take into account the lessons learned by those who have implemented policies on this topic (e.g, the single IRB policy in the United States).

### **III. Proposed key actions**

The regional workshop emphasized the urgency of taking robust and rapid action to revitalize the clinical trials ecosystem to effectively promote health, and the need to define and adopt a specific plan. PAHO's participation and support was recognized as crucial in this regard, and the relevance of an official document from the Organization's governing bodies was discussed as a way to formalize an action plan to revitalize the clinical trials ecosystem to promote health effectively.

Throughout the workshop, the following key actions were proposed as part of such plan:

1. Establish a regulatory cooperative system, which can entail reliance mechanisms or joint reviews, for the authorization of clinical trials that allows NRAs to streamline multi-country clinical trial authorization. To achieve this objective, it is a priority to make efforts to:
  - a. Establish an NRA network in the region, which could be hosted within the PANDRH as a permanent working group on clinical trials.
  - b. Harmonize the requirements for the submission, evaluation, authorization, and control of clinical trials and standardize procedures based on good clinical practices among the countries of the region.
  - c. Develop and approve a regional agreement with binding legal force whose purpose is to harmonize the legal aspects involved in the conduct of clinical trials, such as, for example, the core clauses in insurance policies or the key content of clinical trial contracts. This agreement should also address regulatory gaps (e.g., donation of research products) as well as logistical challenges posed by regulatory frameworks for research.
  
2. Design and establish diverse mechanisms to train groups of experts on regulatory issues to assist research teams and institutions. It is recommended to:
  - a. Establish "regulatory teams" in research institutions, like those in pharmaceutical companies, that are familiar with regulatory frameworks and requirements applicable to research and could be a channel of communication and coordination with NRAs.
  - b. Staff research institutions with lawyers who are experts in regulatory issues and other legal aspects of research. They should be able to facilitate the preparation,

negotiation and signing of agreements related to clinical trials as well as the contracting of reasonable and adequate insurance policies that ensure fair compensation to participants who have suffered research-related harms.

- c. Establish, with the support of PAHO, a permanent forum of experts on regulatory issues to advise the countries of the region.
3. Design and implement mechanisms to avoid repetitive ethics review processes for multicenter studies. For this purpose, it is essential to strengthen the accreditation processes of RECs in the region in order to ensure the professionalization and efficiency of the committees, in accordance with international ethical standards. To further the strengthening of research ethics systems in the region, PAHO should establish and coordinate a regional network of entities responsible for the oversight of RECs, including the accreditation processes.
  4. Collaboratively design and conduct three pilot multi-country clinical trials on priority topics in the region.
  5. Create a regional network for clinical trials -- not limited to clinical trials on drugs and medical devices -- for which PAHO would serve as the secretariat. To strengthen opportunities for collaborative work within this regional network, the following should be available:
    - a. A registry of research centers with the capacity and authorization to conduct clinical trials. Centers should have staff with the regulatory expertise necessary to conduct clinical trials.
    - b. A platform that provides methodological support for clinical trials and can ensure the design and conduct of high-impact clinical trials.
  6. Develop and establish a novel system of incentives for researchers, research institutions, funders (including governments) to promote collaborative research. This system should also encourage mentoring in institutions as a mechanism for training researchers.
  7. Design and implement policies to retain human talent in research, considering not only researchers but also other professionals who have a key role in the conduct of clinical trials, such as those in charge of authorizing and supervising clinical trials in the NRA.

## References:

1. Pan American Health Organization. Catalyzing ethical research in emergencies. Ethics guidance, lessons learned from the COVID-19 pandemic, and pending agenda. Available at: <https://www.paho.org/en/bioethics/catalyzing-ethical-research-emergencies-ethics-guidance-lessons-learned-covid-19-pandemic>.
2. Carracedo S, Palmero A, Neil M, Hasan-Granier A, Saenz C, Reveiz L. The landscape of COVID-19 clinical trials in Latin America and the Caribbean: assessment and challenges. *Rev Panam Salud Publica*. 2021; 45:e33. Available at: <https://doi.org/10.26633/RPSP.2020.177>.
3. Mansilla C, Herrera CA, Boeira L, Yearwood A, Lopez AS, Colunga-Lozano LE, et al. Characterising COVID-19 empirical research production in Latin America and the Caribbean: A scoping review. *PLoS ONE*. 2022; 17(2):E0263981. Available at: <https://doi.org/10.1371/journal.pone.0263981>.
4. Southern Common Market (MERCOSUR). MERCOSUR/GMC/RES. No. 129/96, Technical Regulations on the Verification of Good Clinical Research Practices, 1996. Available in Spanish at: <https://normas.mercosur.int/public/normativas/2045>.

## Annex 1: List of participants

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**Annex 2: Catalyzing Ethical Research in Emergencies. Ethical guidance, lessons learned from the COVID-19 pandemic, and pending agenda. Summary.**

<https://iris.paho.org/handle/10665.2/56585>

# CATALYZING ETHICAL RESEARCH IN EMERGENCIES

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

## SUMMARY



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.*

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

## (CHAPTER 1)

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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.
- Share research results rapidly in order to guide decision-making.
- Include a public engagement plan as part of research protocols.
- 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:

1<sup>st</sup>

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.



2<sup>nd</sup>

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

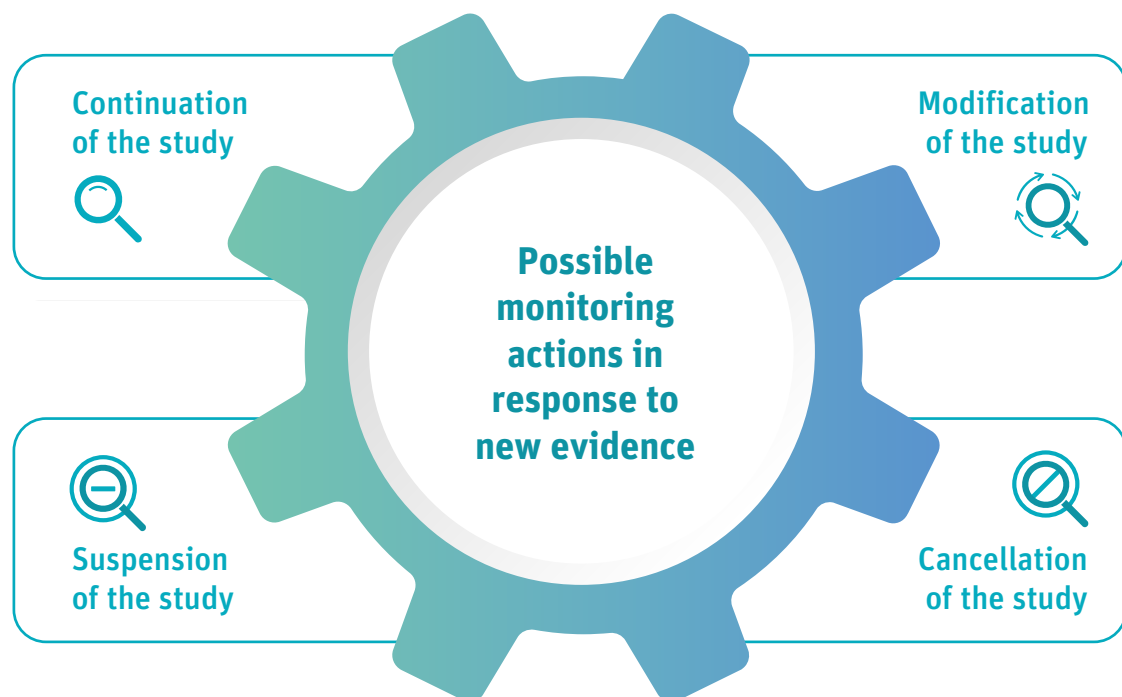
# How can the ethical acceptability of research be ensured in response to emerging evidence?

## (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.*

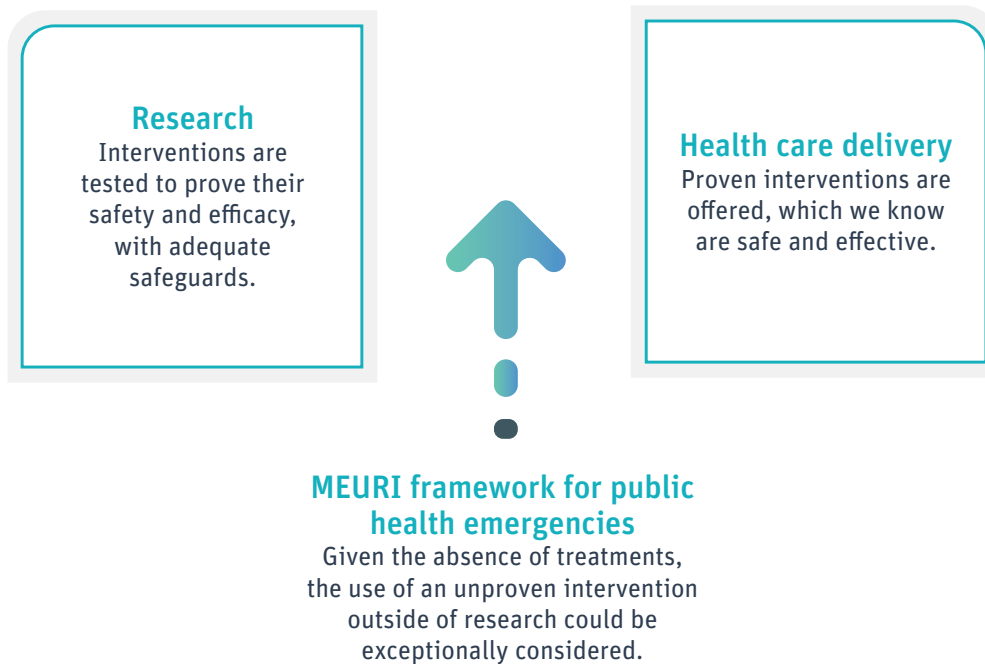
Researchers and RECs are responsible for ensuring that research continues to be ethically acceptable in light of the most up-to-date available evidence.



# 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)

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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
<b>Health authorities</b>	<ul style="list-style-type: none"> <li>• Establish strategies for the oversight of research ethics in future health emergencies.</li> <li>• Entrust the relevant health authorities with responsibility for coordinating research efforts in emergencies.</li> <li>• 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.</li> <li>• 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.</li> </ul>	<ul style="list-style-type: none"> <li>• 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.</li> <li>• Require all clinical trials to be registered in registries that feed WHO's International Clinical Trials Registry Platform (ICTRP) before they begin.</li> <li>• Establish a website that lists the studies with human participants that have been approved.</li> <li>• Continually inform the public about the research conducted.</li> <li>• Strengthen scientific journalism and spaces to disseminate scientific research in the media.</li> </ul>
<b>RECs</b>		<ul style="list-style-type: none"> <li>• Require that researchers submitting a proposal for review report prior reviews conducted by other RECs and to include a copy of their decisions.</li> <li>• Establish communication mechanisms to inform the public about the studies if it becomes necessary.</li> </ul>
<b>Institutions that conduct research</b>		<ul style="list-style-type: none"> <li>• Compensate REC members financially or through another appropriate formal mechanism for their time and dedication.</li> </ul>

Recommendations for action		
Responsible entity	For health emergencies	For ordinary situations and health emergencies
<b>Health authorities and RECs</b>		<ul style="list-style-type: none"> <li>• Review their procedures to incorporate virtual tools, and agile communication and coordination mechanisms.</li> <li>• Allow for different ways of carrying out informed consent processes.</li> <li>• Establish clear and agile procedures to determine which activities constitute research with human subjects and thus require REC review.</li> </ul>
<b>Health authorities and international organizations</b>		<ul style="list-style-type: none"> <li>• Advocate for expanding the scope of ICTRP so that it includes all research with human participants.</li> </ul>
<b>Health authorities, international organizations, and the scientific community</b>	<ul style="list-style-type: none"> <li>• Develop generic research protocols for potential health emergencies.</li> </ul>	
<b>Authorities, RECs, international organizations and the scientific community</b>		<ul style="list-style-type: none"> <li>• Strengthen capacities in research ethics.</li> </ul>

Recommendations for conceptualization	
For health emergencies	For ordinary situations and health emergencies
<ul style="list-style-type: none"> <li>• Design and implement mechanisms for effective coordination of research efforts initiated in emergencies.</li> <li>• Plan a strategy to generate collaborations within the Region to conduct research in emergencies.</li> <li>• Develop mechanisms for the ethics oversight of research at the (sub)regional level.</li> </ul>	<ul style="list-style-type: none"> <li>• Design and implement strategies that streamline the review and monitoring carried out by multiple RECs.</li> </ul>



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