Zika Ethics Consultation:
Ethics Guidance on Key Issues Raised by the Outbreak

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Executive Summary

The document presents the guidance that resulted from the Zika Ethics Consultation convened by the Pan American Health Organization (PAHO) on the issues that affected countries had previously identified as most ethically challenging in the context of the Zika virus outbreak. Ethical duties in the domains of health care delivery, public health activity, and research are explained. With respect to health care delivery, women's moral right to choose among all relevant reproductive options is highlighted. Respecting women's capacity to choose goes in tandem with the ethical obligation to support them and protect their health. Providing all available information in an honest and transparent manner is a crosscutting ethical duty of healthcare providers, Ministries of Health, and governments. The impact on all domains of the ethical duty to undertake research and then share the data and research outcomes to enable prompt responses to the health emergency is stressed, along with the imperative to advance research and surveillance. Because the Zika virus outbreak is a global health issue, solidarity should guide the collaboration among countries in the delivery of health care, advancement of public health, and conduct of research.

Introduction

The current Zika virus disease outbreak was first identified in Brazil in 2015 and spread rapidly throughout Latin America and the Caribbean. Zika virus infection in pregnant women has been linked to microcephaly in newborn infants, which often implies severe brain damage. Zika has also, less frequently, been associated with autoimmune neurologic conditions including Guillain-Barré syndrome (GBS) in those infected. In February 2016, the World Health Organization declared the event a Public Health Emergency of International Concern. This is the first time that a mosquito-borne disease was found to cause severe congenital malformations. Congenital malformations resulting from Zika, referred to as presumed Congenital Zika Syndrome (CZS), include microcephaly and other severe neurological abnormalities that may result in marked mental retardation and disabilities.[1] The causal link between Zika virus and these abnormalities was confirmed in mid-April.[2]

Signs of CZS can only be confirmed late in pregnancy. Zika virus infection is often asymptomatic and there is no treatment or vaccine to prevent infection. Furthermore, diagnosis of Zika virus infection is difficult because existing tests can cross-react with other viruses such as dengue and yellow fever, and laboratory tests are not always available. Diagnosis is therefore often based on clinical and epidemiological criteria.

The Zika virus outbreak is particularly challenging from an ethics perspective because of difficult ethical issues associated with pregnant women. Furthermore, the outbreak is characterized by a high level of uncertainty, for example about the likelihood that an infected pregnant woman at a certain stage of pregnancy will have an affected fetus, or about the prognoses in cases affected with CZS. Public health decisions should be informed by evidence, but very little evidence is currently available. Action is however

[1] Miranda-Filho DdeB et al. Initial description of the presumed congenital Zika syndrome. *Am J Public Health* 2016; 106(4):598-600.
[2] Rasmussen SA et al. Zika virus and birth defects – Reviewing the evidence for causality. *N Engl J Med* 2016 April 18; [Epub ahead of print].

urgently needed to address this public health emergency. A thorough ethical analysis is crucial to determine what guidance to provide in this situation.

The Regional Program on Bioethics of the Pan American Health Organization (PAHO) led an ethics consultation aimed at providing ethically sound guidance in the Zika virus outbreak. The ethics consultation took place on April 6-7, 2016 in Washington D.C. with the participation of ethicists, mostly from the Region of the Americas, and other professionals involved in the response to the outbreak at Ministries of Health, PAHO and WHO. The consultation was funded by the Wellcome Trust. It was preceded by dialogue and consultation with PAHO Member States to identify the specific issues that posed the most pressing ethical challenges and on which PAHO's guidance was sought.

This document presents the recommendations that resulted from the Zika Ethics Consultation on the ethical issues that the countries in the Region had identified as most challenging. The ethical analysis took into account the diverse landscape of the Region in terms of legal frameworks, established practices, resources of the countries, and the beliefs and values of their populations. Against that backdrop, the commitment to the democratic value of respecting different beliefs and values was highlighted. Further, the ethical analysis built upon prior regional consensus among Member States that ethics is the "discipline [that] allows for continual analysis and reflection on the law and on what should be required by law."[3]

All recommendations generate practical challenges to put them into practice, and thus often dictate further priority-setting and action to allow for their equitable implementation. Ethical recommendations to address the issues raised by the outbreak pose challenges that range widely and include resource limitation and legal barriers. The ethical duty to take steps towards addressing these challenges should be highlighted in the context of the duty to respond to the public health emergency and the unique issues raised by the Zika virus.

A salient recommendation that resulted from the Zika Ethics Consultation is the ethical imperative to give all women the capacity to choose among all relevant reproductive options. Taking into account the significant mental anguish about reproductive issues that women experience during the Zika virus outbreak, along with the ethical duties to minimize harms and to allow for decisions to be made on the basis of the beliefs, values, situation, and concrete reality of each woman, the capacity to choose should include the full set of options including contraception and termination of pregnancy. This should be framed as equitable access to comprehensive sexual and reproductive health. Promotion of women's capacity to choose goes in tandem with an ethical obligation to support and protect their health.

Ethical duties in the following three domains were identified: health care delivery, public health activity, and research. Providing all available information in an honest and transparent manner, which implies being explicit about what information is not yet known, is a crosscutting ethical duty of healthcare providers, Ministries of Health, and

[3] Pan American Health Organization Directing Council. Bioethics: Towards the integration of ethics in health. Concept paper. 28th Pan American Sanitary Conference, 64th Session of the Regional Committee. 2012 Sep 17-21. (Document CSP/28/14, Rev.1). Available from: http://new.paho.org/hq/index.php?option=com_docman&task=doc_download&gid=18416&Itemid=&lang=en (Accessed May 12 2016).

governments. The impact on all domains of the ethical duty to share data and research outcomes to enable prompt responses to the health emergency was emphasized. Finally, because the Zika virus outbreak is a global health issue, solidarity was stressed as the principle that should guide the collaboration among countries in the delivery of health care delivery, advancement of public health, and conduct of research.

Domains of ethical duties

1. Health care delivery

Governments and health care providers have the ethical duty to deliver the best possible care, and to do so in an equitable manner. The Zika virus outbreak creates a wide spectrum of health care needs, which include those of pregnant women that may contract or have possibly contracted Zika, children with CZS, and persons developing GBS and other neurological disorders as a result of Zika infection. Women of reproductive age are therefore a key population in the context of the outbreak. A prominent ethical duty towards them is to ensure that they are provided with the capacity to choose among all relevant reproductive options for contraception and during pregnancy. In the Region of the Americas, women are presented with different options for reproductive decisions in different nations. Equity in access to reproductive options should be advanced to ensure that during the outbreak all women across the Region have access to all relevant reproductive options.

What are the ethical duties towards women during the Zika virus outbreak?

The ethical duties towards women during the Zika virus outbreak include:

- *Provision of information:* Women ought to be given honest, complete, accurate and most up-to-date information about Zika virus infection and CZS. The information that needs to be communicated includes what is known and not known about Zika virus infection, the spectrum of CZS, the benefits and limitations of conducting diagnostic tests, the availability and timelines of testing, and the options relevant to test results. For issues in which uncertainty about the virus and CZS prevails, such uncertainty must be explicitly communicated as well. The right of the woman not to know – including her right not to know the results of her tests– should be respected. All information should be communicated clearly and in neutral language based on the best available evidence. The information will allow women to make decisions based on their own beliefs, values, priorities and circumstances. Different means of communication and disseminating information should take into account cultural diversity, especially with respect to indigenous communities.

- *Respect for the right to choose:* It is crucial to secure women's moral right to choose about their reproductive options during the Zika virus outbreak. Women should be provided with the opportunity to choose from all relevant options, including contraception, termination of pregnancy and carrying to term a potentially affected pregnancy. Women should be able to choose after being presented with all the available options, and assessing their risks individually on the basis of their own values and personal situation. Women's right to choose implies the right to refuse tests and interventions, except for those that are legitimately required from a public health perspective. Women's capacity to choose should not be contingent upon a certain

diagnosis or the probability of a negative outcome. The severe mental anguish that women may experience during the Zika virus outbreak as a result of a possible negative outcome justifies the duty to ensure their opportunities to make informed reproductive decisions for themselves. While women themselves should make these decisions, it is appropriate to invite them to consider involving other persons in the decision-making processes, such as spouses, partners, or, in the case of pregnant minors, parents or guardians. Women's decisions about whom to involve in these conversations, and their reproductive choices, should always be respected.

- *Access to comprehensive sexual and reproductive healthcare:* The moral obligation to provide women with reproductive information and choices implies that health authorities have a duty to ensure their access to all reproductive options during the outbreak and, for each option, to provide related support and care for women making the decisions and their offspring. Comprehensive sexual and reproductive care encompasses family planning, maternal health, pre-natal testing, safe termination of pregnancy, counseling, and post-natal care services. Lack of resources and legal barriers challenge access to reproductive options. Health authorities should thus take steps to expand access in ways that make all relevant reproductive options available to women during the outbreak. Health authorities should also ensure that access to reproductive options is not limited by women's socioeconomic, cultural, racial, or religious, status. In order to ensure equity, it may be necessary to prioritize resources to advance access among disadvantaged women.

- *Social support*: Women can only be empowered in their decision-making if all options are appropriately supported. They must not be blamed, punished, or left unsupported as a result of their reproductive decisions. Women and their families have a right to adequate social support for any reproductive decision they may make. Social support includes various forms of assistance to help women and their families handle the difficulties that they may experience as a result of the Zika virus and CZS, such as counseling, psychological therapy, psychosocial assistance, and disability care and other social services. Mechanisms to prevent the stigmatization and discrimination that women and their children and families may experience should be designed and implemented in locally meaningful ways. Health authorities should continuously inform the public about the importance of respecting different beliefs, values, and choices in order to minimize discrimination and stigmatization.[4]

<u>Are there specific duties towards different groups of women?</u>

Different groups of women, depending on their location and collective and individual circumstances, are impacted differently by the Zika virus outbreak and its consequences. Although the public health challenges posed by Zika virus and CZS in any given country vary, the ethical obligation to provide information, capacity to choose, and care that supports women's individual reproductive choices does not vary depending on the prevalence of Zika virus. Women in countries with high prevalence of Zika and women in countries with low prevalence have the same moral rights.

Within any given location, however, different groups of women will have different needs, and these ought to be considered. Child-bearing age women, pregnant women, pregnant

[4] Hanschmidt F et al. Abortion stigma: a systematic review. *Perspect Sex Reprod Health* 2016 Mar 31. [Epub ahead of print]

women with probable or confirmed Zika virus infection, women that are pregnant with a fetus with (suspected or confirmed) CZS, and women (and parents, guardians, and caregivers) of children with CZS have different needs and priorities for information they want, the choices they make, and the care and support that are owed to them. For example, information about contraceptive methods and effective access to their preferred contraceptive option is crucial for women of child-bearing age, while pregnant women have greater need for diagnostic tests, comprehensive maternal health care, and support mechanisms for their reproductive options.

What are the ethical duties to children with CZS and their parents?

Children with CZS ought to be provided with medical care and social support. These children and their parents should not be left unsupported under any conditions, even if it would have been possible to avoid or terminate pregnancy. Children with CZS will suffer from disabilities and need long-term or life-long care. Continuity of treatment should be ensured, along with equity in the provision of both care and support services for children and their families. Persons suffering from CZS –especially those experiencing visible symptoms such as microcephaly— and their families can be the target of stigmatization and discrimination. Women that are pregnant during the outbreak can also experience stigmatization and discrimination, for example in areas where they were recommended to avoid pregnancy during the outbreak. We have the duty to protect the wellbeing of these groups. This entails advancing strategies to prevent negative stereotypes and unfair treatment, and to minimize the harms of stigmatization and discrimination that occur.

How should priority-setting decisions regarding care be handled?

The Zika virus is occurring in settings where resources to meet health needs are often limited and this challenges the ability to meet these additional health needs in addition to ongoing health needs. Responding to the outbreak and its consequences should not take away urgently needed resources from other serious health conditions. If faced with challenging priority-setting decisions when delivering health care, the criteria and justifications used should be communicated transparently and widely to the public.

During the outbreak, health care delivery may also entail the provision of necessary care to foreigners. As a Public Health Emergency of International Concern, the clusters of microcephaly cases and other neurological disorders are global health problem that requires global cooperation and responses.[5] Collaboration and solidarity between countries is crucial to meeting related health care needs, controlling the outbreak, and reducing related harms.

2. Public health

Health authorities are tasked with protecting the health of the population and responding to public health emergencies. An adequate health response requires up-to-date information.

[5] WHO Director-General summarizes the outcome of the Emergency Committee regarding clusters of microcephaly and Guillain-Barré syndrome. 2016. Available from: http://www.who.int/mediacentre/news/statements/2016/emergency-committee-zika-microcephaly/en/ (Accessed May 12, 2016).

To obtain this information, health authorities have the duty to conduct surveillance and to act without delay on the basis of information obtained. In the context of the Zika virus outbreak, surveillance is needed to reduce some of the uncertainty that surrounds the virus and its consequences. Health authorities must ensure that the information is collected rigorously, that all relevant cases are reported, and that data are managed responsibly, always taking the benefit of the population into account. As in other cases of surveillance, in the Zika virus outbreak public health authorities may need to collect personal data or samples. While informed consent may not be required for such data collection, the information must be collected in a respectful manner, safeguarding the privacy of individuals, maintaining confidentiality to the extent possible, and providing information about the data collection in a transparent manner. Public health authorities also have the ethical duty to implement interventions that are already known to work, e.g. vector control.

How should public health activities that involve data collection be distinguished from research?

Not every activity that involves data collection in a systematic manner constitutes human subjects research. Research is characterized by the primary intent to produce generalizable knowledge. Health authorities engage in various forms of research, for which prior ethics approval must be obtained, and in which participation is voluntary following an informed consent process. Health authorities also conduct activities that aim primarily at the direct benefit of the population they serve, e.g. improving their health or addressing public health problems. Even if those activities involve the systematic collection or analysis of personal data, as in the case of surveillance, they do not constitute research with human subjects.[6] Therefore, they are not subject to the rules and regulations that govern human subjects research, such as prior approval of a research protocol by an ethics review committee. Nevertheless, all public health surveillance and other activities must be undertaken in an ethical manner, for example being attentive to minimizing risks for individuals and communities.[7] Appropriate ethical guidance and oversight should be sought, especially in the context of a public health emergency.

It is often difficult to distinguish between public health research and other public health initiatives and activities, particularly during a health emergency. In the Region of the Americas, this was particularly challenging during H1N1 and SARS. Various existing guidance documents and training materials can help distinguish public health research from non-research.[8] [9] [10] [11] The determination of whether an initiative constitutes human

[6] World Health Organization. *Ethics in epidemics, emergencies and disasters: Research, surveillance and patient care. Training manual*. Geneva: World Health Organization; 2015. Available from: http://apps.who.int/iris/bitstream/10665/196326/1/9789241549349_eng.pdf (Accessed May 12, 2016).

[7] Pan American Health Organization Directing Council. Bioethics: Towards the integration of ethics in health. Concept paper. 28th Pan American Sanitary Conference, 64th Session of the Regional Committee. 2012 Sep 17-21. (Document CSP/28/14, Rev.1). Available from: http://new.paho.org/hq/index.php?option=com_docman&task=doc_download&gid=18416&Itemid=&lang=en (Accessed May 12, 2016).

[8] World Health Organization. *Ethics in epidemics, emergencies and disasters: Research, surveillance and patient care. Training manual*. Geneva: World Health Organization; 2015. Available from: http://apps.who.int/iris/bitstream/10665/196326/1/9789241549349_eng.pdf (Accessed May 12, 2016).

subjects research or not should be made by an appropriate third party, like an ethics review committee. If it is determined that the initiative constitutes human subjects research, then the corresponding research protocol must be submitted for ethics review.

How should the health of the public be advanced in the Zika virus outbreak?

A range of public health responses is needed. Their ethical design and implementation requires incorporation of equity, responsibility, solidarity and transparency. Equity entails efforts to ensure that the poor and disadvantaged are not disproportionately burdened by the outbreak. Equity is essential for vector control, for example, because mosquitoes carrying the virus are more prevalent in areas where standing water provides breeding sites, which are more commonly present in poorer areas. Hence the poor are more likely to be exposed to, and infected with, Zika virus. Additionally, the poor cannot afford repellent and nets to protect themselves. Public health interventions should aim at reducing this and other inequities. Public health activities aimed at Zika control should be conducted responsibly and, inter alia, build capacity to improve response to future health emergencies.

Responsibility and solidarity dictate that relevant data should be promptly shared so other countries can act to reduce the harm caused by the outbreak. Responsibility implies attention and responsiveness to environmental conditions that affect mosquito-breeding and life cycles, and exposure to and transmission of the virus. Before approving research or interventions involving the use of genetically modified mosquitoes to reduce the Zika vector, or other new technological approaches, rigorous risk-benefit assessment should be conducted.

The Zika virus and its consequences might present us with thorny priority-setting issues. We should anticipate scenarios in which health systems are overwhelmed and cannot provide care to all persons needing it, e.g. access to ventilators for all patients with GBS. Health authorities have the ethical obligation to provide a public justification of the criteria used for priority-setting decisions. Transparency about the rationale for priority-setting decisions enhances public trust, increases their acceptability, and promotes compliance with related recommendations.

What do health authorities owe to the general public in terms of communication during the outbreak?

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[9] Cash R, Wikler D, Saxena A, Capron A, editors. *Casebook on ethical issues in international health research.* Geneva: World Health Organization; 2009. Available from: http://whqlibdoc.who.int/publications/2009/9789241547727_eng.pdf (Accessed May 12, 2016).

[10] Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada. Tri-Council policy statement: ethical conduct for research involving humans. Ottawa: Canadian Institute of Health Research; 2010. Available from: http://www.pre.ethics.gc.ca/pdf/eng/tcps2/TCPS_2_FINAL_Web.pdf (Accessed May 12 2016).

[11] Centers for Disease Control and Prevention. 2010. CDC's Policy on distinguishing public health research and public health nonresearch. Available from: http://www.cdc.gov/od/science/integrity/docs/cdc-policy-distinguishing-public-health-research-nonresearch.pdf (Accessed May 12 2016) This material includes examples that can help distinguish between public health research and public health activity.

Health authorities have the duty to proactively design and implement procedures for translating complex health information into layperson language and disseminating this widely to patients and the public. They have a duty to provide the most accurate and complete information about the Zika virus and its consequences that is available. Extreme care should be used in communications in order to facilitate comprehension. Health authorities should assume the burden of ensuring that messages are comprehensible as opposed to passing to the population the burden of decoding technical information, which would further increase inequity.

Health authorities also have the duty to provide the population with the general epidemiological information about the outbreak and make relevant information about the public health response publicly available. The population should be aware that data are being collected as part of surveillance efforts in order to improve public health, and that individual data are protected and will be managed confidentially and used responsibly. Providing this information in a comprehensible manner is key for public trust, and this is particularly important in emergency epidemic situations, which tend to be characterized by a background of distrust and resistance to following related public health recommendations. Communication and engagement with local populations and communities also fosters public trust and helps ensure that messages are sensitive to cultural differences and respectful of diversity. Health authorities should lead by example and ensure transparency, in addition to providing truthful, accurate and unbiased information. Partnerships with the news media should be explored as possible means of disseminating information.

How should uncertainty be handled?

People are owed the truth. Public health authorities should be honest and transparent about the information that we do *not* have about the Zika virus and its consequences. They should avoid statements of certainty when it does not exist about a particular issue, and be straightforward about the scope of uncertainty. The communication of uncertainty is important because it enables individuals to make decisions based on their own risk assessments, and avoid the harms that may result if decisions are made taking what is uncertain as a fact. Health authorities have the duty to explain that certainty may increase as more data are collected, and as more research is conducted. Recommendations may change on the basis of the new knowledge we have. More certainty will allow more informed policy-making and individual decision-making.

3. Research

Research is crucial to reduce the uncertainty about Zika virus and its consequences. We have the ethical obligation to conduct research during the outbreak in order to improve prevention and care. Research is essential firstly to understand the disease so that interventions and management practices can be devised, and then to assess the safety and efficacy of any proposed diagnostic tests, treatments, vaccines or management approaches. We should aim at conducting the most rigorous studies that are possible in the current conditions to ensure that we learn as much and as fast as we can. Conducting research can be challenging during an emergency and should not compromise the duty to provide care as outlined in this document.

Populations and communities must be continuously informed about the importance of

doing research during the emergency and also afterwards, and that this requires the collection of samples and data during and after the outbreak. The Zika outbreak highlights the need to conduct research involving pregnant women as human participants, as well as post-mortem studies in fetuses, which have contributed importantly to our understanding of the consequences of Zika virus.[12] Community consultations prior to the initiation of related research are strongly encouraged to ensure that studies address local needs and priorities and that design of studies will be acceptable to host populations. Community consultation will thus build trust, which is vital during an emergency, and essential to the conduct of research that will provide accurate and meaningful information.

This outbreak also highlights the need for ongoing local research capacity development in order to strengthen the ability to respond in outbreaks such as this. As stated in the 2013 World Health Report, unless low- and middle-income countries become the generators and not only the recipients of data then there will never be any great improvements to public health.[13] From an ethical perspective, research capacity development efforts should therefore be considered a priority.

Can we fast-track ethics review during an emergency?

Human subjects research conducted during emergencies must be subject to higher, not lower, ethical safeguards. Ethics approval must be obtained for all emergency research with human participants before studies begin, and the need to accelerate research should not come at the expense of thorough ethics review. Ethics review committees, however, must fast track ethics review for emergency research while ensuring a rigorous ethics review. Mechanisms to fast-track ethics approval processes must be devised, along with strategies to integrate the work of different ethics review committees to avoid duplication. Investigators and research funders may consider seeking ethics review of standard protocols that can later be adjusted and approved in an accelerated process.[14] Involving ethicists in the development of research protocols is recommended.

Particularly during emergencies, ethics review processes should examine accountability of the researchers, institutions, and funders involved to guarantee that studies are conducted ethically. Health authorities and institutions conducting research should enhance the visibility and credibility of ethics review committees to promote trust in research.[15] Trust can be built by informing and engaging communities and local populations about the design, implementation, and probable benefits and outcomes of research, and

[12] See for example Driggers RW et al. Zika virus infection with prolonged maternal viremia and fetal brain abnormalities. *N Engl J Med*. 2016 Mar 30. [Epub ahead of print]; and Mlakar et al. Zika virus associated with microcephaly. *N Engl J Med* 2016 Mar 10;374(10):951-8. [Epub 2016 Feb 10].

[13] World Health Organization. *Research for universal health coverage: World health report 2013.* Geneva: WHO, 2013. Available from: http://apps.who.int/iris/bitstream/10665/85761/2/9789240690837_eng.pdf?ua=1 (Accessed May 18 2016).

[14] Global Forum on Bioethics in Research (GFBR). Meeting report: Emerging epidemic infections and experimental medical treatments. Annecy, France. 3-4 November 2015. Available from: http://www.gfbr.global/wp-content/uploads/2016/03/GFBR-2015-meeting-report-emerging-epidemic-infections-and-experimental-medical-treatments.pdf (Accessed May 12 2016).

[15] For example, enhancing and protecting their independence and providing support and arms length expertise where needed, and especially where non-traditional research methods and innovative trial design will be involved.

continuously informing the public about the research that is being conducted and the various processes and requirements aimed at ensuring that it is ethical. This also facilitates consent processes that tend to be challenging during emergencies.[16]

Is consent necessary when doing research during emergencies?

Existing national and international ethical guidelines that govern research involving human participants apply to all research conducted during emergencies. Accordingly, obtaining informed consent is necessary for research in emergencies involving human participants or their identifiable samples or information. Existing guidelines stipulate circumstances in which the requirement to obtain informed consent can be waived by a research ethics committee when: (a) it is not feasible to obtain consent, and the studies (b) have important social value and (c) pose only minimal risks to participants.

Especially in the context of outbreaks, and in order to catalyze much needed research, the practice of obtaining broad consent for the use of samples and data in future research (including biobanking research) should be strongly encouraged. Unlike traditional consent, which seeks participation in one specific study, broad consent applies to participation in a range of future studies that are not planned or conceptualized yet, but are likely to be designed as new information emerges. In cases of broad consent, future research involving a participant's samples or data should ordinarily be approved by an ethics review committee, and this should be explained to participants as part of the broad informed consent process. Overall, individuals should always know whether they are participating in research, receiving medical care, or participating in a public health intervention. This is vital to instilling and upholding public trust in research and health professionals.

Is it ethically acceptable to conduct research with pregnant women?

Research with pregnant women is ethically acceptable and should be actively promoted because it is critical to providing pregnant women with safe and effective medical treatment, which is imperative for their own health and the health of their offspring. This is true in routine and emergency situations. Without research with pregnant women, we face a dearth of evidence about how to make treatment and dosing decisions. Given that pregnancy can profoundly change the way in which the body metabolizes drugs, and given the importance of ensuring that medicines used in pregnancy have an acceptable risk profile to the fetus, data specific to pregnant women are urgently needed.[17] Research with pregnant women, when conducted responsibly, is both allowed under consensus international guidelines and morally important.

This is critically important in the Zika virus outbreak. Given that Zika virus infection is so potentially devastating in pregnancy, pregnant women are among those we most want to protect from infection. As we move forward generating knowledge to address the Zika virus outbreak and its consequences, different types of research with pregnant women – including vaccine studies— should be expected and promoted. Because of the long time

[16] Global Forum on Bioethics in Research (GFBR). Meeting report: Emerging epidemic infections and experimental medical treatments. Annecy, France. 3-4 November 2015. Available from: http://www.gfbr.global/wp-content/uploads/2016/03/GFBR-2015-meeting-report-emerging-epidemic-infections-and-experimental-medical-treatments.pdf (Accessed May 12 2016).

[17] Lyerly AD et al. The second wave: toward responsible inclusion of pregnant women in research. *Int J Fem Approaches Bioeth* 2008; 1(2):5-22.

lag in achieving herd immunity, vaccine development may need to proceed on the assumption that it should be used in pregnant women. Moreover, given that a predictable proportion of young women receiving a vaccine will unknowingly be pregnant, understanding the safety profile of vaccines given during pregnancy may be critical. All human subjects research must be conducted ethically and in accordance with existing international and national research ethics guidelines. Where such standards are lacking, new guidance should be encouraged and established.

Can samples collected for other purposes be used for research?

Research during and after the outbreak is needed. Samples collected for purposes other than research (e.g. surveillance by the health authority, or left over clinical samples) can be used for research in some circumstances. These include when individuals provide broad consent to the use of their specimens for their future use in human subjects research, or when the public has been informed that left over clinical samples may be used for research after anonymizing them. These studies must obtain prior ethics approval.[18] If broad consent for the future use of samples was not obtained when the samples were collected, ethics review committees might require asking for the consent of the persons who provided the specimens in order to use them for research. Ethics review committees may also assess if a waiver of consent is appropriate.

Do we have a duty to share the results of research?

Yes. As internationally agreed after the Ebola virus outbreak, during a health emergency all involved parties have the duty to share data and research results quickly in order to guide decision-making.[19] Efforts should be made to ensure data are complete and of the highest possible quality. In the current outbreak, research is urgently needed to minimize the harms caused by the outbreak. It is ethically unacceptable to block or delay the publication of research results. Every party involved in research should contribute towards ensuring that research results are shared promptly through channels that are widely accessible (e.g. open access journals) to better inform public health responses to the outbreak. Research teams have the duty to make the results of their research publicly available without delay, and to provide public health practitioners promptly with all relevant information. Research teams also have the duty to advance further research, which implies sharing research protocols and instruments, data and samples to the extent that it

[18] Certain guidelines and regulations for human subjects research are restricted to studies involving persons or their identifiable samples. Accordingly, research with samples previously collected for other purposes can move forward without obtaining ethics approval if these samples are completely unidentifiable for the researchers. This is consistent with international guidelines: The Declaration of Helsinki provides ethical guidelines for "medical research involving human subjects, including research on identifiable human material and data," and CIOMS refers to "research involving human subjects, including research with identifiable human tissue or data."

[19] Leading international stakeholders from multiple sectors convened at a WHO consultation in September 2015, where they affirmed that timely and transparent pre-publication sharing of data and results during public health emergencies must become the global norm: http://www.who.int/medicines/ebola-treatment/blueprint_phe_data-share-results/en/. This commitment to sharing data during public health emergencies has been deemed relevant in the context of the Zika virus outbreak and endorsed by various key partners: http://www.wellcome.ac.uk/About-us/Policy/Spotlight-issues/Data-sharing/Public-health-emergencies/index.htm.

is possible to do so ethically. These duties apply to all researchers, including those at governmental institutions.

The Zika virus outbreak is a global health emergency. Global collaboration and data sharing across national borders is therefore strongly encouraged. Global collaboration should not be restricted to data and research results. When possible, researchers and funders should incorporate designs and activities that build research capacity in low- and middle-income countries and other resource-limited settings.