Template and operational guidance for the ethics review and oversight of **COVID-19-related** research

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SUMMARY

As part of the response to the COVID-19 pandemic, health research has proliferated. Clinical trials and other studies with human participants are being conducted to find efficacious treatments and vaccines for COVID-19. In this context, research ethics committees (RECs) must be prepared and organized to conduct a thorough ethics review of research, and have rapid and flexible procedures in place to do so efficiently, considering the tight timelines and needs posed by this health emergency. This document aims at providing guidance for RECs to develop standard operating procedures (SOPs) for the rapid review of human subjects research related to COVID-19. It supplements the prior Guidance and strategies to streamline the ethics review and oversight of COVID-19-related research.

General considerations

Guidance and strategies to streamline the ethics review and oversight of COVID-19-related research presents alternatives to organize the processes of ethics review and oversight of human subjects research, which relevant authorities can adopt during the COVID-19 pandemic. In some cases, the best option may be establishing a new REC (e.g. an ad hoc committee). In other cases, it may be best to designate an existing REC or one or a few existing RECs (e.g. institutional committees). The choice depends on the context of each country and its response to the emergency. This document presents the key topics that all RECs must incorporate in their SOPs to guarantee a rapid and rigorous review of COVID-19-related research during this health emergency. These topics have been divided into three sections. First, *Preparation of the REC*, includes the SOPs related to the internal organization of the REC to function efficiently during the pandemic. Second, *Ethics review process of COVID-19-related research* presents SOPs to ensure rapid processes of ethics review. Third, *Ethics oversight of COVID-19-related research* includes the SOPs pertaining to the follow-up and monitoring of research during the pandemic. In the left column we provide brief guidance about the aspects that content of the SOP should address; in the right column we illustrate these with a template that RECs can freely use.

The SOPs presented in this document are not sufficient alone when new RECs are established for the emergency, because relevant authorities must consider additional issues (including the governance, composition and resources of the REC); these are discussed in other documents[1]. For existing RECs, these SOPs should be added to their current procedures through addendum.

[1] The following documents provide guidance about these other aspects that RECs must consider:

- World Health Organization. *Standards and operational guidance for ethics review of health-related research with human participants*. WHO, 2011. Available from: https://apps.who.int/iris/bitstream/handle/10665/44783/9789241502948_eng.pdf?sequence=1&ua=1
- Council for International Organizations of Medical Sciences (CIOMS). International Ethical Guidelines for Health-related Research Involving Humans, Fourth Edition. (Guideline 23: Requirement for establishing research ethics committees and for their review of protocols). CIOMS, 2016. Available from: https://cioms.ch/wp-content/uploads/2017/01/WEB-CIOMS-EthicalGuidelines.pdf.

PREPARATION OF THE REC

GUIDANCE	TEMPLATE
1. Composition of the ERC	
In addition to the usual composition of the REC, health professionals with knowledge relevant to COVID-19 should be included. Members who participate in the review of protocols during the declared emergency should have the availability of time to participate in the ERC's activities as well as knowledge of ethical aspects of research in emergency situations.	*During the declared health emergency, the REC must ensure that health experts with knowledge about COVID-19, methodologists, pharmacologists, ethicists, and community representatives are included when reviewing COVID-19-related research; multidisciplinary and gender diversity must be further guaranteed, among other criteria.* *The REC president should identify members to participate in the review of the protocols and ensure that they have the required availability to carry out a rapid review of protocols and knowledge of the ethical aspects of research in emergency situations.*
2. Selection of member conducting reviews	
Members may have reduced availability to conduct a rapid review during the emergency. The SOPs establish the process to pre-identify members before assigning them a project to review.	*The REC president consults members electronically about their availability for a rapid review before assigning them research protocols to review.* *Members will be selected to conduct reviews on the basis of their knowledge and experience related to the COVID-19-related research in question.*

3. Selecting and convening independent consultants	
The SOPs describe the process of selecting and convening independent consultants. For this, it is important to pre-identify experts in topics related to the pandemic with the availability to review research protocols on tight deadlines (researchers, professionals in health or social science, methodologists, ethicists, etc.). The SOPs include mechanisms to identify and manage the consultant's conflicts of interest, and ways to protect the confidentiality of information.	*The REC maintains a list of national or international independent consultants who have been pre-identified based on their experience and knowledge related to the pandemic as well as their availability.* *The REC may seek the advice of consultants taking into account the specific complexity of the COVID-19-related research or when the REC does not have the experience or knowledge necessary for the review.* *Independent consultants can also serve as ad hoc members, with voice and vote, during situations in which the REC needs to include members with the required profiles.* *The president issues a call for consultants through electronic means, at the request of the REC. Before receiving the corresponding documentation, consultants should sign a declaration of conflicts of interest and a confidentiality statement.*
4. Digital registry and documentation archive	
The SOPs establish processes for the digital registry and archive of documentation. These also include measures for guaranteeing the confidentiality of the information.	*The REC's digital documentation will be archived in … (secure cloud-based storage service). Maintaining this documentation is the responsibility of the Secretary. All members of the REC will have access to this archive.* *The digital archive includes electronic the documents received by the REC, digitalized minutes and reports as well as any other information generated during review and oversight processes.*

5. Responsibilities of members	
The SOPs describe the responsibilities of members for ethics review and oversight during the health emergency.	*The responsibilities of members are:* 1. *Establish an email and cell phone and commit to reviewing messages within an appropriate timeframe during the emergency.* 2. *Respond promptly to the president's requests.* 3. *Comply with the assigned deadlines for reviewing protocols.* 4. *Complete and send review reports in accordance with the SOP of the REC.* 5. *Attend virtual meetings or, in case of absence, send comments with their justifications via email.* 6. *Carry out ethics-related follow up and monitoring as decided upon by the REC.* 7. *Promote the registry of COVID-19-related clinical trials in a Primary Registry of the WHO International Clinical Trials Registry Platform (ICTRP)* 8. *Other responsibilities necessary for the adequate functioning of the REC during the emergency.*
6. Responsibilities of the Secretary	
RECs maintain a Secretary to support their activities during the health emergency. The SOPs establish the responsibilities of the Secretary in consideration of the management and use of electronic resources.	*The responsibilities of the Secretary are:* 1. *Provide information to researchers, research sponsors and other relevant parties about the SOPs of the REC during the COVID-19 emergency (requirements for the submission of review requests and internal REC processes, among others).*

	2. *Record documentation submitted to the REC through electronic means and coordinate its handling with the president.* 3. *Manage the timely progress of reviews of research protocols by maintaining close communication with members and researchers.* 4. *Prepare REC meetings, which includes distributing relevant documentation to members, scheduling meetings and guaranteeing quorum.* 5. *Preparing minutes, decisions and other necessary documentation in coordination with the president.* 6. *Maintaining registries and documentation archives, guaranteeing the confidentiality of information.* 7. *Other responsibilities required for the adequate functioning of the REC during the emergency.*
7. **Responsibilities of investigators**	
Research conducted during the health emergency adheres to national and international ethical guidelines and takes into account the primary obligation to provide health care to participants with COVID-19. The SOPs describe the responsibilities of researchers regarding the submission of requests for review, amendments, and any other type of report. Considering the existing evidence around COVID-19 changes rapidly due to the large number of research studies being conducted, researchers are responsible for being attentive to new evidence that could modify their studies. The SOPs also contemplate the responsibilities of investigators to register their studies in national or international registries and	*The responsibilities of the investigator are:* 1. *Establish an email and cell phone and commit to reviewing messages and attending to the REC's calls and messages within a time frame that is appropriate for the emergency.* 2. *Present initial requests for review, progress reports, adverse event reports, amendments and any other information as established by the REC.* 3. *Respond to requests from the REC within the established deadlines and according to the SOPs of the REC.* 4. *Carry out the COVID-19-related research in accordance with national and international guidelines.*

to inform participants about the progress and results of the investigation.	5. *Carry out the COVID-19-related research in accordance with the approved protocol except for when it becomes necessary to act immediately to avoid causing harm to participants and/or interfering with their care.* 6. *Being attentive to new evidence that could modify the study.* 7. *To inform the REC promptly of any changes or deviations made, and the justification for doing so, in accordance with the SOP.* 8. *Registering their COVID-19-related clinical trial in a Primary Registry of WHO's International Clinical Trials Registry Platform (ICTRP).* 9. *Keep participants informed about the progress of the study in comprehensible language, as well as of the results obtained.* 10. *Present to the REC the final research report.* 11. *Other responsibilities necessary to the conduct of the research protocol during the emergency.*

GUIDANCE	TEMPLATE
8. Submission of requests for reviews	
The SOPs establish the process for the submission of requests for review through virtual platforms (such as ProEthos) or other digital means. The SOPs aim to avoid rejecting studies due to concerns about their presentation, and to establish tight deadlines by which investigators must fill in any gaps in information without impeding the start of the rapid review process. The SOPs incorporate mechanisms to determine that studies are effectively related to the health emergency and to ensure that their review is prioritized. The SOPs describe processes for the electronic submission of amendments, progress reports, final reports and other information related to the study. Deadlines for reports about protocol deviations or adverse events are set in accordance with the health emergency.	*The request for review of a COVID-19-related research project should be made a high priority for the REC.* *The protocol and all its documentation should be sent via email to: xxxx@xxx.xxx and should include "COVID-19" in the subject. Before assigning the material, the president reviews it to ensure it is actually related to the health emergency.* *In the case that the documentation is not presented in an adequate manner, the investigator will be notified about it and given a deadline of 24 hours to fix it. This issue does not impede the start of the review process.* *To request the review of amendments to the protocol, a justification and summary of amendments should be sent via email along with the final version of the emended document and a version with changes highlighted.* *Progress reports are presented via email according to the deadlines that are determined in the approval decision.* *Reports about protocol deviations, adverse events, adverse reactions and security are presented via email within 48 hours of the events, which should indicate the reasons and the measures adopted.* *The final report of the study is presented via email at its completion.* *Any other communication directed to the REC should be sent via email.*

9. Documents for initial review	
Along with the documents that are usually presented to the REC (for example, the submission form, research protocol, informed consent forms, the investigator's CV and others), the SOPs establish that the initial presentation of a COVID-19-related research project should be accompanied by additional documentation to facilitate its rapid review.	*For the initial review of a COVID-19-related study, the researcher should present to the REC, along with the usual requirements, the following documentation in the language of the country where the study will be conducted:* ▪ *A summary of the study, in two pages or less, in non-technical language.* ▪ *Previously published and up-to-date evidence, if any* ▪ *The risk minimization plan, taking extreme care to avoid spreading COVID-19 or straining the health system.* ▪ *Material transfer agreements for biological samples and/or data, or their preliminary versions.* ▪ *Plans to publish and disseminate the data and results, indicating the process through which the results will be returned to the affected community and the health authorities.* *In the case of clinical trials, the following should also be submitted:* ▪ *In the case of multi-center studies, the decisions of other RECs or medicines regulatory authorities (in-country and external), where applicable.* ▪ *List of centers in the country where the clinical trial is being carried out, if any.* ▪ *The procedure through which interventions will be made available to participants and to the community if found effective.*

10. Initial review of research by members	
The SOPs for the initial review of COVID-19-related research by members describe processes and deadlines for a rapid review, considering the complexity of the project.	*The protocol and all of its documentation is assigned to at least two primary reviewing members. One of them is a medical professional and the other is not.* *Documents to be reviewed are sent to members via email within 24 hours of receiving the request for review.* *Members will maintain a deadline of 72 hours to carry out the review from the time the email is received. The deadline could be longer in accordance with the complexity of the study.* *The review including the relevant justifications is sent to the email xxx@xxxx.xxx*
11. Additional reviews	
The SOPs for additional reviews consider the process to review amendments, progress reports, security reports, final report and any other documentation that investigators present that may require an assessment or the adoption of a measure by the REC in a timely manner.	*Amendments and reports will be reviewed by members who have reviewed the original protocol.* *Documents to be reviewed will be sent to members via email within 24 hours of being received from the principal investigator. If additional information is needed, the principal investigator should request it within 24 hours of the completion of the member's review.* *Members have a deadline of 48 hours from the receipt of documentation to give a response. The response will be sent via the email of the REC so that the president can communicate to the principal investigator within 24 hours.*

12. Quorum	
The SOPs establish the requirements for quorum. Given the exceptional context of the health emergency, the SOPs can establish a lower than usual quorum. The SOPs consider that members who cannot participate in the meeting may be considered for quorum.	*Quorum for decision-making about a research protocol or other request constitutes … (half plus one, ⅓) of the total number of members. Among those should be members with experience and knowledge relevant to the review of the research in question.* *In cases in which members cannot participate in the virtual meeting, they may be considered for quorum as long as they send in their reviews electronically in advance.*
13. Virtual meetings	
The SOPs describe the process of carrying out virtual meetings. They should take into account, at least, the following topics: ▪ The deadline for carrying out the meeting. ▪ Contacting the investigator for specific consultations or clarifications. ▪ Participation of independent consultants. ▪ Mechanisms for the development and signing of minutes.	*The virtual meeting for the deliberation and decision-making of a COVID-19-related research protocol is to be scheduled within 24 hours of receiving the reports from reviewing members.* *The exact date and time of the meeting are to be communicated electronically by the Secretary to the REC members and consultants (if applicable).* *The Secretary communicates the date and time of the meeting electronically to the investigator so that they are available in case their virtual participation is required to clarify as quickly as possible any doubts that the REC might have.* *The REC should aim to reach its decision by consensus. If this is not possible, decisions should be made via a simple majority vote.* *During the meeting the Secretary, in coordination with the president, takes notes on the deliberation and decision-making processes regarding the research protocol, including who attended, quorum requirements, decisions adopted (approval, conditional approval, or*

	non-approval), along with their justifications, among other information.
14. Staggered review and decision-making	
For cases in which members are unable to carry out virtual meetings, the SOPs describe the processes of staggering review and decision-making processes through digital means (email, instant messaging, etc.)	*For cases in which members are not able to organize a prompt virtual meeting, the review, deliberation and decision-making may be carried out in a staggered way.* *The president, in coordination with the Secretary, sends review reports to all members of the REC through email. Members will send their comments and observations through the same medium. Member discussions can be carried out through email or instant messaging.* *The REC aims at making decisions by consensus. If this is not possible, decisions will be made through a simple majority vote.*
15. Communicating the decisions of the REC	
The SOPS describe the mechanisms for communicating the decisions of the REC electronically. They include the following deadlines: ▪ Deadlines for communicating with the investigator. ▪ Deadlines for receiving the responses from the investigator. ▪ Deadlines for communications with others parties involved with the research as needed.	*All requests to investigators, decisions made by the REC and other communications are communicated via email (xxxxx@xxxxx.com)* *Communications to researchers are made via email within 24 hours from the adoption of decisions by the REC.* *Researchers should respond to the REC within 48 hours.* *Communications to the institution, other RECs, or health authorities shall be made as soon as possible.* *Communications and decisions of the REC only require the signature of the president. Once the health emergency is over they will be countersigned by other members as appropriate.*

GUIDANCE	TEMPLATE
16. Follow-up and monitoring	
To avoid putting members of the REC at risk and affecting patient care and the operation of health centers, the SOPs describe the mechanisms for follow-up and monitoring of COVID-19-related research that may be deferred or conducted remotely. In addition, the SOPs should specify whether the deadlines for follow-up will be given for longer periods of time than they normally are, considering that the existing evidence about COVID-19 is volatile due to the large volume of studies being carried out.	*As part of its decision monitoring and follow-up, the REC can include mechanisms that are specific to the study in question, along with the relevant deadlines.* *Ethics oversight is conducted through reports presented by the investigator remotely or are deferred to be received by established deadlines in a way that protects the privacy and confidentiality of the information.* *The president can designate a member or group of REC members to be in charge of following up on an investigation in question.* *Due to the large volume of COVID-19-related research that is being generated rapidly during the emergency, the REC should conduct ethics-related follow-up and monitoring with a view to the results of the investigations that are being obtained locally and globally.*

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