NUFFIELD COUNCIL ON BIOETHICS

Research in global health emergencies: ethical issues

Call for evidence analysis

2019

Contents

Introduction

On 20 June 2018, the Nuffield Council on Bioethics' working group on research in global health emergencies: ethical issues launched a call for evidence.

Targeted emails were sent to notify over 400 individuals and organisations of the launch of the call, in addition to promotion via social media channels and email newsletter alerts. In total, 58 responses were received.

Very few respondents chose to answer all the questions raised by the call for evidence, with the majority choosing a selection of questions that related to their areas of expertise.

This document provides an analysis of responses, excluding two responses which were submitted without permission to publish or analyse.

Questions 1 and 2: what constitutes a 'global health emergency'?

Question 1

Please comment on this working definition of a global health emergency.

The working definition of a global health emergency (GHE) presented in the call for evidence document comprised five elements:

- It is triggered by a **disruptive shock** – a sudden and significant change from the ordinary course of events.
- This disruption entails **risks of significant harm to health** both for individuals, and at population level.
- The effectiveness of the response is directly linked to the **timeliness** with which the response is undertaken.
- The health threat **may extend beyond national borders and is a matter of regional and international concern**: this may be in terms of the potential for direct impact on other countries and/or in the need for an international element in the response.
- There are **barriers hindering effective response**, for example in terms of scientific uncertainty, availability of resources, or disrupted infrastructure.

Several respondents commented specifically on these elements and their suitability, or lack of, in contributing to an overarching definition of a 'global health emergency'. Other respondents, including UK Research and Innovation (UKRI), highlighted more generally the importance of having "clarity over what constitutes a 'global health emergency'. Events classified as GHEs may require specific responses from those involved in potential research activities including funders, publishers, and the research community, in addition to any humanitarian assistance provided."

Comments on disruptive shock

Comments on disruptive shock were predominantly critical, noting especially that its exclusion of longer-term, slowly-emerging, or ongoing crises was a cause for concern.

> "the idea of "disruptive shock" is very [much] associated with a concept… of an isolated and unexpected phenomenon. We understand that the refugee situation, for example, is not necessarily due to war or natural disaster or associated with human action, but a reflection or expression of a chronic situation of inequalities and lack of access to basic resources for survival. These calamitous but not acute situations can also have local, national and transnational repercussions insofar as they are collectivities that may become involved in migratory movements." *Oswaldo Cruz Foundation*

> "Noting that some global health emergencies are predictable, even if sudden (for example, recurrent annual floods or hurricanes). This has ethical implications in terms of planning research and collaborative approaches." *Humanitarian Health Ethics Research Group*

> "I don't like the inclusion of sudden - was Ebola sudden? By the time it was declared PHEIC more than 6 months had passed from the index case… is this sudden?" *Anonymous respondent*

> "… the proposed definition… stresses the disruptive shock of health-related disease or terrorist event… it is also important to consider the existing conditions that increase the potential for such disease outbreaks (e.g. new zoonosis or zoonosis considered as potential biological weapons) and the longer-term research processes around disease preparedness that are shaping responses to them". *Animals in Science Committee (ASC)*[1]

> "… sometimes shocks occur more slowly, and it is only when things get bad enough that we discover how bad they've been all along. I'm thinking in this instance of Venezuela, a country that is currently in crisis, but we could have seen this coming for some time had we been paying attention internationally." *Gillian McKay*

Annette Rid also commented on the timeframe indicated by the inclusion of disruptive shock in a definition of GHEs.

> "The definition of "disruptive shock" explicitly states that this may be short-lived or protracted. One reading of this is that the definition of public health emergency covers both the acute phase and the reconstruction phase following an emergency, as well as any chronic instability resulting from it. Even if these distinctions can be questioned, it strikes me that the ethical priorities for the acute and reconstruction phase (with or without protracted instability) could be quite different. For example, in the acute phase, the focus is on saving lives and preventing or addressing significant harm, while of course being attuned to pre-existing structural injustices. But in the reconstruction phase, addressing these injustices becomes a greater priority."

Anonymous respondents also asked:

> "Is time an important component – e.g. chronic conflict in Syria becomes new "normal". Does this still constitute an emergency?"

> "Why so much "disproportionate" focus on emergencies in low resource settings or those with weak health systems? This raises a priority setting dilemma – long-standing vs. new crises. If so, what trumps what? – is the risk of infection of outsiders enough of a risk to divert resources?"

In comments in response to question 2, but which link with this element of the working group's definition, Associate Professor Jantina de Vries, Department of Medicine, University of Cape Town[2] drew attention to a further set of circumstances which might be omitted through including an element of 'disruptive shock' in a definition of GHE.

> "… you include in the GHE wars ongoing in Syria and other countries, but those longer-term conflicts would not necessarily be included under what I imagine a 'disruptive shock' to be. Myanmar seems to be a good example: on the one hand, there is a long history of marginalisation of the

[1] Hereafter referenced in this document as: ASC.
[2] Hereafter referenced in this document as: Jantina de Vries

> Rohingya in that country, with severe impacts on their physical and mental health which would not fall under your definition of GHE (and probably should not). On the other hand, the 2017 coordinated military attacks on this ethnic group does fall under it; is that right, and if so, what is the cut-off? How long should a 'shock' last for it to still be considered a 'sudden and significant' change to the ordinary course of events, and when does it become the new status quo?"

Another respondent suggested that focusing on 'disruptive shocks' can shift attention from other emergencies.

> "[I] would like to stress the importance of thinking through the different forms of uncertainty (public health, clinical, personal, global) involved in a global health emergency, and how attention to one set of 'disruptive shocks' might mask or amplify others." *Ann H. Kelly, Department of Health & Social Justice, King's College London*[3]

Comments on risks of significant harm to health

Respondents also expressed concerns over the definition's focus on 'risks of significant harm to health', for example:

> "How do we define significant harm to health? Those of us who have endured long term warlike conditions know and understand that health is not merely physical health and disorders related to mental health, and that the effects on war on health can go through the pathway of suffering (for example humiliation, exposure to violence, human insecurity, uncertainty etc.) which over the life course can lead to diagnosable disease. What do we do with the loss of community, social worlds, dignity and values which we know negatively affect health although maybe not visible necessarily?" *Anonymous respondent*

Respondents also suggested how this element might be edited. Jihad Makhoul from the American University of Beirut,[4] for example, suggested that the following amendments (in italic text) might be made to this element: "risks of significant harm to health *and livelihoods* both for individuals, and at population level and *even beyond national borders*." Other editing proposals included:

> "I would propose to add 'physical and mental' health ("risks of significant *physical or mental* harm to health") to emphasize that the ethical challenges are not just to do with physical harm". *Jantina de Vries*

> "[The] criterion *"This disruption entails risks of significant harm to health both for individuals, and at population level*" may need some refinement. For example, what exactly would be the difference between the Fukushima disaster and the collapse of the sweatshop in Bangladesh in which many workers were killed? A possible reformulation of the criterion could be *"This disruption entails risks of significant harm to health not only for those directly concerned."*" *Raffaella Ravinetto, Chair of the Institutional Review Board, Institute of Tropical Medicine (ITM), Antwerp, Belgium, Marianne van der Sande, Head of the Public Health*

[3] Hereafter referenced in this document as: Ann H. Kelly.
[4] Hereafter referenced in this document as: Jihad Makhoul.

Department, Institute of Tropical Medicine (ITM), Antwerp, Belgium, Anne Buvé, Vice-Chair of the Institutional Review Board, Institute of Tropical Medicine (ITM), Antwerp, Belgium[5]

Comments: effectiveness of response linked to timeliness

Fewer comments focused on this element of the proposed definition. They included:

> "it is not clear to me what 'the response' means – do you mean the response in terms of containment by large international organizations or do you mean the ethics response?" *Jantina de Vries*

> "timeliness depends on the nature of the emergency […] "[there is] a need to act within a time frame that is helpful, limits collateral damage or further disease spread". *Anonymous respondent*

Jihad Makhoul suggested that the following changes might be made (indicated in italic text):

> "The effectiveness of the response is directly linked to the **timeliness** with which the response is undertaken *and also the axes of intervention which in many cases should include addressing the root causes for more durable and ethical solutions*."

Comments on extending beyond national borders, and GHEs as "a matter of regional and international concern"

Concerns expressed about this element and its potential consequences included:

> "[The definition] unintendedly suggests that what is 'local', or an emergency in a particular setting, for instance in Uganda, may not attract sufficient attention if there is NO real / imagined threat to the international community. For instance, Uganda regularly deals with 'local' disease epidemics, which claims many lives, but because such epidemics do not warrant the scale of a global threat, Uganda deals with these all by itself – sometimes with unexpected success. Uganda's effectiveness of dealing with such epidemics could have been improved if the health emergency was upgraded to a 'global health emergency'." *Anonymous respondent*

> "The definition states that the health threat may be a matter of regional or international concern. Yet there seems to be quite a significant difference between public health emergencies that can be dealt with at national level (meaning that disaster response mechanisms are broadly in place, as are, presumably, other institutions to promote social justice) and emergencies that require external assistance (meaning that such mechanisms are not in place, a multitude of national and international actors with different goals and priorities and sometimes limited knowledge of the population affected by the emergency requires coordination, and so on)." *Annette Rid*

[5] Hereafter referenced in this document as: Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé.

An anonymous respondent stated: “I like and appreciate the use of the word ‘may’ in this sentence: “The health threat *may* extend beyond national borders and is a matter of regional and international concern.””

Ann H. Kelly also stated:

> “By foregrounding the disruptive nature of the crisis and the timeliness of the response as opposed to the international dimensions of the crisis (“*may* extend beyond national borders”), I support the effort of this call to avoid reinforcing the forms of public health neglect that a security-focused emergency declaration can bring to a crisis.”

Edits to this element were also suggested (indicated in italic text):

> “The *consequences on health* may extend beyond national borders and is a matter of regional and international concern: this may be in terms of the potential for direct impact *(severity and seriousness to the public’s health)* on other countries and / or in the need for *concerted global efforts to address.*” *Jihad Makhoul*

An argument was also put forward that GHEs may not necessarily be required to cross borders.

> “[A GHE] should not need to be an international threat – it may be enough if [the] emergency overwhelms local system or places many individuals at risk”. *Anonymous respondent*

> “[It] is important that the definition reiterates that global health emergencies do not need to be health threats that cross borders.” *The Ethics, Community Engagement and Patient Advisory (ECEPAS) Working Group of the Global Emerging Pathogens Treatment (GET) Consortium*[6]

Comments on barriers that hinder effective response

Very few respondents commented directly on this suggested element. However, an anonymous respondent listed examples of barriers that might fit into this category:

- “Knowledge, uncertainty about benefit vs. risk of interventions/therapies in emergencies
- Scepticism, mistrust or fear of the health system or of the research enterprise/foreigners among those affected
- Infrastructure for usual care, for research, for transportation, delivery of supplies (for clinical care and research), storage of samples, data security, confidentiality, avoidance of stigma, local customs/beliefs
- Challenges in reaching most vulnerable
- Lack of a therapeutic or a solution
- Lack of coordination and collaboration
- Poor communication, education”

The same respondent also suggested:

[6] Hereafter referenced in this document as: ECEPAS GET.

> "[a further] barrier to conduct of effective and appropriate research is limited *capacity of local researchers* (in terms of numbers and knowledge). Very few local names appeared on papers related to Ebola research / most authors were form US, Germany etc. The insights, skills, languages etc. of local researchers are however crucially valuable for planning and implementation of research– but they may be directly affected (e.g. Haiti Earthquake, family members affected by Ebola etc.) – the may not be able to "think straight" under massive stress".

Jihad Makhoul also observed:

> "There are *perceived and actual* barriers hindering effective response, for example in terms of scientific uncertainty, availability of resources, *conflicts of interest,* or disrupted infrastructure."

Other comments on this definition

Several comments were made in relation to this definition more generally, rather than on the specific elements proposed.

The distinctiveness of different 'global health emergencies'

Some respondents indicated that different types of GHEs should each be treated as distinct entities.

> "I have difficulty in grouping all types of emergencies under the heading of global health emergency. There are different types of emergencies which I do not think should be lumped together. There are natural disasters of different sorts, man-made disasters of different sorts, and this includes wars and conflicts of various durations." *Anonymous respondent*

> "Some aspects remain problematic and deserve more clarification. Looking at the provided examples, for instance, it would seem that the issues relating to research in Ebola/VHF or a respiratory virus with high mortality are very different than health issues for displaced people in Lebanon, even if the latter is part of a regional crisis. It seems that there should be some differentiation, based on the type of emergency (e.g. based on elements such as the type of agent, the type of transmission, the expected mortality etc)." *Myriam Henkens, Clair Mills and Greg Elder, on behalf of Médecins Sans Frontières (MSF); Raffaella Ravinetto, Lisa Schwartz, Ross Upshur, and Grace Ku, on behalf of the MSF Ethics Review Board (MSF ERB)*[7]

The need for a broad approach

Other respondents suggested the need for a broad approach to defining a GHE.

> "[The] definition can only be in broader context since depending on the far-reaching ramifications and implications of the emergency on human, animal and environment". *Ernest Tambo, Africa Disease Intelligence and Response Institute & Universite des Montagnes, Bangangte, Cameroon*[8]

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7 Hereafter referenced in this document as: MSF/MSF ERB.

8 Hereafter referenced in this document as: Ernest Tambo.

> "I am not sure that it will be possible to come up with a single definition. It depends on, among other things, how health is defined. If health is 'well-being' then all humanitarian emergencies are health emergencies. Maybe it would be good to make the point that restricting the term to outbreaks of particular diseases can be unhelpful." *Tim Allen, London School of Economics and Political Science*[9]

> "It is helpful to have a broad definition of global health emergency that is inclusive of man-made and natural disasters, armed conflict, forced displacement, and disease outbreaks as there are many similarities in the ethical questions related to research across these different types of crises." *Anonymous respondent*

In a related point, an anonymous respondent indicated that the concept of a GHE might be better serviced by a description of characteristics rather than a specific definition, "given that emergencies are highly variable and highly complex." The variety of potential GHEs was highlighted by Wissam Doudar.

> "It [GHE] can be of natural source, like volcanic eruption, earthquake, floods, tsunami, or of biological nature, including pandemics and epidemics, or of nuclear activity, like leaks of nuclear reactor or nuclear war, armed conflicts that cause injury, starvation and displacement and other harsh living conditions."

In a related point, Jihad Makhoul commented on the scope of including infectious disease in the definition:

> "… the scope of the definition and consequently, the examples, should widen to include other types of infectious diseases whose spread has gone unnoticed globally up until 2007. The diseases may be described as endemic, rather than sudden in their occurrence, such as the neglected tropical diseases (NTDs). These diseases also cause much suffering, disability and death for millions of people in about 150 impoverished countries of the world. These diseases have slipped from this category of global health emergencies, although they are of global relevance, but have not received global attention in terms of funding or interventions for prevention. Food crises could be another category which should fall into this definition of global health emergencies. Also, another cause of death, suffering and disability, and again in the most impoverished countries of the world as an outcome of multiple factors, including climate change, armed conflicts, mismanagement of resources and an unjust global economic order."[10]

Similarly, Professor Robin Gill questioned whether, in addition to infectious diseases, communicable diseases might also come within the scope of what the project considers to be a 'global health emergency'.

The inclusion of ethics in the definition[11]

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9 Hereafter referenced in this document as: Tim Allen.

10 These considerations lead the respondent to conclude that the definitional elements set out in the call for evidence should be subject to amendment (see respondent's further comments above).

11 See also 'omissions from the definition' section below.

Respondents also explored whether ethical aspects might be included in the definition.

> "I'd perhaps add that global health emergency could be defined in ethical terms. Something like: 'global health emergency is a condition when existing ethical standards and norms are (partially) dismissed to make the most impactful public health response'." *Arsenii Alenichev, The University of Amsterdam*[12]

> "One added feature that could be considered (particularly in relation to 'ethics') is the characteristics of the affected population […] ethical issues are particularly notable in these situations when the affected population also has been traditionally marginalized as a result of historical 'oppression' – and would suggest adding something like this as one of the features." *Anonymous respondent*

Other examples of 'global health emergencies' are required

Some respondents indicated that the list of GHE examples potentially within the scope of the Council's inquiry should be expanded to other circumstances.

> "The examples on the website started by making link to diseases where there is no effective treatment. However, there may be cases where there is effective treatment but it is not available in the country or the rate of spread is beyond national response and so it becomes a potential global health emergency extending beyond the borders of that country." *Dr Rosmond Adams from the Caribbean Public Health Agency (CARPHA)*[13]

> "I would add 'the emergence of a new infectious disease that causes serious harm and for which effective containment strategies are unclear or pose significant feasibility problems for implementation'." *Bridget Haire, Kirby Institute, UNSW Sydney, Australia*[14]

> "Good examples but it does not include deliberate political interference as in The Yemen at the present time, or in Syria, when there is or may be a deliberate policy to starve in some way (e.g. food, water, medical supplies), or incapacitate a population." *David B. Morton (Professor Emeritus, University of Birmingham, UK)*[15]

Criticism of reference to 'global' health

Several respondents criticised the reference to 'global' health.

> "the word "global" is too often (mis)used these days, so the term "health emergency of international concern" could be preferable. For instance, we can hardly say that the earthquake in Haiti was a "global" problem, unless if we link this to the "global" media coverage." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

> "Not necessarily 'global' – what does that mean? (Two countries immediately affected? Do they have to be contiguous?)" *Dr Cathy Roth,*

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12 Hereafter referenced in this document as: Arsenii Alenichev.
13 Hereafter referenced in this document as: Dr Rosmond Adams, CARPHA.
14 Hereafter referenced in this document as: Bridget Haire.
15 Hereafter referenced in this document as: David B. Morton.

Senior Research Fellow - Infectious Diseases, Department for International Development, UK, responding in a personal capacity[16]

"[The working group] may want to rephrase "global" as support [is] needed when local capacities are overwhelmed or not existing. [It] affects [the] highly vulnerable disproportionately. [Or] remove the word "global" from the definition?" *Anonymous respondent*

Reference to other definitions

Respondents also referenced definitions from other sources, including those from the WHO and the International Health Regulations' classification of a 'public health emergency of international concern'.

"I don't see a major difference between the definition of international health as part of the WHO IHR and your global health definition. The core concept is that it is abrupt (unplanned), it has impact on health of people (public health) and it has a cross boarder implication (international)." *Dr Najeeb Al-Shorbaji*

"I'm not sure it's correct to say that there is no single agreed definition of a 'public health emergency of international concern (PHEIC). The revised International Health Regulations (IHR), agreed to by WHO's 193 Member States, represent a pretty high level of agreement on PHEIC." *William Aldis, Office of International Programs, Faculty of Public Health, Thammasat University (Thailand)*[17]

"A PHEIC is also often used as the trigger for additional targeted activities, facilitating the deployment of government resources and activities in response. In addressing the issue of what constitutes a global health emergency, therefore it will be helpful to consider the implications of an event being, or *not* being, thus classified. For example, WHO was criticised for the delay in the declaration of the 2014 Ebola outbreak as a PHEIC which impacted the response (in terms of international provision of support and resources to address the crisis)." *UKRI*

"We accept that the binary choice between a Public Health Emergency of International Concern and 'business as usual' is not appropriate, however the World Health Organization is working to ensure that terminology can capture different kinds of emergencies and the variety of circumstances which occur and require a tailored response." *Wellcome*

"It is *not* helpful to use the term 'public health emergency of international concern'. Despite initial intentions this definition has not helped focus on prevention." *Dr Cathy Roth*

When does a GHE end?

When a GHE 'ends' was raised by a number of respondents.

"One issue that is difficult to capture in any definition is if/when an event, through becoming a chronic situation, no longer constitutes a global

16 Hereafter referenced in this document as: Dr Cathy Roth.
17 Hereafter referenced in this document as: William Aldis.

> health emergency – or whether the long-term nature of some events does not exclude them from the definition (as stated in the background)." *Anonymous respondent*

> "Some emergencies become 'chronic' – for example, decades long war or civil unrest. So, while a disruptive shock may have set them in motion, the situation of emergency may well become, tragically, the baseline. In these cases, the temporal urgency of the situation will be very different than for a sudden onset disaster." *Humanitarian Health Ethics Research Group*

> "The working definition appears to be focused on the near-term effects following the onset of a global health emergency. The health effects following these emergencies may persist long after the initial emergency event. Additionally, research studies may also take many months or years following the initial event. What is the timeframe that this project is considering? Is it limited to the near-term, or is it inclusive of research in the long-term? This is an important question given that armed conflicts may last several years and forcibly displaced persons are often away from their homes for many years or even decades." *Anonymous respondent*

A related point on time was noted by the Animals in Science Committee.

> "it is important to consider responses to global health emergencies in the context of the longer trajectories of research on disease ecologies, animal models, drug development, and licensing processes that are critical in preparing for outbreaks."

Omissions from the definition

Some respondents indicated that the definition omitted particular points.

> "I would have liked to see a distinction between an emergency and a disaster, where an emergency is as you've described it, and a disaster is an emergency which overwhelms existing response capacity. The nature and scope of the response required in the two are different. The examples you give would be in most cases disasters. All disasters are emergencies, but not all emergencies are disasters. Ethical concerns are more intense in disasters." *William Aldis*

In addition, Jantina de Vries suggested that the definition "leaves out (perhaps on purpose)… the relative weakness of an ethics and regulatory infrastructure… I think that the reason there is now a consultation like this one is because of this lack of ethics infrastructure." The same respondent continued:

> "If a GHE were to happen in Germany, for instance, I imagine that there would be sufficient expertise and resources to deal with containing the event in an (ethically) appropriate manner. But the same is not true for e.g. the Ebola outbreak in Sierra Leone […] I think you need to consider whether you would want to include something to this effect in the working definition."

Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé also suggested that information on 'who decides' is omitted.

> "There remains the issue of who decides on whether or not the criteria mentioned are reached. This may depend, for example, on your perspective / position on what is defined as a 'global' threat, when is existing capacity likely to be insufficient, what defines an event as disruptive, sudden and unexpected."

The proposed definition is satisfactory

Some respondents indicated their satisfaction with the definition.

> "I like the focus on the features of the situation, rather than the underlying cause. And I think the features that have been defined are important and comprehensive." *Anonymous respondent*

> "This definition is very good. It captures many of the essential aspects of GHE. It is clear that the focus is on the emergency, and the sudden onset (disruptive shock), as opposed to the chronic, on-going issues." *Dónal O'Mathúna, PhD*[18]

> "It is also important to clarify what makes research in global health emergencies distinct from other global health research, as this definition does well." *Anonymous respondent*

> "… the features listed are useful to understand the definition as well as the examples provided. I agree that the definition might need to adapt to different situations." *Jackeline Alger MD, PhD, Facultad de Ciencias Médicas, UNAH*

> "The definition provides a useful basis to think about what constitutes a global health emergency at the early phase of an event." *Anonymous respondent*

Respondents also suggested how the definition might be put into practical use:

> "The working definition used is comprehensive and inclusive. It will be good to form certain criteria based on impact and magnitude of a condition to include something as a global health emergency. For example a sort of scoring system based on magnitude in terms of numbers affected, or magnitude of the condition, potential harm to the lives of affected and unaffected persons, impact on the economy of the region etc." *Dr Anuradha Rose*

Question 2

What might be the ethical implications of defining global health emergencies in this (or other) ways?

Several ethical implications were highlighted by respondents that can be split, very broadly, into positive and negative categories. Most respondents who chose to address this question highlighted negative implications.

[18] Hereafter referenced in this document as: Dónal O'Mathúna.

Positive implications

Provides a helpful guide

Some respondents indicated that defining GHEs in this way could provide helpful guidance for 'next steps'.

> "Clearly defining what is a global health emergency is important because this will guide us on if we need to fast track research and exempt certain types of research as to enable the speedy collection of data and evidence for response actions." *Dr Rosmond Adams, CARPHA*

> "it gives a direction to the stakeholders to ethically deal with these emergences… It give[s] [a] clear way to act in [a] more systematic way rather than for everyone to jump in and take a situation for granted". *Ms. Tausi S. Haruna (BscN, RN, Masters in Bioethics) from the Hubert Kairuki Memorial University (HKMU) in Tanzania*[19]

Encourages a 'just' response to GHEs

> "Defining global health emergencies based on criteria may minimize the possibility of richer countries, and more dominant societies being responded to earlier than emergencies which affect poorer communities. It will be a more just and transparent system to deploy manpower and resources." *Dr Anuradha Rose*

Negative implications

Overlooks / overpowers other important issues / circumstances

Several respondents indicated that defining GHEs in this way might lead to other important issues and circumstances being overlooked or overpowered.

> "[The] definition – and most others I am familiar with – highlights the scale and suddenness of the potential harm. Both can create an urgency to act, with the possible ethical implication of giving greater weight to saving lives over respecting process or respecting rights. The suddenness aspect also is prone to lead to psychological distortions that can direct attention and resources away from equally bad, or worse, events or situations." *Annette Rid*

> "The biggest danger in my view is that those focused on one area tend to overlook the other, or regard them as being in serious conflict. For example, the rush to relieve a sudden onset disaster should not undermine on-going development work." *Dónal O'Mathúna*

> "… in general, a fixed definition may be heavily influenced by recent events and/or by personal views of those who had the opportunity to participate in the process, leading to possible bias, or limiting inclusiveness". *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé.*

[19] Hereafter referenced in this document as: Ms Tausi S. Haruna.

> "The headline hitting emergencies are generally a threat to Malawi, not because of the context (SARS, Zika, Ebola) but rather because global attention is diverted from the crashing health needs that affect Malawi daily." *Professor Stephen Gordon, MLW, Malawi*[20]

Compromising longer-term outlooks was raised as a further ethical implication.

> "Tendency to focus on here and now only, without necessary consideration on potential distant or long-term effects, rather than (only) immediate effects." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

> "… while the focus here on GHE is fine, I would like to see a comment about how emergency responses should take long-term sustainability into account, and give due consideration for long-term recovery." *Dónal O'Mathúna*

Resource implications

Resource implications were also identified as a negative implication of defining GHEs according to the working definition, or in other ways.

> "there is an impression that as long as a health emergency does not meet the scale / magnitude of a global health emergency, a country will address such a challenge-by-itself. Too much attention and resources will then be reserved to only health emergencies redefined as global health emergencies. I foresee too much attention and resources / planned and redirected for diseases like Ebola, yet in my country there are many other health emergencies/regular challenges which are regular and persistent, for instance cholera, malaria." *Anonymous respondent*

> "Use of the term 'global' risks the approach that action only happens when richer countries fear being affected – implications for equity and access – and also for funding." *Dr Cathy Roth*

What it excludes

Respondents also indicated that a negative implication of the definition could rest in the situations it *excludes* from its remit.[21]

> "As I think about the five bullet points characterizing a global health emergency, it occurs to me that the last four could be subjected to quantification or levels: How severe are the risks? How critical are the time constraints? What is the extent of international spread and magnitude of populations affected or at risk? What is the nature and the magnitude of barriers to response (for example, geography of an affected region may be a barrier, but armed conflict is a much more serious one.)? I mention this because it seems to me that ethical issues might be framed differently depending on the level of severity." *William Aldis*

> "Though the EVD epidemic caused a "disruptive shock – a sudden and significant change from the ordinary course of events", it also involved

[20] Hereafter referenced in this document as: Professor Stephen Gordon.
[21] Other points on what the definition excludes are also discussed in response to question 1.

significant continuities with the ordinary course of events, continuities to which researchers and research ethicists must remain attentive." *Humanitarian Health Ethics Research Group*

"If we take the Palestine refugee situation in Lebanon as a very protracted emergency (70 years of protracted), would it be considered under this definition as a global health emergency? It meets the features – other than perhaps timeliness, but that in itself is an issue. There may be no urgency because the world has been complacent. But these are refugees that have been living with few rights for 70 years. And any research conducted in this context needs to be a different approach than the 'usual' because of that." *Anonymous respondent*

"[A] global health emergency can also be understood in contexts of humanitarian situations – oftentimes whose impacts e.g. disease outbreaks, malnutrition and others may affect more than one country. Examples majorly include refugee crises." *Dr Joseph Kimuli Balikuddembe, Institute for Disaster Management and Reconstruction, Sichuan University, China and Hong Kong Polytechnic University*[22]

"While we find the notion of a 'disruptive shock' helpful in some categories of global health emergency, it seems most useful only in seemingly sudden contexts of GHE. It is not inclusive of the longer term, gradual problems of relentless poverty or conflict, climate change, political or social conflict that lead cumulatively to something that becomes an emergency or should benefit from emergency response. Sudden and disruptive issues deserve careful attention, but they should be seen within a context of wider protracted problems which cause or aggravate the emergencies. For example, the terrible outbreak of Ebola in West Africa was predicated on a lack of public health infrastructure due to poverty and a history of political instability. Cholera in Yemen might have been contained if the war didn't inhibit access to treatment etc." *MSF/MSF ERB*

Other respondents indicated that the definition fails to account for the role of animals in GHE research endeavours:

"We would like to highlight the implications of this (and other) ways of defining global health emergencies on the harm-benefit analysis of animal research, which remains the primary ethical framework for evaluating the use of animals in research and testing." *Animals in Science Committee*

"[Deliberate] killing or maiming or incapacitating humans and animals for a questionable benefit. NB I am including animals under the ethical issues as their suffering also matters and it can be more extreme than many humans". *David B. Morton*

Other suggested negative implications

Other negative implications highlighted by respondents included:

- Suggests homogeneity

[22] Hereafter referenced in this document as: Dr Joseph Kimuli Balikuddembe.

"… global health emergencies cannot be defined as 'One event fits all' and/or not all or [no] law can be applied [when] talking of global health emergencies since [the] event, strength and severity occur and [vary] from [one] place to another from outbreak, hurricane, hunger and famine, man-made disaster, migration and resistance." *Ernest Tambo*

- A disconnect between the elements of the definition

"There is a possible disconnect between the first feature – disruptive shock – and the protracted nature of emergencies. In the first feature, it is stated that: '... a failure to respond adequately to an emergency may mean that it is protracted...'. Indeed, but these protracted situations may not be "… a sudden and significant change from the ordinary course of events.""" *Anonymous respondent*

- Compromised ethical standards

"If… we agree that there may be circumstances that justify compromised ethical standards then we should push for a very strict and limited interpretation of such emergencies and ensure that this determination be made subject to regular and periodic review". *Anonymous respondent*

- Risk of stigmatisation of affected communities

"Labeling an event as a "GHE" might risk in some cases stigmatize rather than support the populations most affected by emergency." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

- A retrospective approach

"[The] definition risks being made retrospectively and also by people other than those affected – so whatever ethical frameworks should be applied may be implemented late and by external people dislocated from the problem." *Anonymous respondent*

Questions 3–5: undertaking research in a global health emergency: whose voices should be heard?

Question 3

Please provide examples of how, despite the urgency and pressure of other aspects of immediate humanitarian response, national governments, local researchers, and affected populations have genuinely been 'at the table' in setting research priorities in a global health emergency.

A range of examples were offered by those who chose to respond to this question. For example, the work of the Partnership for Research on Ebola Virus in Liberia (PREVAIL) was highlighted in a response from Barthalomew Wilson:

"This bilateral arrangement brought together scientific experts, community champions and population stakeholders from both Liberia and the U.S. The PREVAIL team was established, with representatives from each

> country bringing to the table their expertise and experience to conduct high-quality clinical research in the midst of a major epidemic of global public health concern. Functional teams were established with the responsibilities of developing strategies based on their respective objectives, tasks, and project timelines. Each team consisted of representatives from both countries who worked together to quickly resolve challenges and barriers as they were identified."

Also commenting on PREVAIL, Bridget Haire stated:

> "There was certainly community engagement in the Prevail vaccine study in Liberia, though it was limited in that it appears to have been quite focused on negotiating cooperation with the program rather than participating in setting the research agenda. Nevertheless, the process of negotiating cooperation is important, and I believe that there was also two-way communication between community, community liaison personnel (who were Liberians) and the researchers and that this had some impacts on the program roll out."

Other respondents also highlighted the positive approach taken in response to the West Africa Ebola outbreak.

> "The question of who sets the research agenda is pressing in all kinds of international health research. It just is more pressing in GHE, and we should acknowledge that in some settings where a GHE arises, there is a tremendous lack of research capacity. Having said that, in the Ebola epidemic in West Africa genuine efforts have been made and were successful in involving local researchers." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé.*

> "During the West Africa Ebola outbreak, there were patches of good practice, even if these weren't able to be joined up… [There was] a very good REC in Sierra Leone – but its infrastructure wasn't strong enough to stand up to all the other demands placed upon it because of the emergency." *Dr Cathy Roth*

> "In conducting the "EVD-PME study", we encountered examples where some of the groups identified above were genuinely "at the table" in setting some research priorities. The most successful examples were from Guinea, a country that had comparatively robust health research structures and a well-established established health research ethics governance before the onset of the epidemic and was able to draw on these resources to promote key priorities." *Humanitarian Health Ethics Research Group*

> "[An] example of good collaboration is the research undertaken into the therapeutic potential of convalescent plasma in Sierra Leone. Investigations in this area were begun by national researchers, who in the absence of plasmapheresis machines transferred whole blood from survivors into Ebola patients. The work also had considerable public support as it relied on the efforts of Ebola survivors, who expressed pride at being able to support." *Ann H. Kelly*

> "The research laboratory capacity was instrumental in the success of Mali's Ebola response by providing timely and accurate diagnostics".

Seydou Doumbia, Faculty of Medicine & University Clinical Research Center, University of Sciences, Techniques and Technology of Bamako, Mali[23]

The 2018 Lassa fever outbreak was also highlighted as a key example:

> "the Lassa fever research agenda that was started in early Jan 2018 under the leadership of NCDC [Nigeria Centre for Disease Control]. The initiative brought together NCDC, special teaching hospitals in known endemic region including local medical staff with the support and collaboration of international partners." *Anonymous respondent*

The more recent outbreak of Ebola in the DRC was also noted as an example:

> "An assessment of risks was conducted immediately. This resulted in the identification of five active cases. The WHO did point to the fact the success was not in the vaccine, but due to the rapid response from the international community and the national government efforts to build trust in the community. Fast international support, ready availability of funds, support from the government and buy in, good will and trust from the local community enhanced efforts towards setting the research agenda and dealing with the global health emergency." *ECEPAS GET*

In response to question 11, Ann H. Kelly illustrated a community engagement approach undertaken during the Zika virus outbreak.

> "In Rio, during the Zika Outbreak, the *World Mosquito Programme (Previously Eliminate Dengue)* undertook successful experimental releases guided by an impressively nuanced, sophisticated and comprehensive approach to community engagement. A couple features of this programme I would emphasize here: 1) the programme worked through a public institution, Fiocruz, and made use of existing public health resources such as urban vector control teams and community health officers 2) the programme worked with communities to help articulate their concerns not only with the project but with broader set of public health issues 3) consent came via an extensive and iterative dialogic process, multiple avenues were put in place for communities to raise questions and be involved in research design 4) the intervention did not require participants to change any behaviours, for instance they could were encouraged to protect themselves against mosquitoes with their preferred method including using indoor spray and larvicide."

The Zika outbreak was also highlighted by the Oswaldo Cruz Foundation:

> "The recent experience of the epidemic by Zika virus highlighted the ethical constraints and the demand to include people affected by outbreaks or damages since the very beginning of the [formation] of research and ethics protocols."

In addition to specific comments, general comments on involvement were also made:

> "… it is unlikely that international responses will be effective without the full support of affected populations and their representatives. That means

[23] Hereafter referenced in this document as: Seydou Doumbia.

governments of affected states, but also a wide range of other actors. Especially where affected populations are politically marginal, official responses from national actors may not be experienced as well-meaning." *Tim Allen*

"in South Sudan, research has largely been driven by donor interest given that the country is over-dependent on aid. The national government, local researchers and the affected populations generally do not understand and conceptualize the importance of research. As a result, research is 'brought to them'. The local institutional review boards rarely turn down research approvals. In addition, views of senior government officials do not necessarily mean it is the view of the community." *Anonymous respondent*

"Important to recognise that this is not just an issue when foreign researchers undertake research – researchers from the same country as an affected population can feel just as 'foreign' to some affected populations – e.g., remote communities." *Anonymous respondent*

"Getting all concerned parties on one table is essential to stand on the problem from different angles and at all dimensions." *Wissam Doudar*

"once engaged in a collaboration, local researchers should be treated with respect, especially around equity of status among researchers. Continuing communication, involvement in local and international dissemination, and co-authorship is essential. Funding bodies should be aware of this and assist by providing funds earmarked for follow up and shared authorship. Together, foreign and local researchers need to plan in advance how this continued collaboration will be done to ensure local researchers can share in professional benefits from their contributions to research." *MSF / MSF ERB*

"… being 'at the table' is not the only way of influencing research priorities. For example, media or journal articles (especially in high-impact outlets) or discussions with key decision-makers can be highly influential." *Annette Rid*

"Very few local researchers were acknowledged as authors in papers after Ebola". *Anonymous respondent*

"It is important to listen to specialists, professionals of any field of knowledge, especially those who have experience in the affected area." *Instituto Aggeu Magalhães- Fiocruz-PE, Brazil; Federal University of Pernambuco, Pernambuco, Brazil; MERG - Microcephaly Epidemic Research Group*

Examples of where those parties have* not *been able to contribute

Other respondents used this question as an opportunity to indicate some of the situations where national governments, local researchers, and affected populations have *not* been able to contribute to setting research priorities in a GHE, with some indicating scepticism.

"In Uganda, I have not seen such a trend yet. Instead I see the reverse happening, particularly if there is a health threat-which may be easily

> defined as a global health emergency thereby causing disruption, when many researchers flood the country. The national governments may be reluctant to disclose this health threat/emergency to the Global community." *Anonymous respondent*

> "A collaboration between the US and Liberia on Ebola research has been in a spotlight because of its effective collaborative partnership model. In following Ebola vaccine trial in Liberia, I encountered a significant difference between official discourses of collaborative partnership presented in papers / reports, and participants' 'views from below'." *Arsenii Alenichev*

> "It is rare that you can see local researchers on the table with "external experts" during emergency. Locals are busy solving problems on the ground while others are doing research and collecting data. During rehabilitation you might find locals with external experts. The problem is that locals are used to collect data and provide interviews, documentation, pictures but very little contribution in the research itself." *Dr Najeeb Al-Shorbaji*

Ann H. Kelly also highlighted the Zika epidemic in response to this question.

> "During the Zika crisis, the strength of national research infrastructures offered more opportunities for locally driven research. Those capacities, however, did not obviate the power imbalance in collaborating with better resourced partners from the US and Europe; public disputes about attribution underscores the importance of developing safeguards for local investment and contribution in developing mechanisms for sharing data."

The infrequency of 'setting the research agenda' in GHEs

MSF / MSF ERB indicated that the experiences sought by this question may be infrequent.

> "*Setting the research agenda*" during a GHE is not that frequent. It is much more likely that the experience of a GHE will lead to / shape a research agenda in the next GHE, which may happen in another community. In addition, the key role in setting the agenda is often played by non-local-actor players, such as international research institutions that have the power to attract donors, and international donors that have the power to decide on rapid funds' deployment.

> "*Designing and implementing a specific research protocol*" is more likely to happen during a GHE. However, our general sense is that in most cases local actors are not 'at the table" in any consistent or principled way. For the most, decisions are made far from the location, and there is a descending order of appearance at the table (Ministries or government officials, mostly at the national level if IHR involved, and on a sliding scale down from there.) Seldom are affected populations involved, mostly because of the location of the "table". So, a big question is where the table is located and who sets the table in the first place."

Question 4

Please comment on what you believe are the essential aspects of community engagement in an emergency, their ethical justification, and how these can they be achieved.

In addition to tackling the three points set out in this question, respondents also indicated that some clarification may be needed regarding definitions of 'community' and 'engagement'.

Clarifying 'community'

> "[There] is always (whether in case of GHE or not) a general challenge of defining who or what constitutes a 'community'". *MSF/MSF ERB*

> "… academics and researchers are part of community, and this is something that needs to be stressed, as sometimes community is construed as just the group immediately affected by an emergency." *Anonymous respondent*

> "[How] do we define a ''community''? This is an important challenge in international collaborative research in general, but it is exacerbated under the time pressure of a GHE, especially if it takes place in a research-naïf community, or in a community with internal tensions and/or (hidden or visible) oppressive structures. This underlying difficulty may undermine the effectiveness of the following, positive measures." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

> "[Before] "communities" are approached to engage in any activity whether it be an assessment of any type, research or intervention, the process of defining who and what constitutes community (physical boundaries and social fabric) needs to be understood and should be an on-going process. Who is the group/population of interest, what are their characteristics, social norms, dynamics, vertical and horizontal relationships, formal and informal leaders and institutions are some examples of guiding questions. Communities are dynamic systems and understanding "community-ness" helps prevent stereotyping and social exclusion when emergencies hit and the response begins. This could be a part of a rapid assessment with the people themselves." *Jihad Makhoul*

Clarifying 'engagement'

> "[We] need to be cautious about what we mean by 'engagement'. There are many ways to engage a community, some are informational and instructional while others are collaborative and constructive. The first type will be useful for passing on information such as public health knowledge, however it is mainly passive. The second type is more active and invites contributions and sharing of knowledge between communities and GHE responders/researchers. Both are essential and can be done in combination, however they are frequently conflated which can lead to disenchantment and distrust." *MSF / MSF ERB*

> "… there is a difference between community engagement and community sensitization. I think the latter is essential and there is no excuse for not seeking to keep members of affected communities informed about what is

going on… Actual engagement may be more ambitious and hard to do – which is not a reason not to try of course." *Jantina de Vries*

Essential aspects of community engagement

Context: understanding the affected community

The importance of understanding the affected community's context was raised by several respondents.

"One must understand the sensitivities and uniqueness of communities." *Dr Rosmond Adams, CARPHA*

"… during an emergency, sometimes what needs to be done is obvious, and there is not time for consultations, maybe even no need. Sometimes one has to respond immediately as an ethical issue. But this requires that those engaged know and understand the situation and the context. That is, involving locals who have the knowledge, experience, and the skills." *Anonymous respondent*

"One of the essential aspects of community engagement is to take seriously, and respect, the cultural and religious beliefs of that community; international health organisations really struggle with this. Global health has a PR issue - not one of perception to the outside, but of internal perception. Namely, it conceives of itself as secular and therefore is unable to interact fully with faith-based communities and organisations." *Anonymous respondent*

"The concept of 'community' is most commonly used in a descriptive sense to pick out a particular geographic, linguistic, functional or socio-cultural entity with characteristics such as shared interests and experiences, values, common fate or cultural affinity; sometimes a community will have a pre-existing structure, such as a village committee, that may be used as a means of engagement. However, care needs to be taken to avoid assuming that such structures represent all relevant interests in the community; otherwise there is a danger of reflecting prior repressive or coercive structures; also, in some conflict-ridden environments where the social structure has been damaged or destroyed, it is especially important to consider carefully who would best represent the interests of the relevant population." *MSF / MSF ERB*

"Understanding of political context and intra-community power and social dynamics." *Seydou Doumbia*

"Another aspect of more effective community engagement is understanding the context/politics well so that – in engaging communities – we do not increase inequities – but rather try to stabilize them. This entails an understanding of history and politics." *Anonymous respondent*

"Research institutions should actively engage with affected communities while planning research to determine the trial design and understand cultural requirements and challenges which need to be taken into consideration." *Barthalomew Wilson, PREVAIL*

Relatedly, an anonymous respondent also suggested that assumptions about communities should be avoided: “For example, refugee populations may have skills and capacities that go unrecognized and are under-utilized. One should not assume that refugees all come from poverty and lack education.” A further anonymous respondent indicated that “local understanding of the disease and implications for effectiveness of response/research planned” must be taken into account.

Treating affected communities as partners in research

A further essential aspect highlighted by respondents concerned treating affected communities as partners in research during a GHE.

> “Consultation processes should engage people from affected communities in defining research methods.” *Humanitarian Health Ethics Research Group*

> “Consider communities and affected populations as more than participants in research. They should be treated as partners and key stakeholders in the research process, as their inclusion is essential to building trust and improving the relevance of research.” *Anonymous respondent*

> “Involve them in decision-making to ensure interventions are collaborative, contextually appropriate and that communication is community-owned.” *Anonymous respondent*

An anonymous respondent also noted the importance of avoiding an ‘us and them’ approach.

> “One critical thought process in commitment to engaging affected populations is paradigm/mind shift that is often hard to do – to remove ourselves from seeing them only as ‘victims’ and ‘needing help’ and seeing them as agents that YES need support given the features of GHE but also have something to contribute, and that that contribution in itself – is healing and enhances health / wellbeing.”

Ensuring local leadership involvement and representation

Involving local leads in engagement endeavours was highlighted several times.

> “Ensure strong, legitimate and supported local leadership, who can enforce being accepted as in charge and an equal partner by external supporters.” *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

> “Consultation processes should engage with various types of representatives and should not assume that governmental bodies are necessarily/fully representative of their constituents.” *Humanitarian Health Ethics Research Group*

> “Initially, consultation with community leaders is required to gain entry to a community and set up services. There should then be broader relationship building, including with local media if appropriate, to build trust and dispel fear and promote an understanding the interest of

> community members will be served by the intervention(s) being undertaken, through a process of question and answer and deliberation if that is possible in the circumstances." *Bridget Haire*

> "To identify community representatives, it is important to build trust, find people who minimize bias, build relationships over time, and ensure equitable age and gender representation." *Anonymous respondent*

Some respondents also indicated that identifying core individuals or groups in communities was an essential aspect of community engagement.

> "Different sections of the community need to be engaged, i.e. not just leaders or elites. In certain contexts it will be particularly important to engage women, due to hierarchical gender relations and/or the specificities of the health emergency (both of these would have been the case during the Zika outbreak in Brazil). Saying this is necessary is one thing – accessing all sections of a community is much harder." *Dr Adèle Langlois*

> "'Leaders' involved should include those able to have real contact with different aspects of the community as well as national and local leaders as appropriate (particularly ensuring women are not excluded). This need not be about high status – midwives, female nurses, and traditional birth attendants and healers should all be included. (They will also have their own code of ethics which will be very influential in local considerations of what is acceptable. What is also ethically important, is that involving groups who would normally have a voice in traditional power structures helps shift perceptions and have lasting impact.) Religious leaders are also important." *Dr Cathy Roth*

Dr Rosmond Adams (CARPHA) also stated that there it should be understood "who should lead in community consultation – i.e., who are the voices in the community is important […] it must be led by the community."

Ensuring that community engagement is continuous

Respondents also suggested that another essential aspect of community engagement should be that it is continuous, rather than a 'one-off' exercise.

> "Consultation, collaboration, and information sharing should continue after the emergency, and the research studies, end. Information should remain available to research participants, staff, and people in affected communities. Plans for this should be made (and shared with participants and with people from affected communities) *before* the rollout of research." *Humanitarian Health Ethics Research Group*

> "Community engagement is not a onetime event, it is an ongoing process, with an established forum for communication between researchers and community members. This forum can facilitate a bidirectional communication between research team and the community." *Barthalomew Wilson, PREVAIL*

> "Community engagement must not be one-off but must be continuous." *Dr Rosmond Adams, CARPHA*

> "Approaches to community engagement during an emergency should follow the same commitments to open-ended and iterative dialogue that would guide stakeholder consultation for any public health intervention." *Ann H. Kelly*

However, the difficulties of ensuring this approach are noted by a further respondent.

> "Both the difficulties, and the ethical obligation, to engage with the community before, during and after the research, are magnified under the time pressure of a GHE, where there are also higher risks of humanitarian or philanthropic misconception". *MSF / MSF ERB*

Creating awareness

Creating awareness through effective communication was also suggested as an essential aspect of community engagement in a GHE.

> "Community mobilization: create awareness which will facilitate autonomy." *Ms. Tausi S. Haruna*

> "The community needs to understand why this is being done, what is the benefit to this community, the feedback to them and their active role in this process." *Dr Najeeb Al-Shorbaji*

> "Information about studies should be widely disseminated in research-involved communities. Informing participants and their families is not enough." *Humanitarian Health Ethics Research Group*

> "Enabling fair representation of community members in planning emergency will bring "community buy-in" and they will accept the output of a research or an intervention." *Wissam Doudar*

> "Put in place a good and thorough communication strategy, addressing the fears of the community and taking into account local perceptions of what is happening." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

> "… communication should clarify and favour shared decision making, respecting local cultures, traditions, and existing organizational structures. It should always be done with the support of actors of relevance to the communities who hold credibility." *Oswaldo Cruz Foundation*

In a related comment, an anonymous respondent suggested that there should be open channels of communications as part of community engagement work. The respondent called for "transparency; shifting mindset from giving information to gathering information; and from telling communities what to do, to asking questions."

Ethical justifications

Some respondents provided general comments on ethical justifications, including:

> "The ethical values that community involvement brings to a clinical research or public health intervention effort are based on intrinsic factors that influence the conduct and outcome of these efforts. When

communities are not involved from the inception of a research project, they feel like objects of the research rather than partners in the process, thereby leading to distrust, poor communication, rumours and misconceptions, all of which negatively impact the process and ultimately, the outcome of the research. Communities also feel used and coerced when researchers are insensitive to their concerns and issues that affect their lives. As a result, research findings and outcomes are not fed back into the communities for positive actions, making the research benefits to the community minimal or non-existent." *Barthalomew Wilson, PREVAIL*

"There needs to be a constant balance of risk and benefits to the community in question and the emergency team in decisions made to avoid any waste of scarce resources, jeopardizing the safety of everyone involved and improving outcomes. Individual and community level informed consent is a necessary part of the process which especially involves any type of research." *Jihad Makhoul*

Other respondents identified distinct ethical concepts.

- Fostering respect and trust

"… the most essential aspects of community engagement during an emergency is that retains a rigorous standard of respectful and, perhaps counter intuitively, slow engagement, building trust over time." *Ann H. Kelly*

"The ethical justification for this engagement is the same as in non-emergency settings: community engagement is intrinsically valuable because it respects communities and recognises the stake they have in the research, and it is instrumentally valuable because it promotes better research outcomes and better ethical choices about the research (even if more evidence to support these claims is needed)." *Annette Rid*

"Ideally, conducting any [successful] research among others requires support, coordination and cooperation between researchers and communities (participants), particularly in the research scope. This is essential in acquiring the consent of the community (participants), which ultimately helps to overcome any likely ethical concerns, particularly those related to community suspicions of researcher's objectives." *Dr Joseph Kimuli Balikuddembe*

"Poor community engagement can lead people in affected communities to view researchers and research participants with mistrust. E.g. both participants and researchers in Ebola vaccine studies describe feeling stigmatized because of their engagement in research. Some of this might have been mitigated through greater involvement of affected communities in project development)." *Humanitarian Health Ethics Research Group*

"Long-term, supportive, inclusive, collaborative relationship between institutions and communities will generate more efficient response, build trust and allow for a response that is adapted to local needs." *Anonymous respondent*

- Supporting utility

> "It is important for emergency research to explore interventions that will be useful, accessible, and acceptable to people in communities most likely to be affected by the emergency in question. (Leaders in some EVD-affected countries noted that many clinical trials conducted during the epidemic had focused on medications that could not be produced, and may not be affordable, nationally, creating a situation where national health systems would remain unable to handle even small outbreaks without international support.)" *Humanitarian Health Ethics Research Group*

> "Without such involvement, researchers won't get the insights they need to conduct useful research. There are some beautiful examples of anthropological research that may only have had a minor effect on the current response but will be very valuable for the future." *Dr Cathy Roth*

- Supporting autonomy

> "The ethical justification is in the spirit of autonomy, where the community should be fully represented to enable them to make decisions pertinent to all sections of the community. If all sections of the community are not represented, decisions will be made by the dominant sections who will make their way into the group, and this may not uphold the best interests of the other more submissive sections of society." *Dr Anuradha Rose*

- Fairness

> "Community engagement should be respectful, gender sensitive, built on mutual trust, voluntary, fair for community members, an outcome of dialogue with them, and integrated in all phases of any intervention, especially in the assessment and evaluation." *Jihad Makhoul, American University of Beirut*

- Promoting dignity

> "… respect those deeply impacted by the GHE… promote their dignity. This is also done by allowing them an active role in their recovery as opposed to being passive recipients of aid." *Dónal O'Mathúna*

- Valuing resources

> "Past experience also shows that, due to lack of community engagement, resources were wasted in expensive, wasteful planning and expenses." *Anonymous respondent*

- Contributing to future capacity

> "Actively engaging with community members is a mutually educative process, and will enable researchers to learn about communities' cultures and understanding of research- related concepts, and contributes to research literacy by educating the community about key concepts critical for understanding the purpose and procedures of the research." *Barthalomew Wilson, PREVAIL*

Ethical concerns

Related points that focused on ethical concerns were also identified by respondents.

> "Communities and individual participants… might have considerably different expectations about the purpose of the 'community engagement' strategies. Understanding of what are the local precursors of 'community engagement' is a crucial factor for reviewing and evaluating of success / failure of GH interventions." *Arsenii Alenichev*

> "Poor community engagement can also harm people who are not directly involved in research. E.g.: Throughout Ebola-affected communities, there remains widespread confusion about what studies were conducted, and who was enrolled. Many Ebola survivors who did not join clinical trials believe that they were in fact enrolled in trials." *Humanitarian Health Ethics Research Group*

> "Distancing research from the community (link to needs) means that research is done for an academic degree or publishing but not to contributing to solving a problem. The worst thing to happen, ethically, is to study an issue of a human being and never come back to them with a solution or a feedback at least." *Dr Najeeb Al-Shorbaji*

> "In case of a global health emergency, different stakeholders have different needs and priorities. For instance in case of Ebola epidemic, scientists' priority is research and diagnostics. Communities affected have a priority of 'treating and saving lives'. The different priorities set may not be in harmony with each other." *Anonymous respondent*

How they can be achieved

The third part of this question asked respondent to consider how essential aspects of community engagement in GHEs can be achieved. Several suggestions were made.

Through building partnerships with communities

A number of respondents indicated that partnerships should be built with communities.

> "building partnership with communities, strengthening local ethical and regulatory authorities in countries with limited experience in research during emergencies to develop guidelines for study submissions during epidemics." *Seydou Doumbia*

> "… it is important to ensure that before a study is initiated, the community from which participants will be recruited should be consulted about research priorities, preferred trial designs, willingness to be involved in the preparation and conduct of the study." *Barthalomew Wilson, PREVAIL*

> "The essential aspects are that communities should be respected and taken seriously throughout the engagement and research cycle. This requires on-going dialogue where the community is seen as a partner in the work, and not "non-experts" who need to be appeased. The community will have a lot of invaluable information to provide, especially if they live in close engagement with nature." *Dónal O'Mathúna*

> "… involving local people in organizing community meetings and activities towards the emergency responses. Usually emergency responses are

> carried out by NGO's and groups who come from a different state or country and they are immediately laid claim to by the most dominant groups in the area." *Dr Anuradha Rose*

> "For communities in particular, with which we have experience in completing consultations, one does not consult by asking: what do you want or need. This can lead to inappropriate interventions. One needs to ask: what are the problems encountered, then work with community to define what would be the most appropriate ways to solve the problem, or ameliorate it, by steering community to available evidence, and interventions they might not be aware of but can solve some of the problems." *Anonymous respondent*

Supporting communities

The value of supporting communities was also highlighted as integral to achieving essential aspects of community engagement.

> "Support communities with actionable things and support them in identifying what they CAN do." *Anonymous respondent*

> "Support the community/ies designing their own solutions – this is not just education and communicating messages, it needs to include listening, working for and with them. This can be done by community dialogue, focus group, observation, and so on." *Anonymous respondent*

Related points on supporting communities through training and capacity-building were also highlighted.

> "build capacity/skills of community members and preserve protective social structures, values and ways of life while attending to urgent needs." *Jihad Makhoul*

The same respondent stated:

> "Emergency response teams need to have the theoretical training and social sensibility for the work and awareness of the concept of conflicts of interest. This means they need to be trained on the intellectual and social aspects of the work: emergency preparedness as well as community building, community based participatory approaches, community ethics and influences by external funding agencies and others who may have vested interests and could interfere in the work or research with emergency affected populations all in the contexts they find themselves in. Team leaders, or independent ethics advisors, need to be aware of ethical national guidelines if they exist and constantly monitor the team's ethical conduct."

Planning

The importance of planning was also noted as an important element in community engagement endeavours.

> "Community engagement strategies do not appear out of blue. Usually they build upon past interventions, forming a local continuum." *Arsenii Alenichev*

> "At a minimum, a credible attempt must be made to engage and learn from affected people, ideally using tools chosen from a pre-defined suite of options derived from rapid assessment techniques." *William Aldis*

> "Engage communities in training / education around emergency contingency plans well in advance of emergencies e.g. natural disasters, infectious diseases." *Anonymous respondent*

> "Ideally, countries will have fostered preparedness plans in advance, with agreed policies of engagement with affected communities. Waiting to develop a research agenda during an outbreak may miss a critical opportunity to build key evidence on preparing, avoiding or responding to future emergencies... We agree that it is important to undertake a significant body of research and preparedness activities in advance of any potential PHEIC, preparing groundwork for research that may itself only take place during an outbreak." *UKRI*

> "… true engagement should be part of ongoing disaster risk reduction (DRR) planning." *Dónal O'Mathúna*

> "Any community engagement should start with a clear definition / goal / objective of what would be expected within the emergency from this activity." *Anonymous respondent*

> "Ensure feasibility and sustainability of supplies – have a preference for local supplies". *Anonymous respondent*

One respondent also notes the importance of communication in the context of planning.

> "… communication need to be integral part of the response planning to ensure that possible ethical concerns are debated to ensure that research does not have a detrimental impact on emergency response." *Seydou Doumbia*

On communication more generally, a further respondent observes:

> "active[ly] listening to communities and acknowledging that their preoccupation might not be the emergency you are in the field to work for." *Anonymous response*

Working with others

Working with community organisations was also highlighted as a way in which aspects of community engagement might be achieved.

> "Working with community organisations, e.g. women's organisations, will help – these should be as grassroots as possible, to avoid the problem of large international organisations speaking for people (rather than the people affected themselves getting the opportunity to speak)." *Dr Adèle Langlois*

> "Achieved through dialogue with the community members, community leader or religious leaders." *Ms. Tausi S. Haruna*

A further suggestion was put forward that 'mid-level professionals' should be involved.

> "aiming engagement not at the affected communities per se (although their elders and other leaders should be considered for involvement) but also at mid-level professionals who can more successfully be included in consultation and decision-making processes." *Jantina de Vries*

The same respondent expands:

> "If it is unlikely that people could be involved from directly affected areas, then attempts should be made to involve those from similar communities or higher-level administrative or traditional leadership positions. E.g. if the village elders cannot be involved because they are dealing with the immediate fallout of the epidemic, then perhaps the higher-level tribal leaders could perhaps be approached." *Jantina de Vries*

The role of multidisciplinary involvement was also noted.

> "Involving composite/mix (intersectoral and cross-disciplinary) researchers to understand the multifaceted aspects of global health emergencies which varied based on the nature, extent and complexity/ severity and impact on humans, animals and environment." *Ernest Tambo*

Other suggestions

Other comments on how these aspects can be achieved included:

- Transparency and inclusiveness of decision-making, including vulnerable communities and individuals
- Open communication and common meetings
- Ensuring that those who want to contribute their views are able to
- Enabling local contribution through infrastructure and personnel – financially, and through capacity-building
- Seeking and building relationships of trust
- Identifying realistic approaches to engagement that are likely to be successful.

Question 5

Are there *any* circumstances in which research might be so important, and time so short, that this could outweigh the need for local voices to be heard?

Responses to this question were divided broadly between those which answered this question in the affirmative; and those which felt that there were *no* circumstances which outweigh the need for local voices to be heard. Most responses fell into the latter category.

There are circumstances that outweigh the need for local voices to be heard

A limited number of respondents set out example circumstances to support this view, while continuing to emphasise the importance of community engagement. Dr Annette Rid, for example, indicates that "it is hard to imagine such circumstances, but two possible scenarios come to mind:

> 1) A global pandemic with vast numbers of people at high risk of serious harm could be such scenario, provided the research has a real potential to help reduce this risk. It is not clear to me, however, that this kind of scenario is likely enough to specify criteria for waving community engagement in those circumstances.
>
> 2) A threat of a lesser scale that research has a real potential to address might be another scenario, provided there has been prior robust engagement about what to research, and how, in similar circumstances. I'm sceptical, however, that advance planning could anticipate actual public health emergencies and be sufficiently robust in process to justify waving community engagement."

Other examples set out by respondents include:

> "If the impact on human lives is severe and community engagement may prolong response or gathering of evidence, then it may be ethical to move forward with research. However, every effort must be taken to engage the community. Only when this engagement may delay progress that we can override community engagement." *Dr Rosmond Adams, CARPHA*
>
> "Yes, if local voices are too impaired to be heard; there's a parallel here in resuscitation research. It should always be with the patient's consent, except when the patient is not in a position to consent. If the community is too fragmented / damaged to allow meaningful engagement, then for a brief period decisions may need to be made justified by best interest - but I would add that this would rarely be the case, and if it was, only for the shortest time possible until effective community engagement can occur and must be made explicit and carefully monitored." *Anonymous respondent*
>
> "Local voices are important to ensuring that research is ethical, actionable, and responsive to the real needs of individuals affected by the emergency. However, community engagement takes time and research may be time-sensitive or may be generating information that informs ongoing interventions in the current emergency. There may be circumstances where urgent needs outweigh the need for local voices in emergencies, though these decisions will really depend on the situation." *Anonymous respondent*
>
> "In emergencies where the magnitude of the harm and rapidity of death or serious morbidity are very high; in emergencies where large sections of society are cut off, such as floods". *Dr Anuradha Rose*

The feasibility of 'hearing local voices' was highlighted by the Humanitarian Health Ethics Research Group.

> ""Hearing local voices" will be much more feasible in situations where the event occurs in a locale where the event is predictable (e.g. recurrent

> hurricanes) and where prior consultation with communities is therefore feasible. Where possible, such consultations should be undertaken in a structured and deliberate manner. In other cases (e.g. an earthquake), this will not be possible. In those cases, engagement with local authorities and other community leaders is necessary but will be constrained and limited in scope."

Time needed to engage local voices was also suggested as a reason that engagement should focus on other groups.

> "Given the effort and time needed for "community engagement", we do believe the engagement of "experienced research community" is more important than ordinary public. Here, "research community" means investigators and institutions, which know the community (to be studied) well, and with experiences on doing research within this community. Their knowledge would be more direct and efficient during the emergency." *Anonymous respondent*

There are no circumstances that outweigh the need for local voices to be heard

Several respondents stated unequivocally that there are no circumstances that outweigh the need for local voices to be heard. Responses include:

> "No. The only question is how 'quick and dirty' -- how unattractive from the academic perspective – collection and analysis of data gathering on local input must be. In the extreme case, it might consist only of qualitative information gathered over hours or a few days." *William Aldis*

> "… there are situations where research might be so important within limited time to act. However this shouldn't outweigh the need for local voices to be heard." *Ms Tausi S. Haruna*

> "I cannot imagine any circumstances during a global health emergency in which the exclusion of local voices would be justified. As the Ebola Outbreak Response exemplified, appeals to the importance [of] timeliness over public engagement can ultimately impede interventions by engendering distrust with communities." *Ann H. Kelly*

> "there should be no circumstances where it would be justified to implement a study without hearing local voices first. It is crucial to keep the bar high here and maintain the same ethical standards as for other research." *Anonymous respondent*

> "I can't imagine any. I think if you have time to do research, you have time to do community consultation, even if it's very short and only gets to the local leadership." *Gillian McKay*

> "Local voices – in some capacity and form (other than tokenism) – is critical. We risk 'harm' otherwise." *Anonymous respondent*

> "If research is to benefit the community who determines the benefit? Should this not be determined by the community the research is being conducted in? Research should be aligned with local needs which should improve the lives of people. Local voices need to be heard no matter what the situation." *ECEPAS, GET*

> "If the research is so vital, this would have to be because it is impacting people in a serious way. This means there would have to be local impact and therefore those affected should be consulted, even as the research is being implemented." *Dónal O'Mathúna*

> "There is nothing that can outweigh the need for local voices to be heard. Ignoring local voices means imposing solutions, means solutions to problems that may not exist, means the foreigner knows everything and the local has just to shut up and receive charity, provide data, listen and be good and obedient." *Dr Najeeb Al-Shorbaji*

> "Regardless of the challenges associated with engaging communities in clinical research, especially during public health emergencies, the ethical value of listening to local voices should not be compromised at any time." *Barthalomew Wilson, PREVAIL*

> "This question is a bit unclear in intent. If it is meant that researchers would set up and recruit without informing the local community and actors, or against their opinion, the short answer is "no!", since this would really be treating local voices as means alone: we find it hard to conceptualize a situation in which research benefit would outweigh this need. As research can never be premised on assured outcomes and harms are always implicit in the research process (as are null/inconclusive results) it is difficult to justify epistemic interests transcending the need for engaging communities. To attempt it would be an epistemic injustice and would likely be unsuccessful because the findings would be irrelevant in many ways." *MSF/MSF ERB*

A distinct point on the 'urgency' of research was also provided in support of the view that local voices must be heard.

> "While public health action and humanitarian care might have this level of urgency, it is hard to see how research could, given that it necessarily requires some level of forward planning and systematisation." *Bridget Haire*

Equivocal responses

Some respondents did not commit to a 'yes' or 'no' answer to this question, instead suggesting that 'it depends'.

> "In principle not; but there may be situations where decision makers may not be reachable and a decision needs to be taken asap. But the risk for that should be minimized if local stakeholders are working very closely with members of other organisations from the very beginning." *Anonymous respondent*

> "If local voices cannot be included immediately, because of the urgency and/or contextual constraints, their involvement can be planned ad a later stage or as soon as feasible." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

Annette Rid (see also comments above) also states:

> "A lot depends, of course, on what is required for "local voices to be heard" and how much delay this causes relative to other sources of delay in the research process. But I find it difficult to imagine real situations where at least some form of community engagement need not occur."

Related points

Respondents also used this question as an opportunity to raise related issues.

> "The notion of hearing local voices could mean soliciting people's opinions, or views and asking them to contribute to the efforts/activities/research if there is a possibility for that and when the necessary guidance or training is available if they wish to do so. Hearing people's voices could also entail familiarisation by the expatriate workers or those foreign to the social context with the local values, social structure, politics and interests. The local voices should be heard to make the response effective, beneficial, resource friendly, as well as to reduce the possibility of stigmatization and social exclusion of the population in question." *Jihad Makhoul*

> "Engagement that facilitates collaboration rather than partnership between researchers and the community during epidemics is acceptable." *Morenike Oluwatoyin Folayan, Obafemi Awolowo University, Ile-Ife, Nigeria*

> "Since "local voice" is a very inclusive but also very broad term, perhaps it may be mentioned here that local ethics and/or regulatory review should never be skipped as long as local mechanisms exist (any exception to this should be justified)". *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

Questions 6–10: study design and review

Question 6

In your view, in what ways, if at all, should decisions about study design and acceptable risk be affected by the fact that the research will be taking place in a global health emergency? On what basis would you justify any variation?

In what ways should decisions about study design / acceptable risk be affected by research taking place in a GHE?

They should not be affected

Several respondents indicated that these decisions should not be affected.

> "From the Latin American and Caribbean perspective, we strongly disagree with the view (common in global debate since) that placebo-controlled trials were ethically unacceptable in the West Africa Ebola outbreak. There was not the evidence to justify treating the trial arm interventions as treatment - interventions could equally well have been

> harmful or useless, and hence normal research requirements were valid. If there were a problem with using placebo, using 'ring' approaches, which were presented as an 'ethical' alternative, wouldn't solve the problem either: if there would be a therapeutic intervention people were owed, how could you justify the delay in providing it? It is, however, absolutely essential to get the communication right, and ensure that you are not starting research in a context of false beliefs about what an investigational intervention can deliver." *Anonymous respondent*
>
> "The time pressure during GHE cannot be a reason to skip essential ethics and regulatory safeguards." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

The same respondents stated:

> "… decisions about study design and acceptable risk should not hamper the response to the GHE, nor vice versa. There may be a need to be more pragmatic than in "routine research", and there may be a need to anticipate repeated (design) modifications along the study. This should be discussed upfront with the concerned ECs and IRBs, so as to allow them to anticipate such issues, and to be as proactive as possible at the start and with amendments."
>
> "There's a best for the most argument that will often be trundled out - but actually it is not a strong justification to move away from normal processes. Instead we should make the normal processes so streamlined that they can be implemented without delay and shape the studies. The studies will be better for the community engagement in their design, and to take account of their views adds so little additional extra work it is hard to see when it would be a problem." *Anonymous respondent*
>
> "If a research project does not demonstrate conditions to obtain its data satisfactorily, it should not happen, despite its scientific correction". *Oswaldo Cruz Foundation*
>
> "GHE contexts should not affect decisions about study design and acceptable risk in any way - except to make the review even more careful." *Anonymous respondent*
>
> "The time pressure during GHE cannot be a reason to loosen the ethics and regulatory safeguards that should always be in place in medical research. Adapting study design and the risk benefit assessment may be done/motivated on ethical grounds." *MSF / MSF ERB*

Decisions should be expedited

A number of respondents suggested that these decisions should be expedited in GHEs.

> "In cases of global health emergencies, it is important to accelerate processes to adapt to the time pressures. In order to do so, preparedness for outbreaks is of critical importance […] While acceleration is important, this should not mean lowering the threshold of acceptability for ethical and regulatory review processes […] It is important to build capacity on ethics during global health emergencies regionally and/or nationally as

> well to ensure regulatory alignment. In this way, in case of outbreaks, the research response can be expedited." *Wellcome*

The Health Research Authority sets out the criteria its research ethics service will adopt when considering whether expedited review of research is warranted:

- "The time available to complete the approvals process and initiate the research
- The potential loss of valuable data or data quality, or disproportionate effort being required to capture the data
- The potential impact of any delay on public health
- The importance of the research for informing, shaping or defining health policy and services provision."

The HRA also highlighted its experience of expedited review of early phase vaccine and treatment studies at the time of the recent Ebola outbreak in the DRC. It stated:

> "All studies were reviewed within 20 days with the majority reviewed within five days. Subsequently an urgent amendment to one vaccine study was given a favourable opinion in five hours on the same day it was submitted."

Enabling alternative / flexible study designs

The option of enabling alternative or flexible study designs in GHEs was highlighted by respondents, including:

> "Study designs need to be flexible and adapted to the time pressure inherent to the global health emergency and local ethical consideration". *Seydou Doumbia*

> "Given the anticipated (hoped for) transient nature of any epidemic, special innovative design considerations may be required. For example, it may not be possible to do a classic randomised controlled trial or other intervention evaluation with sufficient pre-determined power. Alternate adaptive trial designs may be more pertinent to delivering the strongest evidence on benefits to participants." *UKRI*

> "The best research is not methodologically driven, but question or problem driven. It is arguably lazy to fall back on most frequently used design approaches simply because they are most frequently used. A good protocol will consider the problem and choose a suitable methodological design, not simply try to fit a square peg into a round hole, a choice of design is wrong because it will not work in the setting". *MSF / MSF ERB*

> "Study designs must consider exceptional methodologies that yield timely results with minimal harm to individuals." *Wissam Doudar*

> "In general, researchers should be prepared to adapt methodologies and research designs to respond to changing context in emergency settings." *Anonymous respondent*

A related point was raised by Tim Allen:

> "Study design and hierarchies of evidence are inevitably debated. However, in ongoing emergencies, many study designers (and restrictive ethics protocols) are unhelpful. In the Ebola outbreak, and in other emergency situations, the best information is likely to be ethnographic […] In politically fraught circumstance and where enforcement procedures are being considered, questionnaire surveys and informed consent forms are likely to generate distrust and even alarm."

The flexibility of ethics approval processes was also noted by Wellcome.

> "In relation to regulatory and ethical processes, preparedness means establishing flexible regulatory and ethical approval processes in advance of any global health emergency to ensure they can be applied in different contexts and outbreaks, rapidly as needed."

Decisions on risk

A range of views on how decisions about research risk might be affected by a GHE were offered by respondents. They included one view which suggested that higher risk research endeavours might be acceptable in a GHE.

> "the standard ethical framework for risk-benefit evaluations continues to stand during a public health emergency, but the emergency situation highlights considerations that, while always relevant, are less salient—or are considered, rightly or wrongly, less salient—under non-emergency conditions […] Because the social value of the research can be higher during a public health emergency than under routine conditions, higher levels of net research risk (i.e. risks that are not offset by potential benefits to participant, but justified only by the social value of the research) can be justified." *Annette Rid*

> "May depend on risk of emergency itself – if death inevitable, almost any risk might be acceptable…but does not justify "cowboy" activities". *Anonymous respondent*

> "Particular challenges arise for diseases with high rates of mortality, either where there isn't genuine equipoise, or where there are no available alternatives other than the trial intervention. (NB: these are two different things, and should not be conflated)." *Dr Cathy Roth*

On a related point, Dónal O'Mathúna, PhD highlighted a high-risk scenario.

> "If the risk is high, this might influence some variation. For example, the very high risk of Ebola justified bringing some interventions into human trials sooner than normal because people were dying. What changed was the need to get research done, and so the risks needed to be presented to participants and moved along in research. However, the study design should still have been driven by the study question."

Other respondents suggested that risk is itself a concept that varies depending on context.

> "risk is not a one size fits all determination. So, it is not clear that there is a variation in the way risk assessment is done, just variation in the risk elements to be assessed. It would be wrong to imply that risks are being

> assessed differently in a GHE. Instead we should clarify that the risks are higher in the context, so the risk assessment outcome is different from a non-GHE context." *MSF / MSF ERB*

> "There will be need to define and have a common understanding of what is acceptable risk in related to traditional values, cultural and societal norms in global health emergency interventions or humanitarian emergency response." *Ernest Tambo*

Another respondent argued that risks should be minimised in GHE research.

> "… all efforts must be put in place to ensure that research are well designed and that the risks are minimized as much as possible." *Dr Rosmond Adams, CARPHA*

The appropriateness of placebo

The level of appropriateness of using placebos in GHEs also featured in responses.

> "Studies involving placebos may be ethically very problematic and rejected by communities. A least for viral haemorrhagic fever (VHF) – placebo is indeed not acceptable – when thought efficient aggressive supportive care at least needs to be the acceptable standard of care." *Anonymous respondent*

> "possible decision not to allow a placebo arm even if there is no effective treatment, because receiving an experimental intervention represents a human opportunity to get access to "something more" (whatever the theoretical issues on equipoise)." *MSF / MSF ERB*

Justifications

Some respondents also engaged with the second question included in question 6: on how variation in study design and risk would be justified.

Through the involvement of those affected

The involvement of individuals and communities was identified as another way that decisions about study design and acceptable risk should be affected by research in GHEs.

> "People involved in these kinds of humanitarian responses need to be trained to listen and respect the input of persons knowledgeable of local customs and traditions." *Jantina de Vries*

> "communities and individuals who survived Ebola should be invited to explore these issues and offered opportunities to participate in global efforts to plan for further health emergency responses." *Bridget Haire*

> "Parties that can decide on the best interests (note plural) of the affected communities. Such parties must still have the generic agreement of the community." *David B. Morton*

> "In adjudicating the degree of acceptable risk during emergencies it is important to emphasize the role of local ethics and regulatory bodies in deciding the basis of variation for their populations." *Ann H. Kelly*

> "I question how ethical are study designs which are parachuted from other countries, and where we know such designs have not been carefully scrutinized to check for relevance and acceptability, or even validity locally." *Anonymous respondent*

By reference to existing legislation / policy

Some respondents suggested that any effects on study design and risk should be addressed through reference to existing legislation / policy.

> "I would justify any variation on the basis of existing legislation/regulation/guidelines (international and/or national) on assessment of acceptable risk in emergencies." *Dr Adèle Langlois*

> "Under no circumstances should clinical trials be considered acceptable without ethical clearance in which representatives of the scientific / affected nations / communities participate, including WHO bodies, as referred to herein." *Oswaldo Cruz Foundation*

Other points

Other justifications were also raised by respondents, including:

> "In an emergency such as the Ebola outbreak, I think that it was justifiable to release treatment drugs that had not been fully tested for compassionate use under conditions where data was systematically collected about efficacy and adverse events." *Bridget Haire*

Question 7

In what ways, if at all, could it be morally justifiable to change the 'standard' ethical and regulatory review processes to respond to the time pressures inherent in a global health emergency?

It would *not* be morally justifiable

A small number of respondents indicated that changing standard ethical and regulatory review processes in GHEs would not be morally justifiable. For example:

> "There is no moral justification to change the "standard" of the ethical and regulatory review process, in order to respond to the time pressure inherent in a global health emergency. As a consortium that was involved in reviewing protocols during the Guinea, Sierra Leone and Liberia Ebola outbreak, we feel it is worrisome to talk about changing the standards of ethical and regulatory review process during a health emergency. If anything, these systems should be more robust in order to protect the people who become extremely vulnerable, with increased potential for exploitation and harm, during the emergency." *ECEPAS, GET*

> "Barely. Options exist to either pre-design/pre-approve studies, or to fast track them. Waiting months for an ethics committee meeting is clearly inappropriate, but if much of this red-tape is reduced, the key elements including appropriate engagement with design, consent etc can be acted on very fast. Badly designed studies that the community pushes back against /produce poor data are themselves unethical." *Anonymous respondent*

Dependent on context

Other respondents indicated that an answer to this question depends on context.

> "A lot would also depend on the context where the emergency occurs. Where pre-existing research regulation and oversight are weak, and hence distrust in research can be legitimate, a proportionate approach seems less justifiable." *Annette Rid*

> "Of course, in general, much of the IRB or ethical review protocols rely on principles that are Western and individualistic to begin with, and providing guidance on how to apply important principles in collectivistic societies is particularly critical in GHEs." *Anonymous respondent*

How it may be morally justifiable to change standard ethical / regulatory review processes

Several respondents made suggestions for how it might be morally justifiable to change 'standard' ethical review processes.

General positive comments on expedited processes

Several respondents indicated general support for expedited processes in response to this question, with a frequent additional point that making processes faster should not compromise high standards.

> "… given the time pressure presented by a global health emergency, ethics review committees should put in place mechanisms for expedited review. Expedited review, notwithstanding, should at no time change the standard and principles of the regulatory / ethical review process." *Barthalomew Wilson, PREVAIL*

> "… research protocol review during emergencies can be fast-tracked but all due diligence for proper review of the protocol needs to be maintained." *Network of Ethics Committee Members in West Africa*

> "Perhaps the standard processes should be stimulated by facilitating more rapid IRB processes during emergencies, by identifying how to speed up and harmonize reviews without compromising quality, with minimal bureaucracy". *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

> "The time of the approval process should be shortened in an emergency situation." *Anonymous respondent*

> "Ethics review should be faster but should not cut corners." *Anonymous respondent*

> "Questionnaire can be designed to come directly to the point and consent can be obtained where possible, and in some emergency cases, consent may exceptionally be overlooked to save time in order to reach a way out the soonest." *Wissam Doudar*

> ".. . regulatory review processes may be expedited. In the face of a global health emergency, the Home Office may grant licences [for animal research] more rapidly if required, they may seek external expertise, and licences may be prioritised over other less urgent work." *Animals in Science Committee*

> "… this is not necessarily about changing the 'standard' of review – but rather of accelerating the process, and trying to look more searchingly at the whole, rather than piecemeal. This would be good practice in non-emergency situations too. What's needed is a system as accelerated, frugal and safe as possible." *Dr Cathy Roth*

> "We suggest that outbreak relevant research requires its own standard that is "fit-for-purpose" and responsive to the context and needs of the outbreak. Review should be expedited and efficient. However, expedited review should also not compromise the quality of regulatory evaluation of scientific and ethical aspects of a research proposal. This creates a challenging tension." *Prof Alistair Nichol (lead), Prasanth Sukumar, J-P Byrne, Nina Gobat on behalf of PREPARE WP1*

However, the same respondents highlighted their own research among RECs and regulators based in the EU, "which highlighted how [these] groups are not uniformly ready to expedite review. There are different understanding[s] of what "expedited review" might mean (e.g., 5 days or 45 days) and how to operationalise it."

Respondents also drew on previous experiences of expedited research processes to illustrate their answers.

> "The experience of research during the Ebola crisis has demonstrated the value of accelerated processes of ethical and regulatory review to enable both rapid access to critical experimental interventions and ensuring more therapeutic and preventative options for future outbreaks. That being said, there is a great deal uncertainty around the evidentiary requirements of distinct regulatory pathways." *Ann H. Kelly*

> "during the most recent Ebola outbreaks, as well as for other protocols to be carried out during other public health emergencies, the MSF ERB review timelines were shortened so that turnaround was much quicker than in routine research. However, we can wonder how long the ethics (and regulatory) review bodies could keep on working under emergency conditions, with rapid turnaround time, without negative effects on the quality of the review." *MSF / MSF ERB*

> "[Deadlines] should be significantly shortened, as we have had here in Brazil during the epidemic by Zika virus. This does not mean giving up principles but giving the appropriate response at the appropriate time in an exceptional situation." *Oswaldo Cruz Foundation*

Reference to the urgency / seriousness of the situation

The view that the urgency and seriousness of the situation could justify changes to standard processes was expressed by a number of respondents.

> "Research in emergency situations warrant[s] a certain amount of urgency, and it will be justifiable to have emergency review meetings, with fewer members if there is an assurance that a comprehensive review of the proposal will be carried out, with necessary experts being contacted in the case of rare or new diseases." *Dr Anuradha Rose*

> "The response to time constraints requires the acceleration of the ethics review process." *Dr Alpha Ahmadou Diallo, Ministry of Health, Guinea – Conakry*

> "With due attention and adherence, to the extent possible, to all relevant ethical and regulatory review processes, it is morally justified, and sometimes imperative, to deviate from standard processes if actors – including researchers -- responding to an emergency find it necessary in order to reduce suffering and save lives." *William Aldis, Office of International Programs, Faculty of Public Health, Thammasat University (Thailand)*

> "In situations of a medical emergency with imminent risk of death of the affected, the research design involving these individuals may also be modified under very specific conditions that do not increase their suffering or the risk of death [...] However, these changes can and should be seen as essentially exceptional, that is, by consulting the reference bodies with due urgency." *Oswaldo Cruz Foundation*

However, Jantina de Vries raised a note of caution:

> "it is really important that there is harm also in communities and individuals feeling like they've had 'things done to them' and that they were completely disempowered in the process. So even if there are valid scientific reasons to design interventions in particular ways (e.g. the forced removal and quarantining of sick patients), then we should also consider the perverse effects of such an approach – for instance, in inflicting trauma on the people that is happening to."

Through involvement of the affected community

The role of involvement as a way in which moral justification for changes to standard processes might be achieved was highlighted by several respondents.

> "The example of doing community engagement and going with implied consent during the Ebola crisis is a good example I think, where the regulatory approaches were changed to allow for this (but there was still community consultation)." *Gilliam McKay*

> "… if a decision is made to circumvent certain best practice standards, then that decision needs to be taken with great care, the reasons for taking that decision need to be completely transparent, and people mandated with taking care of the health of the affected communities need to be involved in making that decision. This means, at a minimum,

members of the government of the country where the intervention is required, but much rather scientists, ethicists and others from those countries." *Jantina de Vries*

"May need to be a requirement for local and regional input (locals may be too personally impacted by emergency to be impartial?) to ensure contextual appropriateness, however in some cases a local ERC does not exist or may be disrupted". *Anonymous respondent*

"emergency actors who find it necessary to deviate from standard processes should consult with partners, stakeholders and relevant authorities to the extent possible within time constraints. They must also be held accountable for their decisions in post-emergency reviews." *William Aldis*

"Where possible, especially in local ERCs, community representation would be ideal." *Anonymous respondent*

"During the [Ebola] outbreak, the GET consortium benefited from a pool of experts drawn from a diverse background from all over Africa. In addition, we held virtual meetings, where protocols for investigational products were discussed promptly, without compromising the quality and standard of ethics and review. Our experience demonstrates that with the right combination of expertise in your committee, reduction in unnecessary and redundant bureaucracy such as the need for multiple review and the appropriate use of technology such as the use of online review system/holding virtual meetings can maintain optimal research participants 'protection and avoid compromising on the quality and standard of ethics and review process during a global health emergency." *ECEPAS, GET*

"There definitely needs to be local input into ethical review of GHE research. This is because cultural, political, economic, social aspects of an issue and its response become perhaps even more pronounced in GHE, and have even more potential to create significant harm. So requiring local ethics board approval is critical. However, this should not be taken as a way for IRBs in HIC to release themselves from responsibility." *Anonymous respondent*

The same anonymous respondent also stated:

"Another important consideration for ethical review in GHE is engagement of the community IN that ethical review. IRBs often have requirements to have at least one 'community' member on the board. But that person may not have a clear sense of the GHE issues. I have often wondered if it is possible to create a GHE ethical review committee within/of the affected population (at least for protracted emergencies). How can voice of those affected be enhanced in decisions about research that happen in their contexts/communities?"

Ann H. Kelly, however, noted:

"… supporting national regulatory bodies is of paramount importance. In Sierra Leone, a crippling number of applications for research were submitted, straining capacities for thorough and meaningful review."

Planning: pre-approval / pre-review

Respondents also referenced pre-approval / pre-review of protocols as a potential source of moral justification for deviating from standard processes.

> "Ideally emergency ethical approval is something that should be negotiated prior to a real outbreak or other emergency so that there is some preordained model of what is an isn't acceptable." *Bridget Haire*

> "some way of getting adequate review should be planned and implemented. This may include having a means of pre-assessment in normal circumstances, and then a way of getting rapid final review and approval into place when the emergency arises." *Dónal O'Mathúna*

> "[In] practice, a combination of advance discussion of prototype protocols… or key trial design choices… with timely centralised expert support is likely most sensible. This is because advance discussion, while helpful, cannot anticipate the situation at hand and there is independent value to adhering to a predetermined decision-making process to determine whether studies are acceptable." *Annette Rid*

> "… existing good practices should be encouraged and facilitated: for instance, efforts should be put during the research preparedness phase (i.e., before a GHE occurs) to establish procedures for accelerated reviews, to coordinate in-country and multi-country reviews, etc." *MSF / MSF ERB*

The same respondent suggested further:

> "particular attention is needed for critical aspects such as community engagement, transfer and management of biological samples and medical data, benefit sharing measures etc. However, there should be an established means of deciding how to manage when two or more principles conflict. In such circumstances a procedure for fair, transparent and deliberative decision-making should be considered in advance, as well as a fair appeals process and review of decisions."

An anonymous respondent also suggested that a toolkit might be developed.

> "A toolkit for ethical board to refer to for GHE contexts might also be helpful. It will not take the place of ethical reviews but provide some guidance that might be helpful in advancing debates. And yes, it will never be a complete toolkit as new methods, new GHEs... will always arise but it will be a support, and a continuously evolving kit."

However, one respondent felt that this approach to review was unethical.

> "There is a talk about 'pre-approved protocols', to enable timely research in complex emergencies. One of the reasons is that communities affected would be too busy attending to other crucial matters, for instance saving lives in hospital's isolation units– and so, reviewing and approving research protocols may take longer than expected. In my view, pre-approved protocols are going to promote unethical researches." *Anonymous respondent*

Through oversight mechanisms

Some respondents suggested that the development of oversight mechanisms might morally justify changes to standard processes.

> "Creating a national / international body that oversees research in such situation may be needed. For example, an advisory council." *Dr Rosmond Adams, CARPHA*

> "Perhaps when GHE situations arise, there needs to be an alternate model for review... alternate in process of who reviews, by when, etc (not alternate in terms of the criteria that are judged). For the process to be quicker, there needs to be some time release for faculty members (in places where this is the model for review) to be able to turn around in short time frame. Perhaps there needs to be guidance on some models that have been used at university level, at government level, at organization level of processes that are efficient AND effective for institutions to review and consider. Having a plan in place for the ethical review process in GHE is important for every institution." *Anonymous respondent*

> "The standard processes could be speeded up, e.g. there could be specialist RECs constituted to meet on an ad hoc but fast basis in response to emergencies." *Dr Adèle Langlois*

Bridget Haire made a related point:

> "It might also be justified to have a single ethical review rather than both local and international review."

Comments on ethical review

Some respondents indicated more general concerns about ethics review in response to this question.

> "'Standard' ethical processes: not set up for joined up thinking (e.g., in considering whether a study is really a priority in the particular context, and balancing it against others, given limited places and people available). Processes can also be slow and obstructive. This could be improved with the right mindset and resource – systems tend to evolve by new safeguards being added on top of existing ones, despite obvious risks of duplication. But it takes time and thought to re-think such processes and work out what elements can be done together at the same time, and what is duplicatory and could be omitted. There are also practical hurdles (IT, training, permissions …)." *Dr Cathy Roth*

Other respondents highlighted the importance of always having an ethics review process: that is, that the process might be subject to change in GHEs, but it should not be dispensed with.

> "Under no circumstance should it be considered acceptable for clinical interventions to be made without ethical clearance in which representatives of the affected / scientific nations / communities participate, including WHO bodies". *Oswaldo Cruz Foundation*

> "I think one would have to be extremely careful to ever discard of international (scientific and ethical) best practice because of time pressures, because this can cause tremendous damage to people's future health as well as to the trust they may have in science." *Jantina de Vries*

Other respondents differentiated between regulatory processes and ethical review, indicating that they should be addressed as two distinct elements.

> "The regulatory processes should be adaptable to the time pressures, but not the ethical standards themselves. Research should still be conducted to the highest ethical standards." *Dónal O'Mathúna*

> "In a GHE, the ethics and regulatory review must be solid and sound, to ensure protection of a particularly vulnerable community, served by a (most likely) weakened health system. There should be no derogation on ethics principles." *MSF / MSF ERB*

> "Ethical and regulatory structures are different – not helpful to lump them together." *Dr Cathy Roth*

A related comment was provided by an anonymous respondent:

> "It is important to identify the spirit of what is required for ethical research conduct, and ensure that this is still met, rather than focusing only on procedures (cf distinction between the spirit set out in standard ethics guidance and the procedural way this may be formalized in regulation)." *Anonymous respondent*

Comments on what 'standard' means

One respondent asked:

> "What is this 'Standard"? Who sets the standard? On what basis? How do we move from what is called universal standard, developed in the western world, to standards carefully developed in context? Where is the local voice in this?"

Question 8

If any differences in approach to study design or review can be justified because of the features of a global health emergency, would safeguards, such as an independent declaration that 'emergency' criteria have been met, be necessary?

Yes, they would be necessary

Several respondents indicated that safeguards would be necessary.

> "Absolutely. Any short-cutting of normal processes has to be justified with documented rationale. Perhaps more importantly, that decision needs to be reviewed regularly. And the more serious the shortcut, the shorter the

period between reviews and the greater the level of scrutiny of that decision." *Anonymous respondent*

"Yes. I think that in an emergency situation some normal criteria may not be met. However, very little deviation from internationally acceptable standards should take place. There should be suitable justification for any deviation." *Dr Rosmond Adams, CARPHA*

"Yes, it is important that population must know that it is an emergency or global emergency situation and concerned officials must act promptly and individuals are asked to cooperate for the best interest of their community and for humanity." *Wissam Doudar*

"Yes, it will be good practice to ensure that only situations that fit the criteria for global health emergency be reviewed by "Emergency review processes and IRB's"." *Dr Anuradha Rose*

"Absolutely. All proportionate systems of research regulation and oversight require specifying the criteria under which, for example, a given review mechanism comes into effect. This is why such systems are so complex". *Annette Rid*

"Use of such an "alert" threshold may be useful to officially set in motion the rapid ERC review capacity to acknowledge extra time required by ERC members to meet the need, request assistance". *Anonymous respondent*

"Absolutely! I think it is essential that the process for deciding to trump internationally agreed parameters is agreed before emergencies break out, and that decision-making is completely transparent and as inclusive as possible. This is not optional. I think even in the urgency of dealing with a GHE, what is essential is that we remain mindful of the long-term implications of our decisions, and of how we make decisions. We must ensure that we can explain and justify why certain decisions were made, and be satisfied that in making those decisions, we have minimised the potential negative fall-out." *Jantina de Vries*

"A collective independent declaration of a global health emergency would be essential before considering any deviations from standard research design and review. Other safeguards would include supporting a commitment to meaningful data sharing, local collaboration and meaningful provisions for public health impact." *Ann H. Kelly*

No, they would not be necessary

No respondents who addressed this question stated explicitly that safeguards would not be necessary.

They may be necessary

Equivocal responses to this question included:

"Perhaps – or this could be judged by a REC as part of the ethical review, according to criteria within either existing guidelines (e.g. CIOMS and ICH

both contain provisions on emergency research) or a specialist code of ethical conduct in global health emergencies." *Dr Adèle Langlois*

"Probably, but also there it can be driven by, or delayed by, politics, economics, or other non-health related interests. Risks being just another bureaucratic layer." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

"There would have to be safeguards that are determined ahead of time before the emergency occurs. An emergency declaration might help, but that could become a very legalistic way. The point should always be whether the non-standard approach is justified." *Dónal O'Mathúna*

Other comments

Other related comments received in response to this question included:

"One challenge that may arise here is that declaring a situation an 'emergency' is a political decision. It is possible that some emergencies would not be labelled in this way for political reasons." *Humanitarian Health Ethics Research Group*

"Clinical research advances the understanding of science and promotes human health. However, it is important to remember the individuals who volunteer to participate in research. Clinical research can be justified only if, potential risk to individual subjects are minimized; potential benefits to individual subjects are enhanced; potential benefits to individual subjects and society are proportionate or outweighs the risks." *Barthalomew Wilson, PREVAIL*

"If such changes in the review process exist (some expedited but not less robust), then I think the onus falls on the researcher to justify in one short para in the beginning of the proposal, why their proposal should take this track." *Anonymous respondent*

"A declaration of emergency should be determined in a fair and deliberative manner. Who makes the declaration will be as important as how, and should be from a trusted body." *MSF / MSF ERB*

Question 9

When choosing a study design, is it ever justifiable to prioritise a design that will maximise knowledge and hence scope for benefit for future generations, over a design that maximises the possibility of benefit for people affected by the current emergency; or could this never be justified? On what ethical basis would you justify such a choice?

Comments on the framing of this question

A number of respondents commented on the framing of this question, including whether the two options *were* mutually exclusive.

> "The assumption here is that one contradicts the other? And I am not sure this is correct. If for example there is an immediate need for intervention requiring research, one can prioritize benefit to people as a first stage; then continue by working towards longer term goals." *Professor Rita Giacaman*

> "I would question the way the question is framed. Typically, the salient choice in this clinical trial context is between designs that maximise potential benefits for participants or the affected population that result from conducting the research (e.g. access to a promising study intervention for participants or helping to curb the epidemic with the research if the intervention is safe and effective) and knowledge that, provided regulatory processes for licensing a safe and effective product are in place and funding for wider its wider implementation is secured, could still make a significant impact on the current emergency. As I see it, choices can go both ways, and a lot will depend on the promise of the study intervention and the background risk that participants and the wider population are facing, as well as the value of the information gained." *Annette Rid*

> "Are they really always independent of each other? Allowing the suffering and death of the living for the benefit of those that might be born does not seem a reasonable price." *David B. Morton*

Further points highlighted that the use of placebo may be particularly pertinent to this question.

> "This question seems to be especially related to the dilemmas related to the use of a placebo ("do we provide the new (or experimental) treatment to all patients so that they might benefit from it" or "do we conduct a placebo randomized trial so that we have the best evidence on the efficacy of the new drug"?). This is a very complex issue that is best addressed "outside" an emergency situation." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

> "Placebo use in emergencies would fall under this category and has been questioned, therefore RCT are generally considered not ethical in emergencies. Studies approved for emergencies are generally based on the belief that the intervention is very likely to be effective and therefore a true placebo control group would be unjust, i.e. withholding a potentially beneficial treatment." *Anonymous respondent*

It is justifiable to prioritise a design that will maximise knowledge for future generations

Very few respondents indicated that they agreed with this position. One respondent stated:

> "I will prioritize design that will maximise knowledge and hence scope for benefit for future generations. Local population need to be aware of the risks based on the fact that local conditions may result in different potentially (worse) outcome". *Seydou Doumbia*

'It depends'

Several respondents stated that justification may depend on a number of factors.

It depends on the emergency

> "This depends on the emergency. Maybe the need for immediate knowledge for response may be necessary and may not allow for a research that will benefit future generation. However as much as possible should be done to extend the benefits of any research." *Dr Rosmond Adams, CARPHA*

> "Emergency prioritization depends on the extent, nature and degree of event or disaster consequences or impact on human, animals and environment". *Ernest Tambo*

> "It depends on the severity of the health threat. Where the treat is likely lethal and the conditions under which people die entail suffering that is minimally or un-relieved, I would argue that a trial design that maximises knowledge over maximizing possible benefit for affected people is unethical. There is a humanitarian imperative to put the interests of the suffering first." *Bridget Haire*

It depends on those who are affected by the emergency

Some respondents also felt that it might depend on the awareness of those affected by an emergency:

> "Prioritizing designs that will maximize knowledge over designs that maximize the possibility of benefit for people affected by the current emergency may be acceptable when the people affected by the current emergency express a preference for the latter. Such decisions would require careful consultations with local and national leadership, people in affected communities, directly-affected persons, and potential participants." *Humanitarian Health Ethics Research Group*

> "If the people affected by the current emergency agreed to this it could be justifiable." *Dr Adèle Langlois*

> "I think it can be justified if the persons who will take the intervention (e.g. drug, vaccine) are fully aware of the potential risks and they still agree to be involved". *Anonymous response*

It depends on the benefit

> "If this is a question about direct benefit rather than benefit for the next group of people affected by a GHE, then I think it depends on the scope of the indirect benefit. Where in principle the priority should go to research designs that enhanced direct benefit in the now particularly in GHEs, there may be some design that has significant opportunity to enhance wellbeing of future population groups in a GHE in ways that are very significant, and if we can gather than knowledge during the now, I could see prioritizing that, as long as it does not exacerbate the current problems – so not making the current situation in any way worse." *Anonymous respondent*

Another respondent discussed whether it may be justifiable to prioritise a design that will maximise knowledge for future generations if the benefit is significant.

> "A design to maximize benefits to future generations over the current participants is justifiable if the benefit is very large. However subjecting current participants to irreversible or large magnitude harms by justification of benefits to future generations should not be allowed. The good of future generations should never justify serious harms to current generations no matter how large the benefits, as the scope for exploitation is very large in such a situation." *Dr Anuradha Rose*

It depends on the evidence already available

> "I think that depends entirely on the evidence you already have for the intervention. If you already have evidence of safety or efficacy, then I would think it is extremely hard to justify that you design a study to maximise generalizable knowledge, and you would rather consider designing a study that maximises benefit to the study community whilst also answering important scientific questions about safety and efficacy. But if you have very little or no evidence of efficacy then I think you risk doing more harm than good". *Jantina de Vries*

It is not justifiable to prioritise a design that will maximise knowledge for future generations

Several respondents stated that it is not justifiable to prioritise a design that will maximise knowledge for future generations.

> "… a study must first and foremost aim to save lives, and contribute to restoring normality." *Anonymous respondent*

> "We believe that, in principle, it would never be justified. The situation should be studied specifically for possible adoption, which does not appear to be justified by any usual possibility." *Oswaldo Cruz Foundation*

> "[I] don't have the ethical language for it, but this seems like a justification for lazy science." *Anonymous respondent*

> "Most would not favour potentially harming someone in the present for the benefit of an unknown person or occurrence future? Would be very hard to justify? – exacerbating vulnerability, inequity and increasing harm to those currently affected". *Anonymous respondent*

> "In general, I believe that it is an ethical imperative that research conducted under emergency conditions provides some direct benefit for the people affected. Under certain conditions (e.g. the potential future benefit of a vaccine for local populations) this benefit may take the form of building health capacity in country through training of research workers, improving public health infrastructures or local practice." *Ann H. Kelly*

> "… study design should not unduly jeopardize participants by causing harm to participants for the benefit of future generations." *MSF / MSF ERB*

> "Prioritising is the key word here for me. If this means that people's immediate needs / benefit will be overlooked for the benefit of future generations, then I would say no to this. By definition, a GHE means that people are in serious risk, and therefore this needs to be the priority. If there is a way to benefit current people and future generations, that's great. But assuming serious risks of immediate danger, then these immediate needs should be prioritised." *Dónal O'Mathúna, PhD*

Question 10

Are there any specific kinds of research or innovation that, in your view, raise distinct ethical questions and / or might demand differential ethical treatment?

Respondents suggested that a range of types of research or innovation raise distinct ethical issues, including:

- Epidemiological surveillance research
- Physically invasive research (e.g., that includes blood draws)
- Research with participants who do not have capacity
- Vaccine trials
- The emergency use of unproven interventions
- Research on diseases with unknown natural history
- Research involving bio-samples
- Interventional research
- Preparedness research
- Double blind research: "for example drug trials would be especially ethically challenging, if not impossible, in the emergency setting". (William Aldis)
- Research on areas that are subject to cultural sensitivities, or which "radically [challenge] customs and beliefs" (anonymous respondent).
- Research that involves, or excludes, vulnerable, disadvantaged or stigmatised populations: for example, pregnant women, children, older people, men who have sex with men, or people with addictions
- Novel trial designs, "particularly adaptive platform trials […] We solicited the views of potential research participants regarding their enrolment to APTs during a hypothetical influenza pandemic. Our participants preferred the idea of response adaptive randomization and considered it a "selling point" of the trial design. There is then, of course, the potential to "oversell"." (Prof Alistair Nichol (lead), Prasanth Sukumar, J-P Byrne, Nina Gobat on behalf of PREPARE WP1)

One comment highlighted research with 'vulnerable' research participants.

> "Conducting research during a health emergency situation is complex. The community and those affected by the condition, who are usually the potential research participants, become extremely vulnerable and virtually incapacitated in decision making. In such a situation, rather than making rational decisions, potential research participants and their legal guardians are likely to suffer from the fear of the unknown and inhibit the hope that the products under investigation are the ultimate solution to the problems they are facing. On the other hand, researchers may fear that the epidemic may come to an end too soon and limit their chances of testing the investigational product. This may make researchers exposed

> to these situations, suffer from an acute conflict of interest." *ECEPAS, GET*

MSF / MSF ERB also stated:

> "As already stated, there is no reason or justification to negotiate/derogate on ethics principles with the alibi of a GHE. Conversely, some aspects deserve particular attention, for instance:
>
> - Biosamples management, governance and ownership
> - Data sharing
> - Community engagement
> - Benefit sharing
> - Involvement of local research institutions/capacity building
> - Research in pregnancy
> - Research with especially vulnerable populations."

Another respondent highlighted the case of research involving animals.

> "Preparedness research involving animals may have an important role to play in producing animal models and animal data that will enable the licensing and distribution of medical treatments in an emergency, without going through the conventional stages of clinical trials." *Animals in Science Committee*

In a general comment in response to this question, one anonymous submission stated:

> "any research demands a high level of empathy – or understanding of the perspective of the participants. If we can understand that perspective, we become better partners in a research endeavor. I know this is a very 'blanket' response but this is a difficult question as it may be answered differently by persons with expertise in various disciplines."

Fewer respondents identified types of innovation. Examples included:

- Use of artificial intelligence
- Use of drones

In a general comment on the implications of innovation, Dr Anuradha Rose also stated:

> "… innovations which have huge implications on human health but have issues of accessibility post trial and genetic research should have specific questions and commitments by researchers, and separate standards."

Questions 11–13: making decisions about participation in research

Question 11

Are you aware of any examples of when an emergency seemed to demand a different approach to making decisions about research participation? If so, please explain how any derogation from standard approaches might be ethically justified, and the relevance of the kind of research concerned (for

example research involving physical intervention as opposed to research involving data only).

The small number of examples provided in response to this question focused mainly on Ebola and Zika. One respondent also highlighted an example from Gaza.

Ebola

> "I am aware of some pharmaceutical trials which took place during the Ebola epidemic in Sierra Leone. But still, the pharmaceutical was not efficacious. This raises the question, whether there should be any shortcuts in attempts to save lives. Since there is a thin line between doing research, for research's sake and doing research in order to save lives during complex emergencies, I think it is better for any research to be ethically sound - designed and follow normal research procedures including for vaccines and pharmaceutical trials." *Anonymous respondent*

> "Arguably there was an element of 'research' in medical care during the West African Ebola outbreak in treatment centres (including those outside West Africa, such as the US, the UK and Spain) where clinical teams tried to intensify supportive care to achieve better outcomes. It is important that such endeavours be published. Data about the levels of care in particular treatment centres during outbreaks, and how this related to mortality, should also be published. This kind of data though generally doesn't require consent even under non-emergency circumstances." *Bridget Haire*

> "An issue in SL [Sierra Leone] was that the people did not have the conceptual frameworks to understand what treatment they were being given/offered and the same would be true of a study. If the people believe that the virus is caused by the/a government and involves magic, they will not be easily persuaded about the benefits/risks of a trial medication. But a community-based approach to identify how this might be explained in a way that makes sense from their cultural perspective will allow for informed decisions regardless. I believe this was considered too difficult, or thought of too late as it is not really part of the designers' ethical training." *Anonymous respondent*

> "Some of the issues the MSF ERB consistently raised in its reviews during the West Africa Ebola epidemics were how to obtain truly informed consent of patients facing a high chance of death (which raises challenges similar to those generally observed in desperately-ill patients); in a high-safety environment (where protective equipment create a "physical distance" between the person and the healthcare worker during the consent interview, and makes the presence of a family member or witness impossible); with a high potential for therapeutic or philanthropic misconception, as MSF was the only healthcare provider for Ebola patients in many instances, etc." *MSF ERB*

Zika virus

> "In the "Microcephaly Epidemic", specific agreement among institutions in the early days of the epidemic facilitated the design the protocols in consonance with the guidelines. Researchers should take time to meet

> the representative regional/local authorities in order to: set-up priorities, mobilization/support. Official networks are important but unofficial networks may be as important to allow quick response. Local health care staff and health services should be taken into consideration in order to achieve both quality research and quick response. One sensitive issue during the epidemic was the delay of the reference laboratory to give the results to doctors and patients. At the end of the field work equipment used during research should remain available for routine clinical practice to keep the services running (example – Ultrasound)." *Instituto Aggeu Magalhães- Fiocruz-PE, Brazil; Federal University of Pernambuco, Pernambuco, Brazil; MERG - Microcephaly Epidemic Research Group*

> "Here I would like to point to research undertaken during the Zika outbreak involving the release of *wolbacchia* infected mosquitoes. This and other novel approaches involving the release of laboratory-altered insects, presents an exciting opportunity to reduce the threats posed by emerging and re-emerging diseases, however they clearly raise a range of social, ethical and regulatory concerns. Mosquitoes that incorporate drive mechanisms are meant to operate across ecological and temporal scales calling into question hyperlocal understandings of the relevant community, or punctual and sporadic forms of engagement. The risks and benefits of these technologies are to be shared on an increasingly global scale, demanding new criteria of consent and new processes for their implementation." *Ann H. Kelly*

The same respondent continued:

> "Essentially, the release of mosquitoes strains the ethical traction of individual consent. A person can refuse to be part of the trial, but at some level they (and other citizens in the city) would participate if mosquitoes were released. The constraints of this research for individual consent was reinforced both through processes of collective dialogue and approval, but critically through robust regulatory process, the pragmatic nature of the design and the accountability of a public institution through which the research was implemented."

General comments

A small number of respondents also provided general comments in response to this question.

> "Yes; as with fatal illness, exposed populations should have the opportunity to make crisis-style decisions including group consent." *Professor Stephen Gordon*

> "No obvious differences: there may need to be a creative approach to consent processes, suitable to the context, with appropriate engagement with the community – but this should apply in other circumstances too". *Anonymous respondent*

> "In most emergency situations I have observed, participation is narrow and gate-keeping is rather defensive." *Tim Allen*

Dr Cathy Roth set out a series of general comments on autonomy in response to this questions, including:

> "It is striking how 'autonomy' has emerged as the priority ethical principle in international public health fora and meetings – but for most of the world, and most of the time, individual wishes do not dominate over what is best for a community. For a person to act against prevailing wishes / perceptions may in many cases be almost impossible, and when it happens may lead to harm for that individual."

Comments on how the question is framed

A small number of comments were received regarding the framing of this question.

> "[it] might be helpful to widen the description of 'making decisions about research participation' in order to think about justifications. There is a difference (in terms of justifying actions and actors) between:
>
> - deciding to participate;
> - deciding derogation, such as waiving of consent, is appropriate both generally and in specific cases of patient presentation; and
> - deciding to enrol someone, under a different approach from consent, to emergency research (ER).
>
> I take 'standard approaches' to be favourable ethics review plus an approved informed consent process and documents." *Katherine Sahan, from the Ethox Centre and Wellcome Centre for Ethics and Humanities*[24]

> "On a separate note, we would warn the authors of the document about the wording they use above, i.e. "research involving physical intervention as opposed to research involving data only". This seems to imply that there are no risks in using medical and personal data, while abuses are clearly possible (even if less serious, at individual level, than in interventional trials), and everybody has the right to decide whether and with whom to share personal information." *MSF / MSF ERB*

Question 12

If we consider the giving of valid consent as one element in the 'ethical ecosystem' around research in emergencies, and recognise too that consent is often imperfect, what are the other essential elements of the ecosystem necessary for such decision-making to be considered legitimate?

This question asked respondents to put forward elements, in addition to consent, that legitimise decision-making in GHE contexts. Several elements were suggested.

Engagement

Several respondents highlighted the engagement and/or involvement of communities and countries affected by a GHE as an essential part of legitimate decision-making.

> "having good representation and participation/engagement of the affected population (and host communities) can go a long way in helping to

[24] Hereafter referenced in this document as: Katherine Sahan.

resolve many of the thorny issues that are the basis of these questions. Defining 'good' representation is not easy but it should not be tokenistic, and it should be of persons from the community that have the community's interests (and not their own personal interest) at heart." *Anonymous respondent*

"With some types of global health emergencies (e.g. outbreaks and epidemics), people can be informed about studies before it becomes possible for them to participate. Engaging in widespread and culturally-appropriate dissemination of information about studies + holding consultation and discussion sessions in emergency-affected communities can support meaningful consent. This is particularly important given that people's ability to ask questions, deliberate, and reflect may be limited by circumstances once they do become eligible for participation (e.g. Ebola patient being asked to join a study while already acutely ill, and socially isolated, in the ETU)." *Humanitarian Health Ethics Research Group*

"Quality community engagement where the community as a whole agrees to this research taking place. Consent in many contexts is not an individual decision, it is made in concert with family and community, therefore this will help to ensure that consent is more valid." *Gillian McKay*

"True community engagement is essential here. This helps to promote better understanding all around, and can ameliorate concerns over informed consent, harms and benefits, etc." *Dónal O'Mathúna*

"Genuine, visible (intellectual and other) leadership by the countries affected is essential at all levels, from high-level decision-making to low-level implementation." *Jantina de Vries*

"Genuine efforts to understand the culture and what is acceptable / not should not be too difficult, but often are not undertaken". *Anonymous respondent*

"The approval of a local authority is also needed to help address context specific issues related to the research process." *Jihad Makhoul*

"It is important to take decisions about how legal consenting can be conducted and obtained in due consultation with the communities in those situations. Current consenting processes are still imperfect with imperfection being a reflection of specific contextual issues." *Network of Ethics Committee Members in West Africa*

"Subjects' illiterate or social vulnerability should never be a reason for consent waiver. Rather, adequate and contextualized measures should be proposed for meaningfully inform them, and on a separate note for documenting consent. Community engagement and social science research may both help to develop such measures, hopefully before a GHE occurs, and building on the experience of previous ones." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

Continuous and effective information provision

Respondents also suggested that a further essential element of decision-making was continuous and effective information provision.

> "Global health emergencies can bring an influx of medical and research activities into places where both have historically been limited. As a result, prospective participants are particularly likely to be unfamiliar with research, with distinctions between research and care, and with some of the concepts that will be discussed by study recruiters. Efforts to provide information are particularly important in this situation." *Humanitarian Health Ethics Research Group*

> "A significant effort must be made to seek to provide all participants and those involved in the crisis with a balance between risks and benefits, as transparently as possible." *Oswaldo Cruz Foundation*

Trust-based points

A small number of respondents noted the role of trust in decision-making's legitimacy.

> "perhaps trust? There is a growing body of bioethics literature on the place of trust alongside autonomy / consent in ethical decision-making." *Dr Adèle Langlois*

> "a clear and trustworthy data storage plan to protect the confidentiality of the research information is needed." *Jihad Makhoul*

Clarity of roles

On the clarity of roles of those who manage research and those who treat patients, an anonymous respondent stated:

> "Efforts should also be made to avoid blurring the lines between the role of clinicians and researchers if applicable, especially in terms of clinical research. For example, research onboarding should be done by individuals who are not primarily responsible for the care of a participant or patient."

Beneficence

> "Beneficence is a critical aspect of the 'ethical ecosystem' – a genuine desire to do the best for individuals and communities who are experiencing a health emergency – and a commitment not to sacrifice these interests for the putative benefit of future or distant others." *Bridget Haire*

Intent

> "I believe an essential element (which unfortunately cannot be readily measured) is intent. If the intent of the researcher in an emergency is to protect the health and wellbeing of affected people, then it's more likely that the research will be well located within the 'ethical ecosystem' referred to. However, emergency situations often attract personality types whose main motives for doing research are to advance their careers, get publications etc. That's a conflict of interest; and unfortunately, researchers' home institutions are often complicit." *William Aldis*

General comments on consent in GHEs

Respondents also used this question as an opportunity to put forward general comments on the role of consent in decision-making for research in GHEs.

> "Consent should be voluntary. But it is difficult to understand how a community in distress can be sober enough, and of sound mind to make such decisions." *Anonymous respondent*

> "Quality of consent should also be a factor in the "ethical ecosystem"." *Anonymous respondent*

> "[It's] good to start from a point of considering what valid consent properly aims to achieve. E.g. Capron says it achieves respect for individual autonomy, protection of subject rights and welfare, and intelligent governance of research.[25] Also that in influential conceptions of consent[26], the individual autonomy and authenticity elements are central to the conception. From this starting point other essential elements for decision-making can be analysed. It feels as though other elements should primarily focus on restoring some regard for individuals. This argues that we demand more from consent than just welfare and reputational protection." *Katherine Sahan*

> "Valid consent should involve an assurance that there is no coercion. Lack of incentive to participate is very difficult to ensure in emergency research because of some amount therapeutic misconception in the minds of the public." *Dr Anuradha Rose*

The same respondent stated that there should be "consent from participants and not only community consent in the case of cluster methods".

One respondent suggested that how the question references 'consent' might be framed differently.

> "the wording "we recognize that consent is often imperfect" could be replaced with "we recognize that consent is often challenging", to reflect the fact that difficulties should be seen as a reason to find contextualized procedures, not to short-cut on principles." *MSF / MSF ERB*

Question 13

Are there any circumstances in which participation in research should not be optional?

Yes, with provisos

[25] Capron A (2015) Subjects, participants, and partners: what are the implications for research as the role of informed consent evolves?, in *Human subjects research regulation: perspectives on the future*, Cohen I, and Fernandez Lynch H (Editors) (Cambridge, Massachusetts: MIT Press Scholarship Online).

[26] Faden R, and Beauchamp T (1986) *A history and theory of informed consent* (Oxford: Oxford).

“Probably, if the public health risk is so high, but again under very tight review and very rare circumstances. In the main I believe that there will be enough people willing to participate if the cultural engagement is effective that there should be no need to enforce involvement in a trial.” *Anonymous respondent*

“I would say yes. In rare cases however. Where you may need evidence and it is only collectable from few participants. If these participants do not participate then the situation can escalate and become a greater disaster. For example, in Ebola outbreak or similar.” *Dr Rosmond Adams, CARPHA*

“It’s possible to imagine extreme situations (e.g. the emergence of a novel or poorly understood infection, with high transmissibility and mortality) where the need to identify the agent, trace contacts, prevent transmission, plan for healthcare of those in the vicinity etc. is so great that action without consent is the only reasonable response. But this would be quite exceptional.” *Dr Cathy Roth*

“Perhaps where the risk is high for those unable to give consent, and the proxy consenters (a group representing several key interests and not just one person) should make that decision. The impact of future stigmatisation is a further consideration e.g. survival at the expense of others.” *David B. Morton*

“Research in natural disaster situations, which use geographic areas for selection or which do not have direct interventions on individuals can be non-[optional]. However any research where there is direct intervention on individuals with any degree of harm should always be optional.” *Dr Anuradha Rose*

“In the most unexpected situations of disruption, such as biological attack, chemical or radioactive warfare, participation may not be optional. In the case of epidemic outbreaks, even those of infections with higher lethality, the alternative should be offered, even if it means imposing the quarantine on those that do not accept it.” *Oswaldo Cruz Foundation*

“Consent is generally necessary for interventional research, but the extent to which true informed consent is possible in a health emergency means that there might be time when a ‘best interest’ test might have to take the place of consent for a person to access a productive that does not have regulatory approval (if there is genuine belief and substantiated reason to believe that accessing the agent would be in the patient’s best interest). An example here might be access to an unapproved investigational treatment that has been producing undocumented but good results in others, for someone who is not conscious and where there is no time or ability to get surrogate consent.” *Bridget Haire*

“I think there are a limited set of these circumstances. When there is no other way to find evidence, then I think this can be done. For example, if there is true equipoise over whether adding something to food makes it better for people, and little or no risk is involved, I could see where testing it in some groups and not others could be justified. However, there would have to be independent safeguards in place to ensure conflicts of interest

are not involved, and also that people are given as much information as possible on why the research is being done." *Dónal O'Mathúna, PhD*

"May be acceptable where benefit for community would be greater than harm to individual, and individual harm not considered high – proportionality – however THIS IS CONTROVERSIAL – some feel strongly that collective rights cannot trump individual right to free and informed choice." *Anonymous respondent*

No

"We do not think there are any circumstances in which participation should not be optional as this is a violation of ethical conduct. We saw this with the Tuskegee Syphilis study of 1932-1972; and also, with the syphilis research in Guatemala in the 1940s. Having said that, it is important that research participants are well educated about research and are empowered to make informed choices and decisions. Participation in research, especially in emergency situations is a public good, thus research participants have a moral obligation to participate for the benefit of future generations." *ECEPAS, GET*

"I cannot think of any. Given what we know about the history of unethical research, particularly with 'vulnerable' populations, this could open potential for much harm." *Anonymous respondent*

"NO. We cannot see any reasons to derogate on the principle of respect for persons and autonomy, which would imply overturning the Declaration of Human Rights, the Nuremberg Code, the Helsinki Declaration etc." *MSF / MSF ERB*

"No, under no condition should participation be forced. If incapable of making a rational decision, family members can provide consent. However, if the person rejects strongly participation, that person should not be included in the study even with family consent would be my view. The question is raised here about the degree of danger/risk a refusing participant can pose to community. However, this is not about research ethics, this is about governmental controls and action it would seem to me." *Professor Rita Giacaman*

"I could not think of any (unless data would be completely and irreversibly anonymized like "being part of" national surveillance system)." *Anonymous respondent*

"The moral duty to participate in research without consent is very weak… as patients can't respond to the 'call of duty'." *Katherine Sahan*

"as long as power relations among the researched and the researchers exist, many participants are coerced to participate in studies, particularly during complex emergencies. Similarly, in studies deemed beneficial by participants, for instance when they offer medical care, when they have incentives. I have seen studies where participation was optional, but because of the incentives offered, participants 'blindly' enrolled." *Anonymous respondent*

> "Mandatory participation in research without any type of consent may be allowed in cases where the research is public health surveillance. Sometimes, in public health emergencies it might be impossible to seek and obtain everyone's consent. In my view, one needs an independent decision maker to assess the benefits against the risk. People need to and have the right to know how the research will affect their lives adversely or for the best. But even when participation is assessed to pose minimal risk, it may be somewhat burdensome discomforting, inconvenient or raise expectations. One could argue that it may be acceptable if the research is governmental or sponsored by the state, however in cases of global health emergencies, the state may not exist or may have conflicts of interest or may be coercive with one population group and not another. Although there may be some literature on this subject in public health and medical research, I for one, would be very suspicious of research that is not optional for people and cannot think of other circumstances where it should not be optional… even in emergencies." *Jihad Makhoul*

> "A GHE cannot be a reason to derogate on the principle of respect for persons and autonomy. Participation in research that involves active participation, active intervention, or additional medical procedures or sample collection, esp. but not only in healthy subjects, must always be optional (i.e. a personal, free, informed choice)." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

However, the same respondents go on:

> "In some cases of research with minimal risk and high social value, i.e. secondary analysis of aggregated and anonymized data by/in collaboration with a public health institute (PHI), a consent waiver can be granted by the concerned ECs/IRBs. The same can apply to research on health systems. However, reasoned and justified consent waiver should not be confused with "non-optional participation"."

Questions 14–17: duties at the interface of research, treatment, and public health

Question 14

What, in your experience, are the main ethical challenges that arise as a result of uncertainties in the boundaries between treatment, research, evaluation, and public health? To what extent are these associated with logistical or resource constraints?

General comments on boundaries

Respondents submitted several general comments on boundaries in this context.

> "Research and treatment are different: research aims at producing generalizable knowledge, not directly benefitting the participants (which of course may happen but it's not the primary aim). While hoping to benefit from a trial arm may be understandable, a failure to comprehend the lack

of evidence for that hoped-for benefit borders on therapeutic misconception. However, it is the case that people in trials do better – not because of the benefits of the trial intervention but because they are closely monitored, and the other aspects of their care are more carefully standardized. There is nothing unique here in emergencies – the same issues, for example arise in some cancer research." *Anonymous respondent*

"[The] limits are not so imprecise. This imprecision is assumed when searching for alternatives that facilitate certain choices in cases of conflicts of interest of the researcher / caregiver / sanitarist." *The Oswaldo Cruz Foundation*

"The line between research and response is more blurred than it is often represented". *Wellcome*

"Recognition that many activities in the clinical and public health space, including the medical humanitarian space, are hybrid activities that require squaring at times competing ethical commitments." *Annette Rid*

"[Almost] everyone recognises that a more holist approach is crucial." *Tim Allen*

Ethical challenges re. boundaries between treatment, research, evaluation, and public health

Therapeutic misconception

The challenge of therapeutic misconception in research contexts was noted by several respondents.

"… the biggest providers of medical care in SS [South Sudan] are NGOs. Therefore, when the same NGOs design research studies, people conflate research for treatment. It further gets complicated when dealing with low-literate populations and vulnerable people. In addition, translating 'research' and 'treatment' to local terms may mean the same thing. For example, translating the term 'researcher' to a local language comes out as 'teacher' or local/community doctor.' Therefore, respondents consider researchers as doctors or teachers. In addition, we rarely get people refusing to participate in research because the NGO name is very powerful. This is despite numerous assurances that non-participation in research will not affect provision of health services." *Anonymous respondent*

"There are occasions where concerns about therapeutic misconception are well placed - for example some epidemiological studies, or research collecting samples to identify biomarkers for possible future diagnosis and monitoring, where there is no realistic prospect of direct benefit. However, where studies involve the use of novel interventions in the hope of affecting the course of the disease, then 'participants' take part in the hope that they will (a) be on the active arm and (b) that the intervention will prove to be successful. This raises questions about how the research is presented. There is a fine balance between avoiding raising false hopes by emphasizing that it is not known whether this intervention will be

more effective than any other forms of care, and being perceived simply to be 'experimenting on us'." *Dr Cathy Roth*

"Key challenges include research illiteracy and misconception about research and treatment. Many research participants, especially from low-income countries do not understand the difference between treatment and research. This confusion blurs their ability to engage rationally with researchers, on issues related to their right to participate in the study as well as to refuse or/and withdraw from the research." *ECEPAS, GET*

"I firmly support the concerns raised over the 'therapeutic misconception' and suggest than for GHE the distinction between research and intervention present[s] an ethical cul-de-sac. Rather, I would think that in a GHE the commitment to public health impact should only be reinforced." *Ann H. Kelly*

"people in resource poor settings will often take part in research because it is their best means of accessing healthcare. This highlights the broader ethical issue of inequalities of health." *Dr Adèle Langlois*

"Research may be only way to get clinical care – patients compromise their own values e.g. giving blood samples". *Anonymous respondent*

Confusion in a more general sense was highlighted by an anonymous respondent.

"Patient / participant confusion especially in emergency with unfamiliar circumstances, people, interventions".

Working relationships

Challenges regarding working relationships and responsibilities were also noted by several respondents.

"Between treatment and research, the most difficult ethical issue is the dual role a doctor plays as a researcher with an obligation to ensure that the research is valid, and a desire to find answers quickly in an emergency situation, and as a health care provider with fiduciary duties towards the patient." *Dr Anuradha Rose*

"distinct categories can… lead to tribalism. I was on the response side, and there were times that responders seemed suspicious of people who were primarily doing research, or felt that it was a bonus additional activity rather than intrinsic to the response. The ethical challenge here is… situating the importance of research within the response to an emergency." *Anonymous respondent*

"The research and response communities are often quite separate and need to be clearer on how they can work together, and how data can be used and shared." *Wellcome*

"The ethical challenges due to the fact that the care givers and the researcher are the same person or organization are well known in ethics and biomedical literature, and they can only be exacerbated during a GHE." *MSF / MSF ERB*

Inconsistencies / differences in regulatory processes

Differences in regulatory processes were indicated by a small number of respondents as an ethical challenge in the boundaries between treatment, research, evaluation, and public health.

> "I don't think that the lack of separation between research and public health intervention is related to logistical or resource constraints; but just due to the fact that it is not possible to distinguish well between these sub-categories; and different rules how they handle this issue." *Anonymous respondent*

> "the misconception that evaluations do not need ethical review." *Dr Anuradha Rose*

> "There are too many situations where people focus on whether this activity "requires" ethical approval or not, and then this determines how they approach the activity. Instead, the focus should be on engaging with people in the most ethical ways possible, not matter what we are doing. This fundamentally means treating people with respect and dignity, whether we are conducting research, providing treatments, doing evaluations, or driving a truck." *Dónal O'Mathúna, PhD*

Funding implications

Implications for funding were also highlighted in responses to this question.

> "Part of the problem is about funding, with emergency funding lasting say 1 year, so researchers come in, quickly work on research, maybe even a quick intervention, without building on this knowledge to help capacity strengthen and build sustainable programs for the future. To me, public health research in emergency must combine immediate needs with longer term development objectives. And this has been hard to achieve precisely because of funding cycles which do not take this point into consideration, or because of the sectorization of funding schemes, making it difficult to look holistically at what happens to people's health broadly defined in emergency. Yet, we must always think of addressing emergency by at least not harming previous work focused on development objectives."

Similarly, Ernest Tambo highlighted:

> "pilot and short term funding where a project research in a selected community are abandoned with reasons of funding gaps or discontinuation."

The same respondent raised a concern on "[miscommunication] and some researchers' manipulations of results to suit funding or pharmaceutical companies' suitability for licensure".

Interests of affected parties

Challenges to the interests of those directly affected by GHEs were also highlighted.

> "The challenges of balancing individual autonomy and common good in public health research". *Dr Anuradha Rose*

A further respondent highlighted the role of consent.

> "With regards to evaluations and public health, some of the contentious ethical issues include the lack of agreement on whether or not evaluation should be treated as research, with the main issue being whether or not individuals participating in evaluations should be asked to give informed consent or not." *ECEPAS, GET*

Associations with logistical or resource constraints

The question of the extent to which ethical challenges arising out uncertainties in boundaries are associated with logistical or resource constraints was addressed by several respondents.

> "In LMIC such as India, resource constraints cloud judgement in all areas of medicine, be it therapeutic or research. Logistical constraints are usually easier to sort out, as evidenced by the very large programs run quite successfully, such as the Pulse polio program in India." *Dr Anuradha Rose*

> "… without proper planning enormous challenges in allocating resources and finances required are likely to be experienced." *Dr Joseph Kimuli Balikuddembe*

> "In countries with weak health systems, the advent of global health emergencies and related research can bring influx of resources such that ancillary care available to participants exceeds what would be available outside of such care. This has implications for freedom of consent." *Humanitarian Health Ethics Research Group*

> "[Uncertainty] may be compounded by resource constraints, as such constraints may force research and response work (if such a delineation can be made) to be even more closely interwoven – for example, making questions on how to prioritise use of limited infrastructure and personnel much more acute." *Anonymous respondent*

> "a good example will be the availability and use of experimental drugs as a treatment if no effective treatment is available and at the same time as a research activity." *Dr Rosmond Adams, CARPHA*

One anonymous respondent suggested that these boundaries are *not* associated with logistical or resource constraints.

> "I don't think that the lack of separation between research and public health intervention is related to logistical or resource constraints; but just due to the fact that it is not possible to distinguish well between these sub-categories; and different ethics committees may apply different rules how they handle this issue."

One result of this boundary uncertainty was highlighted as a particular constraint.

> "[Such] uncertainty can slow down the response to an emergency. In one emergency situation I have experience of, some people were reticent to share data as they were not sure whether the recipient's activities constituted research on that data – with concern that the data had not explicitly been collected for research purposes – while the recipient perceived their use to be for direct response purposes (epidemiological analysis to inform response planning)." *Anonymous respondent*

> "Such uncertainty can impact upon the speed at which the response can take place, and the way in which people work together, as research was viewed as an activity requiring much more oversight, and people were scared of getting caught out, 'accidently' doing research without the appropriate oversight." *Anonymous respondent*

In a related observation, an anonymous respondent stated:

> "The following are not affected by logistical or resource constraints, as can be avoided by researchers with integrity:
>
> - Unrealistic expectations.
> - Psychological harm ("guinea pig situation, why do they just leave and I am worse off?")"

Question 15

Is it possible to create a meaningful distinction between the collection of personal data for public health purposes, and for research purposes? What does this mean for consent and for data-sharing?

It is possible to create a meaningful distinction

A small number of respondents suggested that it is possible to create a meaningful distinction.

> "[There] is clear marked and difference". *Ernest Tambo*

> "Yes, it's done all the time. Large registries collect anonymised data on e.g. trauma patients without consent." *Anonymous respondent*

> "Generally speaking yes, but in emergency situations, as we are referring to, an effort should be made to ensure that the possible benefits to patients are always in a more prominent way." *Oswaldo Cruz Foundation*

It is not possible to create a meaningful distinction

Several more respondents indicated that a meaningful distinction is not possible.

> "there is no meaningful distinction between the collection of personal data for public health purposes and for research purposes." *ECEPAS, GET*

> "Some data collected for public health purposes may be of research interest […] Some data collected for research purposes may be of public health interest." *Humanitarian Health Ethics Research Group*

> "This is very difficult because first, even senior people in SS [South Sudan] government do not understand some basic tenets of research. For example, it is not uncommon to hear them demand for names of study respondents, or ask to participate in focus group discussions. In some cases, respondents themselves want to give us their names and we have to explain (again) that names are not necessary. In addition, senior government officials, due to their lack of capacity, want NGOs to do their work for them i.e. collect data for public health purposes. As a result, we often do that i.e. collect hospital use statistics but we keep the research data to ourselves." *Anonymous respondent*

> "The distinctions named only exist on paper but do not exist in real life. When I take part in a study, I am acutely aware about difficulties researchers face with keeping their promises, for instance, anonymity – yet the findings will be published." *Anonymous respondent*

Some respondents also indicated that a meaningful distinction should not be attempted, and that other issues should take precedence.

> "I don't think that is possible, and even if it is, I don't think it is meaningful to try. These lines are blurred at the best of times, with some bioethicists arguing that the distinction between 'research' and 'treatment' is not meaningful even in times of status quo (not GHE) […] to pretend that in the case of a GHE we can try to establish the difference, and get valid consent for either or both, is misleading and actually obscures some of the broader ethical obligations we have. These broader obligations concern our duty to protect the interests of the research participants and to ensure that no harm is done through e.g. the re-use of their samples." *Jantina de Vries*

> "it's more appropriate to focus on the rights and interests at stake when collecting data than on trying to define the activity, especially as data are pieces of information that can be used for more than purpose—in public health emergencies and more generally." *Annette Rid*

> "too much time is spent on trying to make clear-cut distinctions between terms or concepts that have blurry boundaries. What should motivate all these activities is a concern for the respect and dignity of the people involved. This means thinking critically and ethically about how the data could be used or abused. If the personal data could be misused, then mechanisms to anonymised should be introduced as soon as possible." *Dónal O'Mathúna, PhD*

The possibility of creating a meaningful distinction depends on other factors

A number of respondents suggested that the possibility of creating a meaningful distinction between the collection of personal data for public health research, and for research purposes, depended on other factors, including the context in which the collection takes place.

> "This depends on the situation. In an emergency setting (outbreak) it may be possible to collect information without consent and to be shared with different entities ensuring that personal information is protected. However, in non-emergency setting all the applicable standards and guidelines would be adhered to. What is important is that at the onset of the process it is clearly stated if the information is for public health surveillance or for research." *Dr Rosmond Adams, CARPHA*

> "where personal data is collected purely for purposes of surveillance in order to facilitate meaningful prediction and trends for an important public health condition, government entities have a moral obligation to ensure the safety of the public is assured, but without grossly infringing on individual rights. For example, it would be unreasonable for the ministry of health in the Republic of Congo, not to collect personal data that would lead to positive identification and tracking of people infected with the Ebola Virus in Congo, owing to the local and international public health threat posed by this lethal disease. This principle should, however, be used on a case by case [basis], and not be imposed on situations whose gravity does not necessity warrant collection of personal data for public health purposes." *ECEPAS GET*

> "This is not a question that one can answer internationally, it depends on legal instruments in each country. Some countries allow the mandatory collection of personal data for public health reasons, others do not. Hence, there already is this distinction, but it needs to be handled locally or a new agreement needs to be found internationally". *Anonymous respondent*

A further view suggested that the distinction might depend on the 'type' of research.

> "Collection of data as a part of experimental studies, in my view, falls under the research umbrella more squarely. Although that is not to say that such data are not also useful for public health purposes. The blurring is, to me, more acute with observational studies – for example data collection as part of a case-control study in an outbreak situation. In such scenarios people may be reticent to share data/information arising from these studies." *Anonymous respondent*

The same respondent suggested a 'way through' this question of distinction.

> "consider the potential risks associated with the method of data collection and sharing, rather than categorising the purpose of activity as public health response or research. Many of the methods may be the same, and the use may be both to directly inform a specific response, and for generalizable knowledge."

Meaningful distinctions and their effect on consent and data-sharing

The impact of the creation (or not) of meaningful distinctions on consent and data-sharing was commented on by several respondents.

What it means for consent

The question of drawing distinctions and its effect on consent elicited several responses.

> "Researchers sometimes collect data with research in mind, avoid the review process and appropriate consent processes by claiming the data was collected for an audit or for surveillance." *Dr Anuradha Rose*

> "We sometimes have situations where internationals acquire and use locally generated data, but interpret it in incorrect and damaging ways. We need to be sure that interpretation related to a good knowledge and understanding of context. The consent should be obtained after making sure that the participants are aware that data is collected for public health practice/ action purposes and/or for research purposes." *Professor Rita Giacaman*

> "Individuals have to be aware of the gravity of the decision they are making and totally understand the impact of the sharing of their personal health/ research data to make an informed choice, prior to consent. To promote personal dignity, autonomy and respect, individuals should be fully informed whenever personal data is collected, whether for public health or research and be given an opportunity to make an informed choice whether or not they are happy for their information to be collected, stored and shared for whatever reason. Information for this purpose should be easy to understand and precise, to enable individuals to fully comprehend and make informed choices." *ECEPAS, GET*

What it means for data sharing

On how the (potential) creation of distinctions between data might affect how those data are shared, comments included:

> "Data collected for public health purposes-for performance audits, surveillance and monitoring of public health should be released to researchers only after a clear proposal for the intended research is submitted along with detailed descriptions of anonymization processes. All research which is prospective should clearly state that the objective of data collection is research, and involve ethical review and consent." *Dr Anuradha Rose*

> "Sharing of data should be limited in both circumstances although public health officials may not have jurisdiction over researchers and therefore more risk that data will be shared and used beyond initial intent (need to emphasise need for ethics approval for all data sharing and use)". *Anonymous respondent*

> "When it comes to further data sharing, adequate measures should be taken in what concerns data de-identification, ethics approval, benefit sharing etc., and clear governance mechanisms should be set up, to ensure that the communities who originally provided the data will also benefit from the findings of secondary analyses." *MSF / MSF ERB*

Question 16

How could a more coherent approach to the complex relationships between research and other essential services in a global health emergency be developed, so that front-line workers are supported by ethical guidance that reflects the realities they face?

Respondents concentrated predominantly on the second part of this question, focusing on how front-line workers are supported by ethical guidance that reflects the realities they face. Some respondents also provided general comments on the framing of the question, including MSF / MSF ERB:

> "this question is not only about research ethics, but also about medical ethics and at the interface of both."

Development of guidelines

Some respondents commented on how guidelines might support front-line workers with the realities they face.

> "[Context] and population relevant *guidelines* need to be developed for them to refer to." *Jihad Makhoul*

> "I would think a handbook of real-life case studies used for local training might be useful." *Ann H. Kelly*

> "There is the need for specific guidelines to be developed and adhered to that will guide public health workers on how to conduct surveillance or research in the context of emergencies. They must also be aware of such guidelines." *Dr Rosmond Adams, CARPHA*

> "Guidelines should be developed with all stakeholders being involved, preferably involving persons who have experience working in the front line in emergencies. Guidelines should list out the essential services and obligations of service which have to be met before research can be allowed, or how the two can be combined with compromising services." *Dr Anuradha Rose*

Training and capacity building

Respondents also suggested that training may have a role to play in supporting front-line workers.

> "Frontline workers should be trained and be briefed about their fiduciary duty and be given written guidelines. Very often in emergencies, frontline workers will have to play a dual role due to resource constraints, time constraints and logical reasons in emergencies." *Dr Anuradha Rose*

> "the question is not just about teaching people about the rules – it's about equipping people with the tools they need to make good decisions." *Jantina de Vries*

> "[An] approach that aims to support frontline workers involves *building their skills* in working with populations affected by humanitarian disasters". *Jihad Makhoul*

The importance of including ethics in training programmes was also highlighted.

> "Ethical guidance is one thing, but people on the front lines may not be easily able to get their hands on guidelines or advisors. They may only have their own consciences, and that means they will need to have been prepared for the dilemmas. This requires training is dealing with ethical dilemmas, and being given ethical decision-making tools and skills." *Dónal O'Mathúna, PhD*

> "Workers in emergency settings need more ethical guidance than workers in one domestic setting without time pressures and life and death decisions. However, such guidance cannot be formulaic. It may benefit from a values approach. The values of fairness, respect, care and honesty have recently been promoted through a code of conduct for research in resource poor settings, which is now compulsory for EU funding." *Anonymous respondent*

> "[There] is a huge need of a better integration of ethics training into response manuals, and top down and bottom up support". *MSF / MSF ERB*

> "… facilitate local input towards modifications on the way, and integrate ethics in training modules/programs for all stakeholders/front line workers." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

> "Having an ethicist or a trained ethical advisor in the team is also very helpful, albeit ideal, for referring to." *Jihad Makhoul*

The same respondent added:

> "Recent research has indicated that very few organizations working in global health crises have codes of ethical conduct for their workers to follow or refer to. Where available, they are described as generally contextually inappropriate or unclear or hard to understand. The staff reported they are not all fluent in the language and the practice of research ethics, and in many organizations, there is no monitoring or continuing education/training for those who join for short term employment or as volunteers."

A forum for discussion

Several respondents suggested that a forum for discussion would support front-line workers.

> "Engage with/initiate "community advisory boards/groups" as ongoing partners in public health and research at baseline who can become target contacts and focal points in emergencies for research, data collection and community engagement." *Anonymous respondent*

> "I think more open and honest discussions about the issues would be a big help, with those who have more experience within this sphere sharing

with others about what they have faced and how they have addressed them […] Real-time help may also be useful, where someone could try to get guidance from someone more experienced, or ideally have a mentor available to them. If this is not available, then a mechanism for debriefing afterwards would be crucial to all lessons to be learned from what happened in the field." *Dónal O'Mathúna, PhD*

"I think the main problem is getting an inclusive forum for all stakeholders in the first place." *Anonymous respondent*

"The organizations need to hold regular briefing or discussion sessions with frontline workers about the challenges they face and provide guidance on how to resolve issues and how to protect themselves from being affected emotionally or physically in humanitarian crises." *Jihad Makhoul*

"creating opportunities to discuss and debate concerns as they arise. This might mean more resources devoted to ethical training and social engagement and more clearly articulated expectations placed on researchers by the funders that these processes are in place." *Ann H. Kelly*

Planning / background research

Respondents also highlighted the contribution of effective planning / background research for a more coherent response.

"Discuss and agree on principles and needs beforehand (eg when evaluating the previous GHE), acknowledge challenges, and jointly identify possible solutions to those". *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

"Having a sufficiently nuanced understanding [of] the relationships in the first place is key, and at the moment I'm not sure that we have this." *Annette Rid*

Collaboration

A suggestion was also made that collaboration could contribute to a more coherent approach.

"Close collaboration between researchers and humanitarian service providers is important throughout the process. Integrating research into the humanitarian response is one strategy for improving these relationships between research and services." *Anonymous respondent*

Question 17

In the alternative, do you think that there are ethical justifications for maintaining clear distinctions between the activities of 'research', 'health care' and 'public health interventions' in a global health emergency? If so, what are they?

There are ethical justifications for maintaining clear distinctions

To ensure transparency and clarity

A number of respondents referenced a justification of ensuring transparency and clarity.

> "[A] distinction is practically important for transparency and accountability. Research in emergencies will be higher risk than usual research, therefore it is crucial that participants do not confuse this with clinical care or public health and know that options exist to opt out if possible, require fully informed consent etc…stakes are higher for the participants and the researchers both for benefit and risk and therefore research must be clear." *Anonymous respondent*

> "The main justification for me is the clear understanding of the participant of which aspect they are engaged in, of roles, responsibilities, expectations, and consequences." *Anonymous respondent*

> "In cases where there is overlap between research, health care and public health is it important to clarify that the three can have different aims, and loyalties. If patients are the focus of health care, greater good orientations are the focus of research and public health. Establishing competing goals and interests can help identify where vulnerabilities can emerge and how they can be managed. It can help by simply asking "what are the goals of this intervention?" then "who could get hurt, and how are we going to mitigate that harm?" *MSF / MSF ERB*

Risk of unethical research; undermining voluntariness

The suggestion that a lack of distinction could lead to unethical research and undermine voluntariness was highlighted in the following responses:

> "If this does not happen we can have unethical research being classified as public health interventions. This can undermine the trust of public health workers and make the work of public health personnel more difficult especially in the emergency setting when they may need access to sensitive information." *Dr Rosmond Adams, CARPHA*

> "Distinction needs to be maintained, in my view. Research needs to be entirely voluntary in all situations. The other two not necessarily." *Anonymous respondent*

Voluntariness was also highlighted by Jihad Makhoul to illustrate an argument that the distinctions between the three types of activity are *not* the 'issue of concern' here (see further views on this question from this respondent below).

> "researchers, healthcare providers and other workers, need to be aware of their possible undue influence to voluntary consent by the population in question to participate in and contribute to these activities, especially in resource scarce settings and especially if they represent influential agencies. The influence of powerful risk of therapeutic misconception also increases with increased deprivation and consequent vulnerabilities. These risks and others need to be taken into consideration and a plan to

> address them developed. So the distinctions among the three types of work are not the issue of concern as much as the potential influence of the workers and the work itself in a global emergency."

In order to prioritise activities

An argument was also put forward in relation to the prioritisation of activities in a GHE.

> "A distinction between research and health care is justified because in an emergency situation, health care should have priority over research. So a clear distinction of which activities are towards health care and which activities are for research only will help the front line workers to prioritise delivery of services. Similarly, public health interventions aimed at mitigating the emergency should be given priority over research." *Dr Anuradha Rose*

In the interests of the local population

The interests of the local population were highlighted as a justification for maintaining distinctions in a response from Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé.

> "Yes, to ensure that the interests of the local population and patients affected are well represented, as much of the global research community ((collaborative) commercial and non-commercial research groups / NGO / donors…) is driven by 'publish or perish' and the need to be visible, rather than to be serving."

A related point was raised by an anonymous respondent:

> "As researchers sometimes, it feels unethical not to support government officials with information, which might assist them in designing public health interventions given that we have data they do not. However, there should be a distinction."

There are no ethical justifications for maintaining clear distinctions

One anonymous respondent stated:

> "Not really. There's ethical behavior. Research and clinical practice are inextricably intertwined (including often being undertaken by the same people), so why should the ethics of them be separate? The ethics of global catastrophe may be different in some ways to the ethics of a single patient's management in front of you but they need to make up a coherent whole. Otherwise there will always be conflicts at the boundary points and areas that are "too difficult' or not exciting enough to discuss. Those will then, in my experience, be exactly the areas that cause problems when the real situation develops."

Other points

Criticisms of 'distinctions'

Several respondents criticised the focus on distinctions in this context.

> "[In] practice such a distinction is not always possible." *Anonymous respondent*

> "I am not sure that the distinctions themselves are particularly useful – I think perhaps that the differences to keep in mind are that some interventions prioritise the immediate patient, some the wider immediately at-risk community, and some distant/future humanity." *Bridget Haire*

> "From a professional perspective, the activities of researchers, healthcare providers and public health workers are different and are governed or guided by different codes of practice. However, in reality, the boundaries become blurred because of the multiple roles each of them could have and which may overlap at different moments in time during and/or after the emergency." *Jihad Makhoul*

Questions 18–21: obligations to / expectations of front-line research staff

Question 18

Do the exigencies of global health emergencies (for example levels of risk, security requirements, extremity of humanitarian need, rapidity of response) change the obligations on, and expectations of, front-line research staff in any way?

Several comments on the effects of demands of GHEs on the obligations and expectations of front-line research staff were received in response to this question. One anonymous respondent, however, questioned the concept of 'front-line research staff':

> "Not sure about the concept of "front-line research staff" – they may be staff on the frontline that will contribute, participate, lead research – at least for infectious disease they are likely to intervene within an existing framework, structure and so on."

No, they don't change obligations and expectations

Several respondents indicated that the obligations of front-line workers and researchers should not change due to the demands of GHEs.

> "The obligations of the front line staff towards the participants should not change due to an emergency situation. But the expectations placed on them should be considerate of the fact that many of them may be from the affected community itself." *Dr Anuradha Rose*

> "The ASC would expect front-line researchers using animals to seek to apply the same ethical standards as in any other type of animal research." *Animals in Science Committee*

> "Frontline research staff face many serious risks and deserve protections, but their relationship to participants (who may be extremely vulnerable) should not necessarily change." *Humanitarian Health Ethics Research Group*

> "Expectations of ethical conduct for all activities should remain the same". *Anonymous respondent*

> "The ultimate obligations will not change, but there needs to be a greater appreciation of the challenges and difficulties that front-line staff face. Intentional violation of ethical standards, and sloppiness, should not be accepted. But the pressures faced by researchers, and the lack of resources they work with, must be taken into account when reviewing activities. The ideal remains the same, but when the circumstances are far less than ideal, this has to be taken into account." *Dónal O'Mathúna, PhD*

Yes, they change obligations and expectations

Other respondents indicated that the demands of GHEs do change the obligations and expectations attached to front-line research staff, to a greater or lesser extent.

> "Yes. For example in SS [South Sudan], tribe plays a big factor. The most competent research assistant cannot work in an area where his tribe is not welcomed. Insecurity and poverty levels make the situation worse. In sudden outbreaks of violence, research takes a backseat as emergency treatment, nutrition; mothers and children become a priority." *Anonymous respondent*

> "Front-liners are, on the face of it, partly or wholly responsible for subject enrolment. They can identify, approach and recruit. In emergencies it's plausible they can be pressured into recruiting for the research when against the interests of individual subjects. This is particularly so if their role is measured as successful only by how many people they recruit, not the process/manner of recruitment, or other targets." *Katherine Sahan*

> "Practical obligations change – more multitasking, more stress (work and personal), less support, more chaos". *Anonymous respondent*

> "Yes: populations are more vulnerable, so more restraint needed. Front-line researchers are under more pressure, so more mistakes and more scrutiny, both from people suffering and from people on the sidelines. Not always easy to turn this into something positive, so should be anticipated and understood by front-line staff and policy makers in particular, also to ensure this is never a trigger or excuse for not being more responsive to local needs compared to 'normal' situations due to increased vulnerability." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

> "Yes, I think front line staff carry a greater burden and risk when these situations arise, but personally feel that they have dined out on their role in society as a physician for years; abrogating it when the people need you most is just wrong. But again, that viewpoint needs to be challenged by the staff representing other groups with other cultural perspectives. BEFORE we ask them all to respond to the next major health emergency." *Anonymous respondent*

> "Most likely they will depend on the environment where the research is being conducted e.g. in war-torn settings, militarized or autocratic

countries local researchers often are forced to publish research findings that suite the interests of regimes." *Dr Joseph Kimuli Balikuddembe*

"In an extremity of humanitarian need, care needs and public health take precedence over research. I would argue that it might be reasonable for research staff with clinical capacity to provide care rather than conduct research." *Bridget Haire*

"Not fundamentally, although specific obligations may differ given the emergency context. For example, obligations to reasonably reduce risks and compensate for harms always exist, but higher levels of risk might be acceptable when the social value of the research is significant in a public health context." *Annette Rid*

Other observations

Further observations in response to this question included:

"I have been in post hurricane response doing assessments and the population always expects some aid from the assessment team even though there may be another group of persons doing aid distribution. Balancing the two is a very difficult task." *Dr Rosmond Adams*

"[It is] important to remember that frontline staff are people too, with families – we should not require 'heroic' action of them." *Anonymous respondent*

"In health emergencies, researchers are humans with means to support others. If they have to weigh up between saving lives and doing research, it has to be the former." *Anonymous respondent*

Question 19

What constitutes fair treatment of both local and expatriate front-line research staff, and who is responsible for ensuring that they receive such treatment? Can differential treatment ever be justified?

Constituent elements of fair treatment

Parity of treatment, care, and value ascribed to staff

Several respondents suggested that the treatment, care, and value ascribed to both local and expatriate staff should be in parity.

"It is absolutely essential that both receive the best possible care, and that any sub-standard care or treatment of local staff is ethically unjustifiable. If anything, local staff are far more valuable than expatriate staff in the long term – in a country with a scarcity of doctors, nurses and the like". *Jantina de Vries*

"Whether local or expatriate researcher, it is important that both have equal access and rights for conducting research". *Dr Joseph Kimuli Balikuddembe*

> "All must be treated similar. There must not be any distinction in how expats of locals are treated." *Dr Rosmond Adams, CARPHA*

> "A further point of inequity arises in terms of access to novel interventions after medical evacuation: those evacuated had all possible interventions thrown at them, without the claimed need to be part of an RCT." *Dr Cathy Roth*

> "There are ethical – and logistical – issues with providing any form of differential care, whether that be differentiating between international and local staff, HCW and researcher, HCW and other members of the affected community. This is an area where negotiation needs to happen to both provide protection for workers and to ensure that this protection doesn't divert resources, and where possible amplifies them. Where international governments provide directed care for their staff, there must be a reciprocal obligation to also contribute resources for the other affected community." *Bridget Haire*

> "On the front-line no differentiation would be ethical. The main difference will be that expatriate staff have the possibility to leave, e.g. be flown out to hospitals, which local staff will not have." *Anonymous respondent*

> "What is probably more important is that tasks and responsibilities are clearly defined between different partners and that everyone feels integrated and well accepted in the team. This should be guaranteed by the coordinating team." *Anonymous respondent*

In a related point on fairness, a further respondent suggested:

> "Differences between expatriate and local staff are almost unavoidable and inherent in international collaborations. The challenge is in ensuring that this does not result in unfairness." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

Remuneration and other work benefits

A number of respondents highlighted the disparity between ex-patriate and local staff in regards to remuneration and other work benefits.

> "Equal chance and opportunity is needed by mutual trust and respect irrespectively of rank and position, caring listening and compassionate, shared values and open communication as well as same/equivalent incentive in compensation and risk taking in emergency. However expatriate got 10times the salary of the local staff in frontline so how do you expect equal commitment and chance/equity." *Ernest Tambo*

- "Provision of compensation commensurate with the rigors of frontline staff's work. (E.g. during the EVD crisis, many frontline staff had to live away from their families and communities)." *Humanitarian Health Ethics Research Group*

> "All front line workers should be offered/promised the same treatment (including pay)." *Anonymous respondent*

> "There is certainly, and will always be, different treatment of local and expatriate staff, starting with pay scales and benefits. There are other

examples which raise ethical concerns, for example evacuation from war zones. All organizations working in emergencies provide for evacuation, if necessary out of the country, for expatriate staff and their families in the event of deteriorating conditions, sometimes to their home countries. But what about local staff? In the UN system, they can be evacuated to 'safe areas' within the country, but how safe?" *William Aldis*

"the expatriate receives far higher absolute sums, compared to the local researcher. The issue is, for a researcher not exposed to both settings, the variations could be alarming – if the researchers do not live in the same setting, for instance UK and Uganda. But the bottom line should be equitable treatment. If both researchers are living in the same settings and doing the same work, why should there be a big gap between their salaries?" *Anonymous respondent*

"… people with the same qualifications and/or expertise should be given equal remuneration, opportunities, privileges and treatment if they are involved in the same kind of work." *ECEPAS GET*

"If people are employed by different organizations and come from different countries, I think it's difficult to avoid differences in conditions (of e.g. payment, local accommodation, etc)." *Anonymous respondent*

The role of funders, leads, and PIs

The role of funders, leads, and PIs in contributing to fair treatment of local and expatriate front-line research staff was also identified as a key point by respondents.

"The PI of the research grant should ensure fair treatment of all front line staff. Fair treatment will entail making sure differences in treatment are only based on need- for example, immunized vs unimmunized staff, degree of exposure to risk- rather than on local or expatriate, gender or any other unfair bias." *Dr Anuradha Rose*

"Whoever hires the staff is responsible […] Differential treatment is a problem, especially when it comes to med-evac for international staff but not national staff. In these cases, national staff must be provided with a high level of care in country, paid for by the lead partner." *Gillian McKay*

"For the case of professional expatriates like myself, it is my duty to give fair treatment. For example, my research assistants may not have a very good understanding of research but they can speak the local language. I have to go the extra mile and teach them additional research skills, time off to focus on their education as well as provide small loans to help their families." *Anonymous respondent*

"All stakeholders and role players, including research funders/donors, research institutions and each individual researcher have a responsibility to promote fairness in research. For example, donors can set aside a moderate budget in every grant award for research, ringfenced for capacity development, skill transfer, facility development and affair and equitable distribution of benefits that accrue from research." *ECEPAS, GET*

> "International agencies are key to ensuring that front-line research staff receive the support they deserve, but again, commitment and oversight is needed from national bodies, capable of holding researchers and companies to account if standards are not upheld." *Ann H. Kelly*

> "… most of the donors of such work find ways of sub-contracting, so that they are not directly responsible for the well-being of the staff." *Tim Allen*

> "[The] care and training that expatriates receive should be extended to local staff, and this cost should be covered by the international organizations or donors." *Jantina de Vries*

Transparency

Transparency was also identified as a constituent element of fair treatment.

> "research institutions and individual researchers should endeavour to be transparent". *ECEPAS GET*

> "All frontline researchers deserve to be properly informed of the details of the research, reasons for it, reasons for the design etc. before they are required to implement a protocol. This will help them understand how and why it impacts on patient treatment and gives them an opportunity to ask questions that can improve the study pragmatically." *MSF / MSF ERB*

Can differential treatment be justified?

A small number of respondents engaged directly with this question, raising several distinct points.

> "expats may come with more resources but the way in which they are treated must not be different." *Dr Rosmond Adams, CARPHA*

> "The obvious candidate for justifying differential treatment are arguments from utility—for example, that repatriation and best possible care for expatriate staff are necessary for recruiting skilled professionals essential for addressing a given global health emergency. I'm no consequentialist, but I would give these arguments some weight if there is a serious health threat to vast numbers of people and external assistance was absolutely essential at a large scale. But I'm not sure how many global health emergencies share these features". *Annette Rid*

> "It could be argued that foreign staff are taking more risk, having actively come to the emergency situation, and therefore may be entitled to different care e.g. repatriation in case of illness that cannot be cared for locally (highest achievable state of health in country of origin). This security may motivate knowledgeable people to go to emergency areas where they have a high impact. However if limited supplies of a specific curative medication is available locally it may not be just to reserve these stocks for expats? (even if one accepts increased risk taken by expats)." *Anonymous respondent*

> "Expatriation of local staff for better life-saving care outside could be justified as they are also putting themselves at risk in working with infected persons etc. This would be equitable care with that given to

expats who get expatriated. However, if this is dependent on which agency the local staff work for (MOH vs. NGO), which may have different approaches or capacity to achieve this, this creates significant inequity among the health care workers. Also, to what grade of local staff would this apply? This may create inequities within local staff at different grades." *Anonymous respondent*

Other observations

Other observations provided by respondents who answered this question included:

> "[In] some instances local capacity is there and there is no need for deploying international researchers. Yet we find that sometimes international and humanitarian groups bring in internationals, set up shop, hire international and local staff and conduct research and interventions themselves. The question is what for? And why not work with already existing local groups, if they are there and active in interventions and research?" *Professor Rita Giacaman*

> "Unfair partnerships, disproportionate power for decision making, institutions having a competitive advantage to compete for funding over others and any power imbalance in the control of resources, data sharing, authorship, acknowledgement and the goals and terms of partnership create an inequitable ecosystem for research." *ECEPAS, GET*

> "Expat workers are not 'honorary nationals' and if they are employed in emergencies under the aegis of major international organisations, they have a legitimate expectation that their safety will be protected to the extent possible (e.g., appropriate security provision). However, it is a matter of concern that some such staff (particularly more junior ones) appear to believe that they would not be deployed 'unless it was safe' – they may have an unrealistic assessment of the risks from which they cannot in practice be protected." *Dr Cathy Roth*

> "Differential treatment is unpleasant, but given that whatever ethical guidelines we use have to operate in the real world, it is likely to remain the case. I think there is a case for differential treatment for healthcare workers who will then go back in to the fight…" *Anonymous respondent*

Question 20

What mechanisms are there, or should there be, to help ensure that obligations to front-line research staff are honoured?

Several mechanisms were identified by respondents.

Using formal documentation / processes

> "These mechanisms should be written into the work health and safety protocol under which people are employed, and a reasonably safe workplace should be part of the standard." *Bridget Haire*

"written documents of obligations and signing of contracts" *Dr Anuradha Rose*

"Auditing by the funder and/or by the project lead to ensure all these things are in place. Audits should include interviews with all levels of staff free from fear of firing if they complain." *Gillian McKay*

"Perhaps the IRBs/ECs should look at these aspects when they evaluate the initial protocols and the periodic reports." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

Effective forward-planning

"There must be clear rules guiding the research process. A very good communication strategy or plan must exist to avoid conflict with researchers and other front-line staff. The justification and rationale of the research must be clear." *Dr Rosmond Adams, CARPHA*

"consideration should be paid before the start of research as to what support and resources these researchers will have access to once research ends; for instance, are there provisions in place for further training? Have there been arrangements between government bodies and research organizations as to opportunities for future work?" *Ann H. Kelly*

Making resources available

"Resources should be made available to support research staff including contingency planning for when research concludes." *Ann H. Kelly*

"I could imagine particular incentives such as ongoing training and capacity building (that starts before outbreak and goes beyond the end and includes for example subscription to Master or PhD programs; personal mentoring), responsibility sharing, bonus payment; paid leave after the end of the emergency, etc)." *Anonymous respondent*

Agreement on future publications

"Honouring front-line research staff roles should enable them to benefit from the publications and career advancement that international researchers receive. Easing follow up and continued communication and collaboration is essential for this." *MSF / MSF ERB*

Effective in-country leadership

"I think this is where genuine leadership by people from the countries who are affected becomes key. It is those kinds of leaders who can detect double standards and question international organizations about them at the highest levels." *Jantina de Vries*

Onerous consequences of not honouring front-line research staff

"Name and shame? But with what consequences? First, research staff should be made aware of their rights. Obligations should be made public,

part of the standard research procedures." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

Other mechanisms were suggested in brief by respondents, including:

- health insurance for frontline staff
- having a rapid process in places to rectify errors
- using health and safety requirements as a vehicle to ensure obligations are honoured
- effective logistics, including transport, money, translation services, and IT support
- employing 'staff wellness' practitioners via human resources mechanisms
- considering if RECs can consider obligations when considering research protocols
- news and social media advocacy

Question 21

What ethical responsibilities do front-line research staff in emergencies themselves hold?

A wide range of ethical responsibilities were suggested.

To act with compassion

"To show empathy and understanding to the affected group.
To be understanding of the situation.
In the event they are offering care, to offer care as a priority and then research." *Dr Rosmond Adams, CARPHA*

"responsibility to place well-being of persons before research needs." *Dr Anuradha Rose*

To carry out effective research

"they hold responsibility for doing their research role effectively and responsibility for treating research subjects appropriately. However, within this there are some complex questions about who they are in relation to the subject, and what professional or other relationships are set up, even in the time-poor setting of the emergency." *Katherine Sahan*

"To get the answers that matter to the affected population as quickly as possible, as accurately as possible, and with as little waste, inequity and use of e.g. suboptimal consent as possible." *Anonymous respondent*

"We also encourage them to utilize their informal networks and alert researchers on any rumours in the community that might affect participation in research." *Anonymous respondent*

"I think ethical conduct stipulates that researchers would make sure to investigate an issue which has not been investigated previously, ensure that design and method and relevant to the research questions, and ensure that data analysis and interpretation are sound […] Of course, in

> an emergency one needs to act fast. This is why quick rapid appraisals, but then ethically, researchers must commit to further, more in depth and longer term research precisely because rapid appraisals allow for immediate action, but are far from complete if one is to eventually provide for need but at the same time think of longer term objectives." *Professor Rita Giacaman*

To carry out research in accordance within established standards

On a related theme, Dr Anuradha Rose suggests the following responsibilities:

- "responsibility to place well-being of persons before research needs
- responsibility to maintain confidentiality and privacy especially in sensitive issues
- responsibility to report important health issues or emergency issues to the health care providers or the research managers
- responsibility to impart information to mitigate harms due to the emergency
- responsibility to protect their own health and safety, and that of their colleagues"

Other respondents also indicate that established standards are key to this question:

> "To adhere to their standard operating procedures. If this is impossible, they need to be redefined – or whether or not the research is feasible should be reconsidered." *Bridget Haire*

> "The ASC would expect front-line researchers using animals to seek to apply the same ethical standards as in any other type of animal research." *The Animals in Science Committee*

The issue of abuse by front-line workers is noted by Professor Robin Gill

> "'[The] risks of abusive behaviour by those on the front-line' only gets a single sentence in your project outline […] it is obviously vital for a discussion of professional standards".

To seek advice if needed

> "To conduct themselves ethically. To not think that just because it's an emergency that shortcuts can be taken. To care for themselves and consider how the emergency will impact on them personally and to be aware that sometimes the best thing to do is to say "I need help" and to take a break." *Gillian McKay*

Similarly, an anonymous respondent stated that they should have "awareness of their own capacity to function effectively" and, in addition, "[awareness] of colleagues' capacity to function effectively."

Collecting and sharing information

> "To collect information as soon as possible." *Dr Rosmond Adams, CARPHA*

> "They also are privy often to information that can be helpful to more macro responses (and this may also blur the relationships between research, public health, health services, etc), and have responsibility to share that in a timely manner with appropriate agencies." *Anonymous respondent*

> "if treatment and research are both present, the ability to make triage assessments and to explain all activities that have no personal benefit, only future benefit." *Anonymous respondent*

Their responsibilities are no different from other research workers

A number of responses indicated, however, that responsibilities for front-line research staff are 'no different' to other research workers.

> "They have all the same ethical responsibilities as any other researcher. However, the extremely difficult circumstances in which they work have to be taken into account in how these obligations are addressed." *Dónal O'Mathúna, PhD*

> "Since they are part of the research team, I would generally think that their ethical responsibilities differ little from other members of the team. One additional responsibility, particularly in the case of front-line workers during an epidemic, would be to ensure liaison with public health teams insofar when they gain relevant insights for surveillance." Annette Rid

> "Front line workers have the same ethical responsibilities as any working in research, except that their responsibility may be heightened (particularly when they are local) as a result of a sense of trust they are imbued with by the local population, and a sense of solidarity/belonging/identification with the affected population." *Anonymous respondent*

> "I would believe these are the same as those involved in any medical research in situations with compromised health infrastructure." *Ann H. Kelly*

> "In principle, they are the same as in any research." *MSF / MSF ERB*

Questions 22–26: what are the challenges of effective collaboration in global health emergencies?

Question 22

Can you provide examples of where collaboration has worked well in enabling valuable research to take place in global health emergencies? What were the key success factors?

Collaborative examples provided by respondents included:

- The 2015 Ebola outbreak
- Zika virus outbreak response

- Polio immunisation response (for example in Africa)
- The response to the Fukushima power plant emergency

Key success factors

To accompany these example of collaboration, a range of success factors were highlighted, including this account from ECEPAS GET on work undertaken during the Ebola outbreak in West Africa:

> "Key success factors were/are: strong leadership, effective communications & logistics planning, team of African consultants who knew the terrain and cultures/customs, strong community engagement, building and harnessing the survivor network, including a humanitarian approach in addition to clinical research by partnering with World Food Program and other governmental and non-profit organizations."

Another respondent also highlighted from West Africa:

> "… the situation in Sierra Leone in early 2000s, when 60% of the country was controlled by an extremely violent rebel group, the Revolutionary United Front (RUF). Although collaboration was primarily in emergency response operations, there was also joint research and sharing of findings; for example, research into the epidemiology of Lassa fever (a haemorrhagic fever virus with high lethality, related to Ebola) in contested areas." *William Aldis*

Meaningful cooperation / collaboration

Respondents indicated that cooperation and collaboration between stakeholders could be a key factor for success.

> "Strong internal communication mechanisms within research teams that make it possible for people on the front lines of research to inform aspects of research design". *Humanitarian Health Ethics Research Group*

> "NGOs and research institutions worked closely together during Ebola, NGOs had the treatment centres, and the research bodies had the new drugs. There were some challenges as NGOs (or mine at least) was not used to doing this level of clinical research and so needed to be walked through the process, but it did work out in the end. Key successes included the reputation of the research institution, a clear working group with ToR to manage the process, and a willingness for the research institution to hire their own staff to conduct the treatment programme so as not to impede day to day operation of the treatment centre." *Gillian McKay*

> "There must be understanding of all groups concerned, researchers, pharmaceuticals, home country. However, this must be guided by someone with power and authority like the WHO who will provide independent monitoring and guidance." *Dr Rosmond Adams, CARPHA*

Highlighting the role of the military during the Ebola outbreak in Sierra Leone, one anonymous respondent stated:

> "The military were able to facilitate and access some of the research going on in Sierra Leone which was a definite positive. Unfortunately as the networks were forming on the hoof, these collaborative efforts happened very late in the outbreak after various contacts were formed and preconceptions/biases were overcome. Pre-agreement would have been far more effective. This is not just about research, this is about the entire response, but the problems are the same."

Consideration of local knowledge and priorities

In this category, Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé also highlighted the importance of "strong local leadership". Other comments included:

> "Collaboration works well when local priorities are taken into account, and there is technical input by technical people based in the research settings. Many studies in Uganda presently have local as well as foreign collaborators. As long as power relations are minimized, it is possible to even integrate more useful objectives in the study – and leave out others." *Anonymous respondent*

> "Recognition and support of investigative capacities and empirical concerns of local investigators". *Ann H. Kelly*

Effective use of technology

The use of technology in collaborative examples was also noted by respondents.

> "Good internet [is] critical. Using teams who already know each other is very helpful. A Skype-based Ebola vaccine DSMB [data and safety and monitoring board] worked very well." *Professor Stephen Gordon*

On data-sharing more generally, Ann H. Kelly suggested:

> "Provision in place for data-sharing but also collaborative data-use, whether in the form of future publications or future research grants – or in other words, a thoroughly going commitment to the collaborative afterlife of research".

Question 23

Can you give any practical examples of ways in which ethical concerns have impeded successful collaboration in research? What would have helped resolve them?

Practical examples

A range of practical examples were offered by respondents.

> "Lack of a data sharing agreement prevented analysis of blood test results and outcomes between two facilities on the same site. That is just insane. Another collaboration was halted as it was felt that one site might be seen in a bad light in comparison with the centres. The current system

allows ego to get in the way of the benefit the research should bring. Researchers who are worried about the intellectual property of their research over the importance of their results for patients are being twisted by a system where their research exclusivity is what guarantees their funding. A coherent research agenda a priori adapted to the situation and with all stakeholders involved up front might mitigate against this sort of territorial competition." *Anonymous respondent*

"Sometimes we were not allowed to share previously analyzed data with other research groups or the wider public (restriction by the Ministry of Health or funders). This may limit future collaborations." *Anonymous respondent*

"We received a proposal to 'partner' on a project looking at stress levels of Palestinian refugee parents (using some biomarker) as it was related to their treatment of their children. We shared our concern that the implication of that research would be at the individual level, and potentially victim blame these parents. We were not against the use of biomarkers of stress, but felt it was critical to also expand the scope of possible determinants to capture social and political determinants so that the crux of the issue might be highlighted, and solution proposed at that level. Our concerns were not acknowledged, and we refused to 'partner' on principle that a continued attention to blaming the victim is unethical." *Anonymous respondent*

"Ethical concerns are also present in the relationship between academic partners. Our institution was approached several times to ''partner' with academic institutions in the US on projects they were undertaking with refugees residing in Lebanon. Many times, their objectives, protocols, and method were already developed and decided on, they were not open to feedback, did not really seem to acknowledge context, and it often seemed as if they only reached out because (1) they needed a local IRB, (2) they needed language translation. We refused to partner in these situations as they are at their base unequal partnerships that continue the legacy of colonialism and oppression, and enhance differential power." *Anonymous respondent*

"Consider looking at experiences with Indonesia and sample sharing following the suspension of sharing samples of H5N1." *Anonymous respondent*

Other shorter factors listed by respondents included:

- Possible delay due to ethical review process
- Various review committees expressing different views on the same project
- Funders inhibiting collaboration

Non-specific examples of where research might be impeded were also provided.

"Outside of the GHE context, but probably equally relevant to them: the somewhat lazy assumption of moral and intellectual superiority on behalf of researchers, universities and organizations based in Higher Income Countries vs those based in Lower Income Countries." *Jantina de Vries*

> "Personal greed or gain perhaps. The Oxfam paradox and the self-interest of paedophiles? Possibly also personal beliefs e.g. religious?" *David B. Morton*

- "Research where the objectives are more towards academic interests and impact of publication and not as much focused on improving treatment outcomes or mitigation of the emergency are unethical and can prevent local researchers from co-operating.
- When the benefits are largely skewed towards the researchers and overseas collaborators, with very little benefit for the local researchers and population
- When data or samples are being taken out of the country with no clear descriptions of how they will be used
- Inadequate post trial provisions for the participating community". *Dr Anuradha Rose*

Ann H. Kelly noted, however, how research might go ahead *despite* ethical concerns.

> "To some extent, ethical clearance given to studies in West Africa masked the problem of a limit of scarce resources. In Sierra Leone, for instance, a number of research studies were approved based on rigorous international ethical review, however the question of which studies to prioritize was not adequately raised. The situation created a competitive environment, leading to some ethically questionable practices around access to patients."

What would have helped to resolve issues?

Indications as to what might have helped to resolve issues included:

> "The local research team should be involved from the beginning of the planning of the research. There should be transparency in the planning process and the objectives." *Dr Anuradha Rose*

> "What would have helped was more timely community consultation and greater scope from institutions to respond to issues raised." *Bridget Haire, Kirby Institute, UNSW Sydney, Australia*

> [Re. example from Lebanon above] "What would have helped resolve them is a partnership that is based on the principles of equitable partnership, acknowledging strengths of both institutions, and co-creating a proposal. There is often an assumption of the need for one-way 'capacity building' – north to south, whereas in fact it is a two-way capacity building or learning that is needed." *Anonymous respondent*

Criticism of the question

One respondent criticised the framing of this question, stating:

> "we note that the question would have been more complete, if it had also been asked if there are examples of unethical research that was/could have been prevented by ethics concerns, or that could have been prevented by a (more rigorous) ethical review." *MSF / MSF ERB*

Question 24

Can there be said to be an ethical obligation to work collaboratively rather than competitively in the context of global health emergencies? What might such an obligation entail and what are its limits?

Yes, there can be said to be an ethical obligation to work collaboratively

Views that answered the first part of this question in the affirmative included:

> "I strongly believe that it is an ethical obligation to work collaboratively rather than competitively in the context of global health emergencies based on mutual respect and trust, research collaboration for (south-south, North-south) for co-working in development and implementation. Moreover [it is important to foster] co-funding and co-production partnership, articulated shared benefits based information / data sharing for all, all-inclusiveness". *Ernest Tambo*

> "Global health emergencies are characterized by a lack of resources and of infrastructures. By sharing limited resources, the involved actors should reasonably reach better and faster results by pooling their efforts. Collaboration should therefore be the guiding rule considered, and it is likely to be more fruitful than competition in such circumstances." *REACTing-Inserm*

> "Hell yes. It is limited by the practical constraints of the current system and their potential impact on researchers' livelihoods so should not be underplayed, but a grown-up system should aspire to address these issues. If grant awarding bodies were to strongly support collaboration and if academic institutions were to accept contribution as sign of output rather than just money won and papers authored then the rests should follow." *Anonymous respondent*

> "Yes, collaboration is a key success to responding and containing global emergencies. Worth example is the multi agencies and countries which were involved in the response that led to winning of the battle against 2014 West Africa Ebola epidemic." *Dr Joseph Kimuli Balikuddembe*

> "Yes, in a context of limited resources, competition is detrimental to health and wellbeing of populations. Research based on competition in these contexts can be harmful in a variety of ways (including duplication of effort), and decrease trust." *Anonymous respondent*

> "I would think so, and not just in emergencies. Insofar as collaboration avoids redundancy of efforts and promotes learning and timely research outcomes, it should be part of the norms for researchers. The obvious counter-argument is that competition fosters innovation, but I'm not sure, at least in global health emergencies with a limited window of opportunity for research, how strong this argument is." *Annette Rid*

> "[There is an] obligation to cooperate and maximize benefit, utility and efficiency / share research resources, collect data/samples

simultaneously, share ideas, findings, build on each other's progress, share dangers and harms early etc." *Anonymous respondent*

"I think this obligation exists in all research because there are limited resources available for research. In a GHE, however, there is the added burden of the urgency of trying to find successful solutions. If two research teams are competing with one another when they could work together and find a better solution sooner, then the ethical obligation to benefit participants should take priority over the competition. I know that sometimes competition is good to bring the best out of everyone, but in an emergency, collaboration and benefit much take priority." *Dónal O'Mathúna, PhD*

"A moral duty to collaborate rather than compete is a prima facie obligation." *MSF / MSF ERB*

"Absolutely. Unless the main research aim is not saving lives – or finding innovative solutions for a particular problem. Why for instance should there be over 10 vaccines trials in one micro setting? These resources could be pooled together, and donors have a moral responsibility to ensure that this happens in the near future." *Anonymous respondent*

"for a successful emergency response collaboration is key." *Anonymous respondent*

There may be an ethical obligation to work collaboratively

A response that there 'may be' an obligation to work collaboratively included:

"I am not sure because you cannot force collaboration. Collaboration resets on the idea that partners would have the same approach, inclinations, values etc. I think it good to encourage collaboration should groups have these in common and are willing." *Professor Rita Giacaman*

There is not an ethical obligation

No respondents explicitly supported this view.

What might this obligation entail?

A small number of suggestions for what this obligation might entail were indicated:

"The aim will be to harness all the necessary information and to work collectively using the principle of solidarity to ensure that answers are arrived at as soon as possible. There must not be any competition or hiding of information. Data and information sharing should be encouraged." *Dr Rosmond Adams, CARPHA*

"The obligation of cooperation entails a commitment to sharing information about proposed research objectives at the very least." *Anonymous respondent*

"mechanisms would need to be in place for researchers to gain adequate recognition for collaborative work, in promotions, fundraising, and so on." *Annette Rid*

"Data sharing is an essential first step in collaboration – you can't collaborate without sharing information." *Anonymous respondent*

"It is critical then that local researchers from the affected countries are not only suitably acknowledged but that provisions are put in place to protect those who might be put at a disadvantage through research collaboration." *Ann H. Kelly*

"This must include an expedited strategic approach to testing new interventions, and ensuring that commercial interests including branding opportunities do not get in the way of achieving optimal outcomes, including optimal outcomes for the most affected communities." *Bridget Haire*

"The PIP Framework is… a good example. It required agreement prior to collaborative work, and builds in obligations for collaboration in public health emergencies." *Anonymous respondent*

What are its limits?

Suggestions as to the limits of an obligation to work collaboratively included:

"Unfortunately, one can scarcely expect collaboration from organizations that often have missions and mandates that conflict or where they are naturally competitors." *MSF / MSF ERB*

"A global health emergency might necessitate the building relationships and partnerships more rapidly and in a more ad-hoc manner. This might mean that collaborations which did not pre-exist have to be set up which may create an amount of difficulty. Particularly, as good collaboration relies on mutual trust which can be challenging to build in such constrained circumstances and tight timeframes. Additionally, global health emergencies require partners from multiple sectors who may not often be brought into discussions such as NGOs, civil society, religious groups and regulators among others to work together." *Wellcome*

"The only challenge I see here is that there is no-one-research funds coordinating entity. Therefore, such competitive ventures are unavoidable. I see that until this day, even call for applications for research grants are similar across main health research funders." *Anonymous respondent*

"it should not lead to large (international?) consortia dominating and claiming most of the funding, while excluding others/new comers/outliers from access to study sites or funding, nor to lack of competitiveness to have the better ideas sharpened." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé.*

"In practice, quite a bit depends on personal relationships." *Tim Allen*

Question 25

What are the obligations of funders to promote collaboration in a global health emergency?

General comment on the role of funders raised by respondents included:

> "Funders are well-placed to bring together people working together in different institutions – even those working as competitors. They can bring together people with a great idea, with others on the ground who are able to implement it." *Dr Cathy Roth*

Making collaboration a requirement of funding

Respondents suggested that funders might have an obligation to promote collaboration through making it a requirement of funding awards.

> "Funders must ensure that there are levels of collaboration. This must be a criterion for funding or for evaluating proposals. How collaboration will work must be clearly laid out and not just be mentioned." *Dr Rosmond Adams, CARPHA*

> "funders should make collaboration a requirement, if success of the work they support would be more likely." *Animals in Science Committee*

> "They are the funders, as such they have the mandate to require collaboration, and, ideally, to support the identification of suitable partners in-country. No grant should be signed to a Global North country without a collaborating partner in the Global South if the research is to be conducted in a Global South country." *Gillian McKay*

> "Funders can promote collaboration in global health emergency when they make it a requirement that scientists from the affected countries are co-researchers, co-applicants. This will improve the research objectives." *Anonymous respondent*

> "Concretely and directly support first the local and then regional research (not only through other international partners) … Ensure that local populations are always involved along the way." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

The importance of encouraging diverse collaboration was also noted.

> "Ensure it is not always just the usual suspects who are involved, which all know each other well, meet in the same fora all over the world, are invited to each other's events for key note speeches, etc. and scratch each other's back (as long as considered opportune)." *Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé*

However, a cautionary note on funders' emphases on collaboration was highlighted by other respondents.

> "There is a balance to be struck between completely open calls, and actively mandating collaboration (for example through the use of consortia) in applications. The latter risks giving priority to well-funded

> institutions in high income countries who have the infrastructure, contacts and money to put together such consortia quickly. What are needed are 'softer' ways of generating collaboration, including active involvement by funders, taking on a role as a broker matching up expertise, skills and experience from different institutions and places (for example by starting a call inviting brief concept notes, rather than fully-formed consortia and plans). There are lots of different models." *Dr Cathy Roth*
>
> "I am not convinced that funders should impose collaborations using a top-down approach. They can of course support different teams and facilitate collaborations." *Anonymous respondent*

Encouraging high-quality outputs / standards

An obligation to encourage high quality outputs and standards was also observed.

> "There is a moral obligation to lead, to set standards, to have harmonized policies, and to implement and monitor standards and practices." *David B. Morton*
>
> "The focus should be on producing effective, equitable outcomes, maintaining a focus on protecting human health and avoiding exploitation." *Bridget Haire*
>
> "Building robust and quality evidence for global health support and impact". *Ernest Tambo*
>
> "Their role is crucial in setting the standards for what will count as good practice. This includes forcing people to collaborate (especially with partners from the affected countries) but also e.g setting standards for whether and how samples should be exported in the case of GHEs, in setting the parameters for data sharing (e.g. instant sharing of data should be a requirement) etc." *Jantina de Vries*

To coordinate with other funders

One anonymous respondent suggested:

> "The Ebola epidemic also provided some examples where coordination between funders would have been very beneficial (in order to avoid duplication, set research priorities, and optimally use potential participants)." *Anonymous respondent*

Ensuring indemnity

On the role of indemnity, Ann H. Kelly stated:

> "One area that needs further consideration and discussion is the indemnity of clinical research and what insurance funds are available to non-profit organizations. During the Ebola Outbreak, companies were required to assume some of the liability for experimental products, I do believe it was national governments who had to indemnify the WHO, while the WHO had to obtain insurance coverage for the benefit of recipient countries in the case of accident. For future research in GHEs,

> further considerations need to be paid as to who will provide insurance and how it will be funded."

Question 26

What are the key requirements for good ethical practice in sharing (a) data and (b) samples in a global health emergency?

A general note on the concept of sharing was indicated by an anonymous respondent to this question.

> "good ethical practice would show sensitivity to the different activities that come under the umbrella of data and sample sharing. The word sharing can mean different things to different people, and may include many types of activity, from sharing within a collaboration, to open access data, to exporting samples. In addition, not all data relevant to a global health emergency will be health data. Mobile phone data, geolocation data, travel passenger data among others, may be relevant. As noted in the background, samples are also a finite resource that would require a prioritisation process for use."

Key requirements

Several respondents chose to answer both points together, listing requirements that they argue should apply to sharing both data *and* samples.

Ernest Tambo, for example, listed the following requirements:

- "Well-understood and commonly shared agreements
- Cultural and anthropological values maintenance
- Mutual cooperation and trust
- Sample or data sharing, tiered-party and ownership including biobanking in stem cell production or organ transplant
- Process of mining and release or dissemination
- Benefits sharing and intellectual property rights
- Rationale for termination and separation"

An anonymous respondent also suggested, for both parts of the question, on consent:

> "consideration of appropriate consent models depending on the type of data, and that account for future uses of data and samples, including broad consent."

Raffaella Ravinetto, Marianne van der Sande, and Anne Buvé also set out requirements for (a) and (b).

- "Always involve the people/teams who collected the original data or samples when reanalysing them, as well as representatives of the population in which the data or samples were collected: better quality, more trust. Failure to do so should be explicitly justified
- Always include clear and transparent benefit sharing plans

- Always set up clear, transparent and balanced mechanisms for the governance of biobanks and data repository"

Involvement of local community

The involvement of the affected local community was highlighted as a key requirement.

> "this is about ensuring genuine, visible intellectual leadership by individuals in the country or region affected by the epidemic, transparency in decision-making, and adherence to agreed-upon standards. What would help a lot is if the international community would commit to developing standards for registering the numbers and types of samples collected, exported etc. – i.e. an agreement by international organisations likely to be involved in the epidemic… specifying how they are going to record the samples and data they collect and export. Similarly, there ought to be a commitment by these actors that data and samples emanating from GHEs will be broadly available to the scientific community post-epidemic." *Jantina de Vries*

> "citizens of the country where the data is collected should be integral to the collection, storage, sharing and write-ups for the data. I see it far too often that researchers "parachute" in during crises, conduct research and then go home only to publish without considering how to build capacity among local research institutions. During the Ebola crisis Sierra Leone insisted that any publications arising from the outbreak's data must include a Sierra Leonean author, and I think this is completely right and should be considered best practice." *Gillian McKay*

In a related point, an anonymous respondent highlighted:

> "Feeding results back to those from whom data / samples were collected."

Making the information publicly available

> "there ought to be a commitment by these actors that data and samples emanating from GHEs will be broadly available to the scientific community post-epidemic." *Bridget Haire*

> "Also all data should be shared as quick as possible for global researchers to conduct research that could be of immediate benefit to the response, but that researchers from the country should still be enabled to contribute to the publications (the case of Zika in Brazil where the researchers put their data into a repository and then another group from outside Brazil published about it first is unfair and unethical)" *Gillian McKay*

However, one respondent raised the following note of caution:

> "in one of our experiences one funder dictated that data should become public within one year of having completed the field work and analysis. This was a real problem, as the locals would have needed 3-4 years to analyse the results, beginning with what is immediately needed and continuing to publish articles for voice, and also documentation from those who belong to community. And this would have meant that locals

would not have been able to complete with internationals who have much better infrastructure and time for research and paper production, yet with locals having the know-how to analyse and interpret results properly."

On a related point on benefit sharing with the affected community, an anonymous respondent stated:

> "Equitable sharing of benefits with populations from whom the data/samples originate, and academic rewards and recognition."

Trust

> "Trust and governance: this is often discussed as an important part of sharing data/samples. In an emergency context, however, people come together from diverse background and organisations with different norms. There may be issue of trust between the population from whom the data/samples have been collected and their government/representatives. Governance processes may also be weak, and disrupted. As such, good ethical practice may to some extent boil down to the practice of individuals and their moral compass." *Anonymous respondent*

Storage of data / security

> "Due to the sensitive nature of (at least some) data, the platform must be secure. It should be scalable, and be able to operate across multiple stakeholders and potentially countries […] [It should] allow each organization to decide who accesses which kind of the data (for what purpose)." *Anonymous respondent*

> "Transparency about what is stored where, and about decision-making processes." *Humanitarian Health Ethics Research Group*

Question 27: other issues / considerations

Several other issues and considerations were put forward by respondents. Novel points made by respondents included:

> "When a public health emergency/situation is declared, and the incident management system is activated, a research group/subgroup should be activated to assess if research will be needed and what research." *Dr Rosmond Adams*

> "Navigating presence of 'former' armed troops who function as a hidden 'community advisory group'. Male community influencers and rebel leaders are often interchangeable and it's not easy to discern their interests and how they influence participation in research especially for women and girls." *Anonymous respondent*

> "[P]ay more attention to the potential suffering of animals in such emergencies". *David B. Morton*

> "Protection of researchers themselves is something that has not been raised. This is especially important given the dangers researchers may

face in dangerous environments, conflict, or with infectious diseases. This needs to be seen as an ethical obligation on all stakeholders involved in getting researchers into these settings." *Dónal O'Mathúna, PhD*

"There is an ethical imperative to research and develop more comfortable and user-friendly protective clothing for healthcare workers during infectious disease outbreaks. If a person can be outfitted to walk on the moon, it is unacceptable that people caring for the desperately ill are expected to wear impossibly hot, uncomfortable clothing that still left too many vulnerable and made performing medical care terribly difficult. This is a priority that can readily progressed in non-outbreak conditions." *Bridget Haire*

"Maybe considerations related to recent hot topics like big data, artificial intelligence [and] mobile technologies could be [considered]." *Anonymous respondent*

"The interactions between research and chronic poverty (and discrimination) need to be given more ethical consideration." *Dónal O'Mathúna, PhD*

"Ethics committees need feedback after the emergency and studies so they can understand their own processes better and evaluate their own performance". *Anonymous respondent*

"It's important for emergency research to include plans for what happens after research ends. Will frontline staff and participants be able to reach researchers when necessary?" *Humanitarian Health Ethics Research Group*

"As a military respondent, NOT using me or my data when it could be made available is wrong - it is intentionally turning away from resources that are already there, and especially in these contexts that is indefensible." *Anonymous respondent*