Appendix B. Guidelines for Review of Protocols during Emergency Outbreak

Adapted from the WHO Guidelines for Rapid Review of COVID-19 Research

Background

To date, there are no approved treatments or prophylactic products known to be safe and effective for COVID 19, which is similar to previous outbreaks such as Ebola, Zika, or Lassa fever. Consequently, conducting research on new medications or vaccines during this pandemic is essential. Research conducted during pandemics or outbreaks, while in the best interests of communities that are presently affected or could be affected in the future, raises many unique ethical issues.

Different countries will be in different stages of readiness to review epidemic-relevant research. Regardless of preparatory work that has been done so far, there are things that ethics committees can and should do now to prepare for rapid review of COVID-19 protocols. It is necessary that research ethics committees be prepared to rapidly review COVID-19 research.

There have been many articles and reports published after the 2014 Ebola outbreak that address ethical issues in research during outbreaks and research ethics governance. [1,2,3,4,5]. Of note, issues were raised about time sensitivity and the balance between the quality and time to review and ensuring the protection of participants in clinical trials, many of whom are in desperate need for any management protocols, lest they lose their lives.

Recently, two workshops were held to address important issues in this context: 1) "Ethics preparedness": Facilitating *Ethics Review During Outbreaks*, organized by ALERRT[6] (**A**frican coa**L**ition for **E**pidemic **R**esearch, **R**esponse and **T**raining)& WHO (World Health Organization) in Dakar, Senegal in March 2018, and 2) "*Ethics review of research on Lassa & other infectious disease outbreaks*", organized by WHO in Abuja, Nigeria in October 2018. These workshops provided recommendations for addressing how National/Institutional (Research) Ethics Committees (N(R)ECs) and other research review committees should

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[1]World Health Organization (WHO). Guidance for Managing Ethical Issues in Infectious Disease Outbreaks. WHO 2016. ISBN 978 92 4 154983 7

[2]Schopper D, Ravinetto R, Schwartz L, et al. Research Ethics Governance in Times of Ebola. Public Health Ethics 2016; doi: 10.1093/phe/phw039 First published online: November 1, 2016.

[3]Nuffield Council of Bioethics. Conducting research and innovation in the context of global health emergencies: what are the ethical challenges? Notes of workshop held on 9 December 2016: 10:00–13:30 28 Bedford Square, London WC1B 3JS.

[4]Upshur R, Fuller J. Randomized controlled trials in the West African Ebola virus outbreak. Clinical Trials 2016: 1-3. DOI: 10.1177/1740774515617754.

[5]The Challenge of Timely, Responsive and Rigorous Ethics Review of Disaster Research: Views of Research Ethics Committee Members. Matthew Hunt, Catherine M. Tansey, James Anderson, Renaud F. Boulanger, Lisa Eckenwiler, John Pringle, Lisa Schwartz. PLOS ONE | DOI:10.1371/journal.pone.0157142 June 21, 2016.

[6]Abha Saxena, Peter Horby, John Amuasi, Nic Aagaard, Johannes Köhler, Ehsan Shamsi Gooshki, Emmanuelle Denis, Andreas A. Reis. The ALERRT-WHO Workshop and Raffaella Ravinetto. Ethics preparedness: facilitating ethics review during outbreaks - recommendations from an expert panel. BMC Medical Ethics 2019; 20:29

prepare for changes that may be necessary to their Standard Operating Procedures (SOPs) in order to respond efficiently during this pandemic.

Specific Guidelines

To facilitate the rapid or time-sensitive reviews, the following additions or changes to the ethics committees' existing standard operating procedures are being recommended.

It is important to note that this guidance should come into action once an outbreak is declared as a public health emergency. This declaration will come from the public health authority of the country. To speed up time to start the research, many processes (e.g., drafting documents, translations, approvals, etc.) will be happening in parallel rather than sequentially as is the case in non-emergencies.

When a protocol is being considered for submission in a language different from that in which the review is conducted, the synopsis, plan, documents of consent/assent, and data collection tools/forms at a minimum should be submitted in the official language of the country where the review will take place. Other documents in the reviewing country's language should be submitted as soon as possible.

A. Documentary Requirements

1. A checklist including the following items should be included in addition to the ethics review form (if used by the research ethics committee):
    a. An option to identify the research as epidemic/outbreak-related in order to facilitate fast-tracking;
    b. An opportunity to describe whether prior research data about the disease exists;
    c. Inclusion of at least one PI or co-PI of the country where research and review is taking place;
    d. Qualification of key investigators, including a description of previous track record with outbreak-relevant research among the research group; and,
    e. An indication whether the protocol is part of a multicenter trial. If yes, an opportunity should be provided to describe the status of ethics approval of the master protocol or the ethics approval of the sponsoring country.

2. Apart from the basic documents submitted for review (Protocol, CVs, etc.), the following should also be submitted:
    a. Letter of collaboration in the form of a Memorandum of Understanding (MOU) or Memorandum of Agreement (MOA) with sponsor institution(s) and the funder(s) of the research along with declarations of Conflict of Interest when possible;
    b. Monitoring and safety management plan for the project, as provided by the study sponsor;
    c. Both data sharing and material transfer agreements (MTA) for data and human biological material, especially if samples are being exported out of the

country, while honoring the laws of the land (a draft may be submitted initially);

d. Clear processes and procedures/expectations for follow-up dissemination and publication, co-authorship, co-presentation, and Intellectual Property Rights;
e. Procedures for dissemination of findings to the affected community (important to ensure maintaining contact and upholding trust of the affected populations, especially research participants); and,
f. May include local requirements on insurance policies, particularly on trials/interventions.

B. Meeting Requirements and Procedures

- ***Considerations***
  1. To prepare for the review of COVID-19 research, RECs should agree on a process for rapid review and communicate this to researchers (and communicate any anticipated delays for non-COVID-19 research).
  2. Also, practical aspects like: identify surge capacity for review, set up systems for remote discussions (which software platform, does everybody who needs it have access and know how to use it, what will you do if internet isn't functioning etc.)

- ***Membership and Quorum***
  1. It is essential that a certain number of members be pre-identified who will share the major burden of review. These members would require specialized training (or equivalent experience) in reviewing research in outbreaks so that they are able to rapidly review research proposals without compromising the ethics. Additional members should be identified and called for review at times when demand increases.
  2. Once an outbreak is imminent or ongoing, the chair or the secretary of the review committee should alert members and ascertain which members would be available for the rapid review.
  3. Identification as well as contacting in advance subject experts (technical) and people with strong knowledge of ethics (both in-country and abroad) willing to serve as ad hoc or co-opted members during outbreaks, as there is a likelihood of receiving multiple projects that need to be reviewed in a short time.
  4. The quorum shall abide by the ICH-GCP requirements.
  5. If pre-identified REC member submits their review but is unable to join the meeting, they should be considered as part of the quorum requirement.

- ***Procedures***
  1. The new SOPs should be circulated to all members of the review committee

2. The review meetings could be virtual or electronic especially if the risk of face-to-face meeting in highly infectious outbreak like COVID-19 may be risky to the members
3. Protocol submission **should** be done electronically to save time with submission of the hard copy, which if mandatory can follow. PIs should contact RECs as soon as possible to communicate their intention to submit as well as a high-level overview of research (is it a trial of new medicine, vaccine, observational study, survey, etc.) so that RECs are aware of protocols that may be forthcoming.
4. Face to face meetings with the PIs should not be mandatory and if necessary electronic and or virtual venues may be adopted.

- ***Timelines***
  1. Protocols should be sent to reviewers within **24-hours of submission**.
  2. Each reviewer should complete their reviews within a specified period of time (usually **3 calendar days** is sufficient and appropriate during an outbreak).
  3. Consolidated review and suggestions (or approval) should be communicated to the PI within a specified period of time (usually **within 5 calendar days**).
  4. The complete review process until issuance of approval should not exceed **14 calendar days**.

C. Communication

1. Electronic or telephonic communication with PIs **should** be initiated to seek clarifications, thus saving time.
2. The PI **should** respond to the review within 48-hour
3. Focal points/persons for communication in respective institutions and RECs/NECs should be identified as early in the process as possible.

D. Documentation and Archiving

All communications **should** be documented and archived following the research ethics committee's standard operating procedures.