STRENGTHENING STAKEHOLDER ENGAGEMENT IN CLINICAL TRIALS THROUGH THE ETHICS REVIEW PROCESS

IMPLICATIONS FOR COVID-19 TRIALS - updated 20 November 2020

The current COVID-19 pandemic underscores the importance of robust engagement and ethics review processes for clinical trials.

1. FACTORS IMPACTING ENGAGEMENT AND REVIEW PROCESSES

- Urgency - A need for rapid yet sound decision-making, as the context is one of emergency.
- Uncertainty - Gaps in knowledge e.g. about pathogenesis, immunity and transmission, and few approved treatments of prophylaxis, makes this research essential.
- Disruption - Social and public health disruptions and restrictive public health measures (e.g., lockdown) may affect traditional face-to-face methods of engagement and ethics review
- Overwhelmed resources - Diminished capacity of various systems to respond e.g. health or regulatory systems.
- Anxiety and mistrust - Stakeholder fear or suspicion triggers the need for heightened transparency.

2. RESEARCHERS' ENGAGEMENT RESPONSES IN COVID 19 TRIALS

Researchers should:

- Be informed by the Good Participatory Practice guidelines for emerging and re-emerging pathogens (GPP-EP) which recommend that "research protocols" include GPP-EP plans and activities, with ample budget allocation and enough time to facilitate participatory approaches (GPP-EP 2016).
- Ensure that stakeholder engagement for COVID-19 clinical trials will be inclusive (involving groups such as civil society advocates and government officials); sustained across the life-cycle; and dynamically responsive to context, as well as adequately staffed and funded.

3. REC REVIEW RESPONSES IN COVID 19 CLINICAL TRIALS

RECs should:

- Assess the "adequacy" of stakeholder engagement plans and activities (GPP-EP 2016).
- Ensure that stakeholder engagement plans are explicit in the ethics review process.

4. RESOURCE DOCUMENTS - USEFUL EXTRACTS AND SUMMARIES

RECOMMENDATIONS FOR RESEARCH ETHICS COMMITTEES

WHO- PAHO 2020 Guidance and Strategies to streamline ethics review and oversight of COVID-19 related research

RECs should:

- Ensure that ethics review and oversight processes are rapid, rigorous, and adapted to the emergency context.
- Ensure that review mechanisms are flexible and suited to country characteristics.
- Ensure that procedures enable communication, co-operation and harmonization between RECs; and avoid duplication of efforts and delays/ loss of valuable time e.g. ad hoc RECs for COVID or institutional, provincial, national or regional RECs.

WHO & ALERRT 2018 Facilitating Ethics Review During Outbreaks: Recommendations arising from a joint ALERRT (African Coalition for Epidemic Research Response and Training) and WHO workshop: Dakar Senegal 20-21 March 2019.

RECs should:

- Have 'peace-time' (non-emergency) review of partial or full protocols to support rapid review of final, contextualized protocols.
- Have clear 'model' Standard Operating Procedures for public health emergencies, including how multi-site review will be managed to avoid unnecessary duplication.

WHO 2020 Guidance For RECs for Rapid Review of Research During Public Health Emergencies (PHEs)

RECs should:

- Acknowledge different stages of readiness for ethics review during Public Health Emergencies.
- Agree on a process for rapid review (as protocols are submitted versus waiting for scheduled meetings) and communicate this to researchers (e.g. review and communication to Principle Investigator (PI) in 5 days, communication back from PI in 2 days).
- Consider remote/ virtual/electronic meetings and review processes.
- Add to review form items relevant to studies in Public Health Emergencies.
- Request documents from PI, e.g. results dissemination plan for community stakeholders.
- Pre-identify members who will assume the burden of reviews and support as necessary.
- Engage subject experts as needed; and
- Identify persons for communication with stakeholders.

WHO 2017 Vaccination in Acute Humanitarian Emergencies: A framework for decision-making

RECs should:

- Use credible regional or international RECs where there is no/ little appropriate local expertise.
- Verify that care/ service-delivery needs are not undermined by the conduct of research.

WHO-TDR 2020 Forum for Ethics Review Committees in Asia and Western Pacific (FERCAP) Statement during the COVID 19 pandemic

RECs should:

- Have "efficient systems to improve turn-around time" and "facilitate timely review".
- Use single or joint review mechanisms to streamline review of multicenter protocols within one state or region.
- Define timelines for efficient ethics review.
- Ensure that research does not "aggravate existing situations of injustice".
- Ensure mechanisms for "input and feedback" from vulnerable study populations.
- Develop expertise to address ethical issues in a timely fashion.
- "(A)dopt relevant guidelines and Standard Operating Procedures".
- Use virtual platforms to convene meetings for these emergency-type protocols.
- Develop informed consent templates for outbreak research.
- Train REC staff for efficient documentation and communication of review/decision.
- Conduct research about review procedures to share good practices with other RECs.

Saxena et al, WHO 2019 Ethics Preparedness: Facilitating Ethics Review During Outbreaks - Recommendations From An Expert Panel

RECs should:

- Develop a national Standard Operating Procedure for emergency response ethical review, including for communications between (N)RECs and National Regulatory Authorities.
- Have support to achieve robust but rapid research ethics review.
- Be cognizant of the impact of outbreak uncertainties on participants' risk of harm.

WHO 2020 - 2019 Novel Coronavirus Global Research and Innovation Forum: Towards A Research Roadmap

RECs should:

- Ensure accelerated ethics review through mechanisms such as the advance review of generic protocols (without compromising human participants' protection).
- Avoid unnecessary duplication in review.
- Learn from previous outbreaks in shaping future response efforts.
- Note that ethics review may be diminished due to outbreak or inadequate expertise/ resources.
- Support and coordinate local capacities for independent ethics review.

WHO 2020 Key criteria for the ethical acceptability of COVID-19 human challenge studies: 6 May 2020

RECs should:

- Review such studies in conjunction with "expert review" by a "specialized independent committee" with expertise in science and ethics of challenge studies (e.g. by WHO).
- Ensure rapid ethics review without compromising stringency.

4 RESOURCE DOCUMENTS - USEFUL EXTRACTS AND SUMMARIES

RECOMMENDATIONS FOR RESEARCHERS

WHO 2020 Ethical standards for Research during Public Health Emergencies: Distilling existing guidance to support COVID R&D:

Researchers should:

- Engage **communities** at all stages of research, if feasible; ensure **local stakeholders** take part in decisions about design, implementation, and evaluation; take reasonable steps to ensure that **all those concerned**—including those who are the **most vulnerable and marginalized**—are included; and establish **community** engagement networks in advance as part of emergency preparedness, ensure collaborative partnerships in determining, conducting and ensuring benefits to **participating community**.
- Build review capacity of **Institutional Review Board/Research Ethics Board/Research Ethics Committees**, or establish other independent review mechanisms if needed; ensure local and international review, avoid unnecessary duplication; employ generic advance protocols/ templates/ tools to help rapid review without compromising protections.
- Not impede **emergency response efforts** or take away personnel, equipment, facilities, and other resources required for outbreak response, ensure that research priorities and activities are consistent with **response efforts**, share findings with response efforts.
- Not take capacity from **routine public health services**, ensure collaborative partnerships in ensuring benefits to health systems for future emergencies.
- Coordinate with **other researchers** to avoid wasteful duplication and underpowered studies.

WHO 2017 Vaccination in Acute Humanitarian Emergencies: A framework for decision-making

Researchers should:

- Not impact the **emergency response**, nor vaccination intervention and ensure that medical care and service delivery take precedence over research in resource-limited settings.
- Obtain the permission of key gatekeepers, such as **community leaders**, where possible, and where possible the input of **affected groups** should be obtained.
- Contain clear plans for returning results to **participants,** recognizing that they may relocate in the months following the humanitarian crisis.

WHO 2020 - 2019 Novel Coronavirus Global Research and Innovation Forum: Towards A Research Roadmap

Researchers should:

- Engage with **communities** to bring their voices to decision-making processes.
- Translate existing ethical standards to salient issues, e.g. impact of restrictive measures.
- Generate high-quality evidence to achieving the goals of **public health response** plans.
- Promote the prioritization of knowledge needs according to epidemic dynamics.

WHO 2020 - R&D Blueprint novel Coronavirus Good Participatory Practice for COVID-19 clinical trials: a toolbox

Researchers should:

- Consider the context – time, place, restrictions.
- Appreciate other planned research activities.
- "Recognize that different types of research (e.g. hospital-based phase 1 vaccine trial vs a multi-facility, multi-country RCT) will likely require different forms of engagement."
- Identify and respond to impacts on the **community**.
- Keep track of **community** priorities as well as concerns raised, and responses.
- Be truthful with (…) **communities** to maintain trust.
- Keep in touch through Community Advisory Boards (CABs) and stakeholder engagement.
- Ensure **stakeholders**' involvement in shared outputs.
- Ensure **stakeholders** can raise concerns and input into study planning and implementation.
- Consider that "lockdown may necessitate the increased use of social media."

WHO 2020 - Working with Community Advisory Boards for COVID-19 Related Clinical Studies

Researchers should:

- Ensure that CAB/G members are not placed at risk of harm (infection, stigma).
- Ensure interactions with CAB/Gs do not undermine, and ideally support local stakeholders particularly Ministries of Health and NGOs.
- Use possibilities like Zoom, Skype or WhatsApp groups or telephone discussions, adapted to low-income communities.
- Begin by working with CAB/Gs that are already in place; set up new CAB/Gs where necessary and possible; or consider whether alternative networks can undertake aspects of CAB/G roles, e.g. networks of Community Health Workers and frontline staff - where pandemic responses will not be undermined.

WHO 2020 Key criteria for the ethical acceptability of COVID-19 human challenge studies: 6 May 2020

Researchers should:

- Consult with **public, relevant experts and policy-makers** with "rapid, rigorous, mutually informative" activities.
- Engage with the **public**
  - At local, national and international levels.
  - Immediately, continuing throughout, and afterwards.
  - To assess acceptability, respond to concerns, and understand impact.
  - To use methods appropriate to context e.g. online engagement.
  - To ensure these are regularly updated.
- Engage with **experts such as RECs, policy-makers** (e.g. in department of health), and others.

Nuffield 2020 Research in Global Health Emergencies: Ethical issues - 28 January 2020

A call to action for research funders, governments, and others: (....)

- Invest in putting community engagement mechanisms into emergency research.
- Ensure engagement is a central part of local health systems in the longer term.
- Promote collaborations between **research institutions** and partners in HIC and LMICs.
- Consider how **communities** will be involved in planning the research, and whether the research will be sensitive to local values (cf. "ethical compass").