

## Strengthening national research ethics systems in the Americas to improve its ethics preparedness and response to emergencies

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Since its creation in 1993, the Regional Program on Bioethics of the Pan American Health Organization (PAHO) – which serves as the Regional Office for the Americas of the World Health Organization (WHO) – has strengthened capacity in bioethics in the Region (1). During the 28<sup>th</sup> Pan American Sanitary Conference in 2012, PAHO Member States resolved to advance bioethics and integrate ethics in all health-related activities, primarily in research and public health (2-3). During the 56<sup>th</sup> PAHO Directing Council in 2018, the outcomes of this 2012 regional mandate were assessed, and PAHO Member States decided to escalate their efforts to integrate ethics into various areas of health (2-4). Regarding research ethics, Member States drew attention to the fact that, despite the significant progress achieved, some challenges remained for the Region, such as the establishment of research ethics systems capable of ensuring that research is always conducted ethically (4).

To promote a systemic approach to research ethics (i.e., taking a comprehensive view of research ethics that considers all relevant aspects of research and fosters coordination with all research stakeholders), PAHO’s Regional Program on Bioethics devised a strategy that includes two lines of action: (1) strengthening research ethics systems to ensure all research is ethical; and (2) strengthening ethics preparedness for emergencies. For each line of action, corresponding objectives and indicators were developed (table 1) (5-7).

**Table 1** – Objectives and indicators of PAHO’s strategy to strengthen research ethics systems

Objective	Indicator
<i>Line of action 1: Strengthening research ethics systems</i>	
Adopt ethical standards for research with human participants in accordance with international guidelines	1. Number of countries with legislation or other legally binding instrument governing health-related research with human participants that is consistent with international ethical standards, including requirements for ethics review by an independent committee

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Objective	Indicator
Establish effective mechanisms for the ethics oversight of research	2. Number of countries with a national body tasked with the oversight of ethics review committees, including establishing mechanisms for registration, training, and compliance
Enhance ethics capacity among researchers and ethics review committees	3. Number of countries with policies that support research ethics training for investigators and ethics review committees
Advance transparency in research	4. Number of countries requiring the prospective registration of clinical trials in accordance with WHO standards
	5. Number of countries with policies on responsible conduct of research
<b>Line of action 2: Strengthening ethics preparedness for emergencies</b>	
Strengthen the capacity to conduct research ethically during emergencies	6. Number of countries with established procedures to do thorough accelerated ethics review of research during emergencies

PAHO evaluates countries' research ethics systems using these indicators in order to understand their current situation, tailor technical cooperation plans to each countries' needs, and identify progress. PAHO's Regional Program on Bioethics actively supports countries throughout the process of fulfilling the indicators, e.g., developing national research ethics policies in accordance with international ethical standards and considering the countries' needs, advocating for their approval, facilitating national consultations, coordinating with key stakeholders, and supporting the implementation of the policies approved. PAHO is committed to periodically reviewing and updating its indicator-based strategy to strengthen research ethics in the Region. This approach can also be used in other countries or regions to catalyze research ethics.

In a recent study, PAHO's indicators were used to assess 22 countries in the Latin American and the Caribbean region (7). The results show that most of the countries already achieve two indicators: 1) having legally binding instruments governing health-related research involving human beings, and 2) having a national body responsible for the oversight of research ethics committees (RECs). The indicators that still require more work to achieve are those related to the responsible conduct of research and the establishment of procedures for the rapid ethics review of research during emergencies (table 2). Regarding this last indicator, it is important to note that the study did not include the measures taken specifically in response to the COVID-19 pandemic.

**Table 2** – Number of countries that achieve PAHO’s indicators

Indicator	Achieved	Partially achieved	Not achieved
Existence of legally binding instruments for health-related research with human participants in alignment with international guidelines	12	9	1
Existence of a national body responsible for the oversight of research ethics committees	12	7	3
Existence of policies that support research ethics training for investigators and ethics review committees	7	10	5
Existence of the requirement of the prospective registration of clinical trials in accordance with WHO standards	1	12	9
Existence of policies on the responsible conduct of research	1	2	19
Existence of established procedures to conduct thorough accelerated ethics review of research during emergencies	1	2	19

## Ethics preparedness and response to health emergencies

The COVID-19 pandemic has stressed the importance of improving countries’ ethics preparedness and response to emergencies, which includes the capacity to conduct research ethically. Countries in the Region that experienced the 2016 Zika virus outbreak had already recognized the value of conducting ethical research in emergencies. Indeed, this public health emergency of international concern led to the consensus that research is an essential component of the response to health emergencies, and that it must be conducted in adherence to international ethical standards, which includes being reviewed by RECs in a rapid yet rigorous process (8).

When WHO declared the COVID-19 pandemic, PAHO quickly escalated its existing work strengthening the Region’s ethics preparedness for emergencies, issuing ethics guidance aimed at catalyzing ethical research (9-14). At first, the support provided by PAHO was mainly focused on the establishment of mechanisms to ensure accelerated yet rigorous ethics review and monitoring processes of RECs (10, 11). Ten countries of Latin America rapidly adapted their research ethics review processes in line with PAHO’s recommendations to streamline the review of COVID-19 studies and ensure their adequate monitoring (15).

However, challenges remained in the Region to conduct ethical research in response to the COVID-19 pandemic. For instance, despite the considerable number of clinical trials conducted in countries of Latin America and the Caribbean studying the safety and efficacy of interventions to prevent and treat COVID-19, a trend toward small and repetitive studies incapable of producing meaningful conclusions was identified (16). Additional prominent challenges in the Region included the monitoring of ongoing research in the context of rapidly emerging evidence, and the emergency use of unproven interventions outside of research. PAHO thus produced guidance on both topics and worked closely with health authorities and other relevant stakeholders to support their implementation. PAHO also held several regional dialogues throughout the pandemic, which have also included RECs, health authorities and investigators, to share experiences and discuss what has worked and what continues to pose challenges (17). The goal of these dialogues was to identify the lessons learned from COVID-19, and the pending agenda for the Region to improve its ethics preparedness and response to future health emergencies. This regional reflection led to PAHO's publication: *Catalyzing ethical research in emergencies. Ethics guidance, lessons learned from the COVID-19 pandemic, and pending agenda* (18).

*Catalyzing ethical research in emergencies. Ethics guidance, lessons learned from the COVID-19 pandemic, and pending agenda* was published in Spanish in June 2022 and subsequently in English, Portuguese and French. The publication revises and integrates prior guidance documents for emergencies issued by PAHO, includes the lessons learned during the COVID-19 pandemic, and develops final recommendations to improve ethics preparedness and response in emergencies, as well as to strengthen research ethics in general (table 3). A summary version of the publication has also been published in Spanish, English, Portuguese, and French (19).

**Table 3** – Chapters of PAHO's publication: *Catalyzing ethical research in emergencies. Ethics guidance, lessons learned from the COVID-19 pandemic, and pending agenda*

Catalyzing ethical research in emergencies. Ethics guidance, lessons learned from the COVID-19 pandemic, and pending agenda	
Chapter 1	Lessons learned from the Zika outbreak and challenges during the COVID-19 pandemic
Chapter 2	How can trust in research conducted in emergencies be strengthened? Transparency and public engagement
Chapter 3	How to ensure that the ethics review and monitoring of research conducted by research ethics committees are agile yet rigorous in emergencies
Chapter 4	How can the ethical acceptability of research be ensured in response to emerging evidence?

<b>Catalyzing ethical research in emergencies. Ethics guidance, lessons learned from the COVID-19 pandemic, and pending agenda</b>	
Chapter 5	How can the ethical use of unproven interventions outside of research be ensured in health emergencies?
Chapter 6	How to ensure that data and samples are shared ethically for future research
Chapter 7	Final recommendations

The publication’s final recommendations are divided into recommendations for action, which can be implemented immediately, and recommendations to conceptualize the specific actions needed. In both cases, the recommendations may apply specifically to health emergencies or may be relevant for both emergency and non-emergency situations. All the recommendations constitute the pending agenda for the Region and establish the stakeholders in charge of their implementation or further conceptualization.

For example, for health emergencies, the responsibilities of health authorities are to establish a strategy for the ethical oversight of emergency research, coordinate research efforts, and get involved in the research conducted in response to emergencies from the beginning to ensure their populations benefit from the research’s potential benefits. Along with international organizations and the scientific community, health authorities should also develop generic research protocols for potential health emergencies.

Most of the recommendations have been conceived for emergencies and ordinary situations in order to foster research ethics in general. For instance, health authorities should always require the registration of clinical trials in registries that feed WHO’s International Clinical Trials Registry Platform (ICTRP) and make public all studies involving human participants that have been approved (20). RECs are tasked with the responsibility of establishing communication mechanisms to inform the public about the studies they are supervising. Health authorities and RECs should incorporate virtual tools into their processes, as well as mechanisms for agile coordination between the actors involved in research, and allow alternative ways of carrying out informed consent processes, so they are not restricted to face-to-face processes. Another important recommendation resulting from the regional reflection on the experience during the COVID-19 pandemic pertains to recognizing the contribution of members of RECs, whose time and dedication is indispensable to conduct rigorous reviews promptly. Research institutions that establish RECs should compensate their members, financially or through another appropriate mechanism.

In order to put these recommendations into practice, PAHO continues providing support to relevant stakeholders. Issuing ethics guidance does not suffice to ensure such guidance is actually followed. PAHO’s Regional Program on Bio-

ethics works closely with Member States on the implementation of ethics guidance and encourages the development of trusting relationships established prior to the emergency, as it facilitates the implementation of ethics guidance during emergencies. Advancing ethics preparedness and response to health emergencies in the Region is an ethical imperative to which PAHO and its Member States are truly committed.

### **From the COVID-19 pandemic to the Monkeypox (mpox) emergency**

On July 23, 2022, WHO declared the outbreak of mpox as a public health emergency of international concern. By November 14, 2022, 52,875 confirmed cases had been reported in the Region of the Americas. (21). Building on the COVID-19 pandemic experience, ethics has been embedded in PAHO's response to the mpox emergency from the beginning. For instance, PAHO's Incident Management System includes ethics as a formal component in the response to mpox, and the Regional Program on Bioethics has worked in coordination with PAHO's response teams on several topics, including the emergency use of unproven outside of research (MEURI framework), and the ethical criteria for equitable vaccine allocation.

Following the recommendations issued by WHO in relation to mpox (22), MEURI protocols for tecovirimat have been developed where clinical trials could not be initiated. In this sense, PAHO's Regional Program on Bioethics has provided support to ensure that the exceptional access to tecovirimat in view of its possible benefit is monitored to protect people and contribute data to the generation of evidence in accordance with the relevant ethics guidance (14, 23).

Additionally, PAHO's Regional Program on Bioethics has been actively engaged with PAHO's Revolving Fund for Access to Vaccines. The Revolving Fund has provided access to most vaccines used in Latin America and the Caribbean for more than 40 years (24), and access to mpox vaccines was approved by Member States in August 2022 (25). To ensure equitable access to these vaccines, ethical criteria for allocation and a plan to operationalize them through the Revolving Fund have been developed with the support of PAHO's Regional Program on Bioethics. To date, 130,000 doses of third-generation mpox vaccines have been secured for Latin America and the Caribbean (26).

## Final considerations

Strengthening research national ethics systems in the Region of the Americas is an ongoing responsibility of Member States and PAHO. Prior health emergencies, including the COVID-19 pandemic, have shown that lessons to improve the capacity of the Region to conduct ethical research in response to health emergencies do get learned. As described in *Catalyzing ethical research in emergencies. Ethics guidance, lessons learned from the COVID-19 pandemic, and pending agenda*, Latin America and the Caribbean have actively taken action to advance the conduct of ethical research during the pandemic. However, further efforts are needed – as evidenced by the recommendations in the document – to be better prepared for potential emergencies in the future (18). PAHO's Regional Program on Bioethics will continue to support Latin America and the Caribbean in the strengthening of regional capacities to ensure that research involving human participants is always conducted in adherence with the highest ethical international standards, and that ethics is integrated in all the other areas of work in health.

## References

- Pan American Health Organization. *Regional Program on Bioethics*. 2022. Available from: <https://www.paho.org/en/bioethics>
- Pan American Health Organization. *Bioethics: Towards the Integration of Ethics in Health, Concept Paper*. 28th Pan American Sanitary Conference, 64th Session of the Regional Committee of WHO for the Americas; Sep 17–20, 2012; Washington, DC: PAHO; 2012. Available from: <https://iris.paho.org/bitstream/handle/10665.2/4457/CSP28-14-e.pdf?sequence=1&isAllowed=y>
- Pan American Health Organization. *Bioethics: Towards the Integration of Ethics in Health, Resolution CSP28.R18*. 28th Pan American Sanitary Conference, 64th Session of the Regional Committee of WHO for the Americas; Sep 17–20, 2012; Washington, DC: PAHO; 2012. Available from: <https://iris.paho.org/bitstream/handle/10665.2/3693/CSP28.R18-e.pdf?sequence=1&isAllowed=y>
- Pan American Health Organization. *Bioethics: Toward the integration of ethics in health: Final report* 56th Directing Council, 70.a Session of the Regional Committee of WHO for the Americas, Washington, D.C. September 23 to 27, 2018. Washington, D.C.: PAHO; 2018. Available from: <https://iris.paho.org/handle/10665.2/49706>
- Pan American Health Organization. *Indicators for strengthening national research ethics systems*. Washington, D.C.: PAHO; 2021. Available from: <https://iris.paho.org/handle/10665.2/54869>
- Neil M, Saenz C. Advancing research ethics systems in Latin America and the Caribbean: a path for other LMICs? *The Lancet Global Health*. 2020;8(1):e23–e240. Available from: <https://www.thelancet.com/action/showPdf?pii=S2214-109X%2819%2930441-3>

- Aguilera B, Carracedo S, Saenz C. Research ethics systems in Latin America and the Caribbean: a systemic assessment using indicators. *The Lancet Global Health*. 2022 June (online). Available from: <https://www.sciencedirect.com/science/article/pii/S2214109X22001280>
- Pan American Health Organization. *Zika ethics consultation: ethics guidance on key issues raised by the outbreak*. Washington, D.C.: PAHO; 2016. Available from: [https://iris.paho.org/bitstream/handle/10665.2/28425/PAHOKBR16002\\_eng.pdf](https://iris.paho.org/bitstream/handle/10665.2/28425/PAHOKBR16002_eng.pdf)
- Pan American Health Organization. *Ethics guidance on issues raised by the novel coronavirus disease (COVID-19) pandemic*. Washington, D.C.: PAHO; 2020. Available from: <https://iris.paho.org/handle/10665.2/52091>
- Pan American Health Organization. *Guidance and strategies to streamline ethics review and oversight of COVID-19-related research*. Washington, D.C.: PAHO; 2020. Available from: <https://iris.paho.org/handle/10665.2/52089>
- Pan American Health Organization. *Template and operational guidance for the ethics review and oversight of COVID-19-related research*. Washington, D.C.: PAHO; 2020. Available from: <https://iris.paho.org/handle/10665.2/52768?locale-attribute=es>
- Pan American Health Organization. *How can research transparency be promoted? Actions for national health authorities during the COVID-19 pandemic*. Washington, D.C.: PAHO; 2020. Available from: <https://iris.paho.org/handle/10665.2/52768?locale-attribute=es>
- Pan American Health Organization. *Guidance for ethics oversight of COVID-19 research in response to emerging evidence*. Washington, D.C.: PAHO; 2020. Available from: <https://iris.paho.org/handle/10665.2/53021>
- Pan American Health Organization. *Emergency use of unproven interventions outside of research: Guidance for the COVID-19 pandemic*. Washington, D.C.: PAHO; 2020. Available from: <https://iris.paho.org/handle/10665.2/52429>
- Palmero A, Carracedo S, Cabrera N, Bianchini A. Governance frameworks for COVID-19 research ethics review and oversight in Latin America: an exploratory study. *BMC Med Ethics*. 2021;22(147). Available from: <https://bmcmethics.biomedcentral.com/articles/10.1186/s12910-021-00715-2>
- 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 from: <https://doi.org/10.26633/RPSP.2020.177>
- Pan American Health Organization. *Regional Program on Bioethics, Dialogues about research ethics during the pandemic: Challenges and lessons to learn in Latin America and the Caribbean*. 2022. Available from: <https://www.paho.org/en/bioethics/bioethics-webinars>
- Pan American Health Organization. *Catalyzing ethical research in emergencies. Ethics guidance, lessons learned from the COVID-19 pandemic, and pending agenda*. Washington, D.C.: PAHO; 2022. Available from: <https://iris.paho.org/handle/10665.2/56139>
- Pan American Health Organization. *Catalyzing ethical research in emergencies. Ethics guidance, lessons learned from the COVID-19 pandemic, and pending agenda*. Summary. Washington, D.C.: PAHO; 2022. Available from: <https://iris.paho.org/handle/10665.2/56586>
- World Health Organization. International Clinical Trials Registry Platform (ICTRP). 2022. Available from: <https://www.who.int/clinical-trials-registry-platform>
- Pan American Health Organization. Monkeypox cases – Region of the Americas. 2022. Available from: <https://shiny.pahobra.org/monkeypox/>

- World Health Organization. Second Meeting of the International Health Regulations (2005) (IHR) Emergency Committee regarding the multi-country outbreak of monkeypox. 23 July 2022. Available from: [https://www.who.int/news/item/23-07-2022-second-meeting-of-the-international-health-regulations-\(2005\)-\(ihr\)-emergency-committee-regarding-the-multi-country-outbreak-of-monkeypox](https://www.who.int/news/item/23-07-2022-second-meeting-of-the-international-health-regulations-(2005)-(ihr)-emergency-committee-regarding-the-multi-country-outbreak-of-monkeypox)
- World Health Organization. *Emergency use of unproven clinical interventions outside clinical trials: ethical considerations*. Geneva: WHO; 2022. Available from: <https://www.who.int/publications/i/item/9789240041745>
- Pan American Health Organization. PAHO Revolving Fund. 2022. Available from: <https://www.paho.org/en/revolving-fund>
- Pan American Health Organization. Final Report CDSS2/FR. Special Session of the Directing Council, Special Session of the Regional Committee of WHO for the Americas (Virtual Session), 5 August 2022. Available from: [https://www.paho.org/sites/default/files/cdss2-fr-e-final-report\\_0.pdf](https://www.paho.org/sites/default/files/cdss2-fr-e-final-report_0.pdf)
- Pan American Health Organization. “PAHO calls for more collaborative action to stop monkeypox outbreak in the region”, 27 september 2022. Available from: <https://www.paho.org/en/news/27-9-2022-paho-calls-more-collaborative-action-stop-monkeypox-outbreak-region>