Ethics of using convalescent whole blood and convalescent plasma during the Ebola epidemic

Interim guidance for ethics review committees, researchers, national health authorities and blood transfusion services

World Health Organization

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1. Background

WHO convened a Consultation on Potential Ebola Therapies and Vaccines in Geneva, Switzerland on 4–5 September 2014. In the absence of proven treatments, participants widely agreed that convalescent whole blood and convalescent plasma, among other experimental interventions, should be considered for use for people with Ebola virus disease. Any such use should be scientifically studied through carefully designed research studies. If, however, convalescent whole blood and convalescent plasma are used for treating people with Ebola virus disease outside research studies, this use should be considered "monitored emergency use of unregistered and experimental interventions", a term coined by WHO in the context of the current Ebola outbreak to refer to an exceptional use of experimental interventions outside clinical trials, and to reflect the urgent need to collect data on their efficacy and safety *(1,2).*[1]

This document specifically analyses the ethical issues surrounding the potential use and study of convalescent whole blood and convalescent plasma in both research and clinical settings.

2. Ethically relevant facts

2.1 Context constraints

The Ebola epidemic is occurring in countries in western Africa that are not adequately prepared to respond. Standard operating procedures for using convalescent whole blood and convalescent plasma among people with Ebola virus disease do not exist. The current situation in the affected countries is as follows.

- They lack the functional health care systems necessary to treat the people who are sick and adequate public health systems and personnel to prevent the spread of Ebola virus disease.

- There is poor public understanding of Ebola virus disease, which has sparked rumours and fears about its causes and treatment and has led to a lack of compliance with recommended infection control practices, such as safe burials.

- There is an insufficient number of health-care workers to provide care. These countries faced critical human resource shortages in the health sector before this outbreak, and Ebola virus disease has taken a high death toll on this population subgroup: health-care workers who become infected have an estimated case fatality rate of 59% *(3)*. This critical shortage, the lack of adequate training and protective equipment for health-care workers and the widespread public distrust of health officials and health-care workers tremendously affect their commitment to work and reduce the number of health-care workers per capita. This further complicates efforts to control the epidemic.

- The availability of basic blood transfusion services in some of the affected countries could ease the use of convalescent whole blood or convalescent plasma for Ebola virus disease. However, collecting, processing and using convalescent whole blood and convalescent plasma are more challenging than routine blood transfusion activities because of (1) the risks associated with contact with people with Ebola virus disease during blood transfusion and (2) the difficulties of maintaining a registry of people with Ebola virus disease who have recovered, especially those

[1] Monitored emergency use of unregistered interventions may be achieved through existing regulatory mechanisms that contemplate the use of unregistered interventions under specific emergency circumstances, such as the notion of emergency use of an investigational new drug by the United States Food and Drug Administration.

who live in remote and hard-to-reach areas and (3) the limited feasibility of obtaining blood or plasma donations from donors in the midst of overwhelmed health-care systems with limited infrastructure capacity and human resources.

2.2 Uncertain therapeutic efficacy of convalescent whole blood and convalescent Plasma for people with Ebola virus disease

It is unknown whether convalescent whole blood and convalescent plasma can effectively treat patients with Ebola virus disease. There is theoretical reason to expect that antibodies in the blood or plasma of individuals who have survived Ebola virus disease would reduce the viral load of individuals who are acutely ill due to the virus, but this remains unproven.

Transfusion of immune plasma is a standard therapy for South American haemorrhagic fevers caused by arenaviruses, and it has been used successfully for treating people infected with other infectious agents *(4)*. For instance, in Hantavirus infection, convalescent plasma was safe and reduced the case fatality rate to 14% in 29 treated cases versus 32% in 199 untreated cases *(5)*. Nevertheless, only anecdotal evidence suggests the possible efficacy of convalescent plasma *(6)*, and evidence of the efficacy of convalescent whole blood among patients with Ebola virus disease is disputed *(7,8)*. Some existing experimental data have even indicated the absence of efficacy of immune plasma and of whole blood transfusions in non-human primates infected with various filovirus strains (which include Ebola viruses) *(9–11)*. However, monoclonal antibody cocktails *(12–14)* and immunoglobulin preparations from vaccinated and challenged monkeys *(15)* have been effective in preventing Ebola virus disease and treating monkeys with Ebola virus disease in the monkey challenge model.

2.3 Uncertain therapeutic safety of convalescent whole blood and convalescent plasma for people with Ebola virus disease

The safety of convalescent whole blood and convalescent plasma therapies for people with Ebola virus disease is not fully known, and there is a theoretical concern and some experimental evidence about antibody-dependent enhancement of Ebola virus infection when these therapies are used in cell culture *(16)*. However, the use of convalescent whole blood and convalescent plasma for other conditions is generally considered safe if standard precautions *(17)* and blood safety strategies are effectively implemented, such as screening donated blood for transfusion-transmissible infections. Thus, if these precautions and strategies are followed, and donors are people who have fully recovered from Ebola virus disease *(18)*,[2] transfusing convalescent whole blood or convalescent plasma for treating patients with Ebola virus disease is expected to be safe.

2.4 Medical and psychosocial condition of convalescent people

People convalescing from Ebola virus disease often remain ill for weeks after recovering from the acute phase: residual fatigue, poor nutritional status and joint pain are common *(19)*. More severe complications can also be seen, associated with immune recovery *(20,21)*.

In addition, they may be affected by long-lasting mental distress because of the trauma of isolation in Ebola treatment facilities, survivor's guilt, social stigma, the loss of relatives or close friends, material losses and rejection by their community *(22–25)*.

[2] To be released from care and eligible to donate, these patients should have a negative result on reverse-transcriptase polymerase chain reaction (RT-PCR) on two blood samples (drawn 48 hours apart).

All these conditions make convalescents especially vulnerable to even slight coercion or to additional physical burdens if blood donations are to be considered.

3. Ethical analysis and recommendations

The WHO Ebola Ethics Working Group emphasizes that priority should be given to providing basic supportive care to everyone with Ebola virus disease and to preventing the spread of the epidemic. For the sake of efficiency, and to maximize the benefits of efforts, interventions with known benefits should be given priority. In the context of experimental interventions, for the sake of fairness, priority should be given to studying promising interventions that (if proven to be safe and effective) could reach the most affected individuals and prevent the greatest number of people from becoming infected or save the lives of people with Ebola virus disease. Given the high mortality resulting from Ebola virus disease and the absence of proven cures and vaccines, providing people with a potentially beneficial intervention – such as convalescent whole blood or convalescent plasma – is ethical, even if its efficacy is unknown *(1)*. The ethical acceptability of providing convalescent whole blood or convalescent plasma is partly supported by the presumed positive risk–benefit balance of these therapies when standard blood safety strategies are being implemented – that is, the risks of negative side effects are considered low when blood safety measures are in place, and theoretical and some anecdotal evidence indicates that people with Ebola virus disease may benefit from these therapies. In addition, the WHO Ebola Ethics Working Group considers that the following issues are ethically relevant in providing convalescent whole blood and/or convalescent plasma to people with Ebola virus disease.

3.1 Gathering evidence

In its deliberations on 21–22 October 2014, the WHO Ebola Ethics Working Group reiterated that *(2)*:

> There is an ethical imperative to carry out research on potential therapeutic agents against Ebola virus disease.
>
> Even in the context of a public health emergency, unregistered and experimental drugs and therapeutics must be tested for safety and efficacy using rigorous methods and simple but properly designed clinical trials. In the context of the current Ebola epidemic in West Africa, WHO has already published recommendations that it is ethical to make investigational therapeutics available outside of clinical trials for "emergency use" provided clinical data from their use is systematically collected and shared. Such "emergency use" should not preclude or delay the initiation of more conclusive investigations of the intervention in properly designed clinical studies. The latter, if appropriately designed and executed, may yield generalizable conclusions that result in greater societal benefit.
>
> The WHO Ebola Ethics Working Group proposed that the term "monitored emergency use of unregistered and experimental interventions (MEURI)" should be used in this case instead of "compassionate use" – a term that can have other meanings, such as use of an investigational intervention for patients outside of an ongoing clinical trial or the indicated scope of utilization.

It is therefore ethically imperative to learn whether convalescent whole blood and convalescent plasma are safe and efficacious for treating people with Ebola virus disease through carefully designed and executed research studies. All efforts must be made to systematically gather relevant data. This includes collecting safety data from transfusions of convalescent whole blood and convalescent plasma, whether under research or monitored emergency use of unregistered and experimental interventions, analysing these data and making them publicly available in an expedited manner without compromising standard and supportive care, donor or recipient confidentiality or

health worker safety. Most crucially, immediate action should be taken locally and internationally to respond to the new risk–benefit information that results from research related to convalescent whole blood and convalescent plasma and to other experimental Ebola interventions. Examples include closing clinical trials or treatment in the context of monitored emergency use of unregistered and experimental interventions if relevant evidence is presented of harm to the donor or the person with Ebola virus disease.

3.2 Disseminating results

Whether such treatment is successful or unsuccessful and whether it is part of research or monitored emergency use of unregistered and experimental interventions, the results should be disseminated as widely as possible to maximize their value in the Ebola epidemic. An important priority in the dissemination plan is to provide for communication in a differentiated form with all relevant audiences, including donors, people with Ebola virus disease receiving convalescent whole blood or convalescent plasma, clinical practitioners and the wider public. People with Ebola virus disease and other stakeholders should also be updated as the trial proceeds and promptly informed on the results obtained.

3.3 Community engagement[3]

Engagement with local communities may be challenging in the context of the Ebola epidemic but is of paramount importance to ensure fair processes in developing and implementing convalescent whole blood or convalescent plasma programmes. This means that stakeholders should have a fair opportunity to participate in deliberations about the future of the community and in the decisions that may affect their lives. Communities should understand the rationale behind interventions with convalescent whole blood and/or convalescent plasma, be involved in developing these programmes and be able to decide whether these therapies are locally acceptable. Community engagement should start early and be as inclusive as possible. The role of families in engagement practices should also be considered, especially since they may be able to offer even more compelling reasons for individuals to cooperate with their community and health systems. However, familial coercion is a concern and should not be ignored (see section 3.6.1).

Community engagement processes need to identify the best ways of conveying not only the uncertainty inherent in research but also seemingly contradictory messages: that contact with the body fluids of a person with Ebola virus disease will transmit the disease and must be avoided, but transfusion of blood from someone who has recovered from Ebola virus disease is safe, if the donors' blood is properly screened for infections and is compatible with that of the recipients, and might help treat the people with the disease. All efforts should be made to avoid misunderstandings, since they can potentially lead to increased contagion, fuelling public distrust of officials and health-care workers, and creating even more difficulty in controlling the spread of the epidemic. This is especially important in the context of the affected populations, in which anxiety about blood theft, sale and vampirism is not uncommon *(26)*.

Communication efforts should also consider relevant cultural issues, since these may affect the acceptability of donation in communities. For instance, community engagement strategies could consider incorporating an educational component to address the fears of people who have recovered

[3] WHO interim guidance on community engagement and education, recruitment and retention of people recovered from Ebola as potential blood donors for convalescent blood and plasma (being developed) will provide further information on WHO recommendations on community engagement practices.

from Ebola virus disease. Given the current stigma attached to Ebola virus disease, community engagement could additionally provide an opportunity to foster understanding in the community about the disease and facilitate the reintegration of survivors into the community. As the number of people who have recovered from Ebola virus disease grows, they should be encouraged to help in leading community engagement efforts. For example, survivors could take an advisory role in ethics review committees reviewing trials using convalescent whole blood and convalescent plasma.

Once convalescent whole blood and convalescent plasma start being collected, requests will probably be made for sharing this resource across national borders. As an act of solidarity, sharing convalescent whole blood and convalescent plasma seems to be a laudable practice, but there are potential safety and product liability issues as well as ethical concerns related to ownership, fairness and justice that need to be analysed further. As recently introduced in Europe, setting up an international panel of experts in infectious diseases and transfusion medicine that includes ethicists should be encouraged to address these issues in a practical and timely way.

3.4 Donors and recipients as research participants

Convalescent whole blood or convalescent plasma should preferably be used within a framework of research (see section 3.1), without compromising health worker safety or the health care provided in the health facility. In the research setting, the donor's plasma might be subjected to further scientific investigations (such as for anti-Ebola antibody titres), and both the donor and the recipient would become research participants; this needs to be clearly explained to them prospectively so that they can voluntarily decide whether they want to participate. Participants' right (both donors' and recipients') to withdraw from the study at any time without penalty or loss of benefits (such as standard of care) should also be clearly communicated.

3.5 Ethical oversight

Even though the Ebola outbreak constitutes a public health emergency, any research that is undertaken must adhere to high ethical standards. Local ethics committees should therefore provide rigorous ethical review for research protocols and should seek assistance from international and other organizations when needed For example, to help assess the technical and scientific validity of newly proposed study designs. In turn, international and other organizations have a moral duty to provide such assistance to local ethics committees in a timely manner. Similarly, the use of convalescent whole blood or convalescent plasma outside research should be governed by the ethical principles of non-maleficence, beneficence, justice and respect for persons.

3.6 Donor-related issues

This section outlines ethical issues related to donors of whole blood or plasma, whether they are asked to donate for a research study or as part of monitored emergency use of unregistered and experimental interventions.

3.6.1 Autonomy

3.6.1.1 Voluntariness

All blood and plasma donation should be voluntary and non-remunerated *(27,28)*. A strictly voluntary approach to blood donation is consistent with emphasizing the importance of donors' altruistic contribution and the principle of human dignity insofar as not using a human body or its parts as a source of financial gain *(29)*. Identifying donors of convalescent

whole blood or convalescent plasma may be straightforward during the epidemic, since potential donors are likely to have been treated in a facility for treating people with Ebola virus disease. One might ask survivors when they leave a treatment facility whether they would be willing to volunteer to donate blood or plasma after they have fully recovered. Such a request should be done in a manner that does not exert undue pressure; for example, by providing counselling services.

3.6.1.2 Obtaining informed consent[4]

An informed consent process for donors is essential both for research studies and as part of the monitored emergency use of unregistered and experimental interventions. Potential donors should be well informed about the rationale for donating their blood or plasma, the potential benefit of their donation to other people with Ebola virus disease and the risks connected with the procedure to them so that they can make informed decisions. For illiterate donors, a witness should be present during the informed consent process. Where applicable, potential donors should also be informed that they could be contacted again for further donations, and they need to be given the option to opt out at any time.

3.6.1.3 Avoiding coercion and exploitation

Respecting donor autonomy also means that potential donors should be neither coerced nor exploited. In the context of donating convalescent whole blood and convalescent plasma, coercion refers to threatening people who have recovered from Ebola virus disease to donate, whereas exploitation refers to any practice leading to an unfair distribution of the burdens of and benefits from donation. An example of exploitation is accepting repeated donations from one person who has recovered from Ebola virus disease irrespective of his or her health status. Since the demand for convalescent blood and plasma may exceed the supply and the intervention has the potential to save lives, communities and families are likely to have huge expectations from people who have recovered from Ebola virus disease. Several options exist to protect people convalescing from Ebola virus disease from undue pressure, coercion and/or exploitation to donate.

- Independent counsellors could be made available to approach potential donors and provide them with relevant donation-related information in a neutral manner regarding the individual risks of donation, the use of donations, community benefits and the voluntary nature of donation, so that donors can – if they so wish – refuse a donation without feeling pressured or obliged to accept becoming a donor.
- Donors' safety should be scrupulously safeguarded, especially through setting limits on the age of the donor, the quantity of blood to be donated at one time and the interval between subsequent donations to avoid compromising the potentially fragile health of people convalescing from Ebola virus disease. The criteria for assessing donor suitability should be based on WHO guidelines and effectively implemented. Donors' well-being should be sought and monitored for, and donation-related injuries and adverse reactions should be promptly managed and recorded.

[4] For an example of an informed consent form for the donation of convalescent whole blood or plasma to treat Ebola virus disease, please refer to the WHO technical interim guidance on use of convalescent whole blood or plasma collected from patients recovered from Ebola virus disease for transfusion, as an empirical treatment during outbreaks *(30)*.

- Sites should consider banking convalescent whole blood and convalescent plasma donations rather than giving them directly to patients with Ebola virus disease. This would help protect the identity of donors and prevent exploitative practices.
- Communities and families should be informed that the blood of every person convalescing from Ebola virus disease may not be useful and that certain tests may be required to ascertain the usefulness of a blood donation. Such messages could protect people convalescing from Ebola virus disease who voluntarily decide not to donate blood or plasma or who are otherwise unfit for donation from possible harassment by community members.

3.6.2 Fair selection of donors

Donations from people who have recovered from Ebola virus disease should only be accepted when the donation is considered safe for the donor and when mechanisms are in place to guard against the exploitation of potential donors. This should be rigorously assessed by a competent health-care worker.

Children

The minimum age of donation should be in accordance with international guidance on blood donation and national legislation on consent. Because children are at increased risk of vasovagal reactions and adolescents have higher iron requirements, children who have recovered from Ebola virus disease should in principle be excluded from donation (in accordance with WHO guidelines for donor selection *(31)*) due to a lower benefit–risk ratio. If there are a disproportionately high number of people who have recovered from Ebola virus disease within this age group, however, relaxing the minimum age of donation to include minors older than 16 years of age may be ethically permissible if: (1) the minors fulfil the standard physical and haematological criteria required for blood donation and (2) the minors and their parents provided appropriate informed consent. Minors should be able to fully comprehend, be properly informed and agree to the donation of blood and/or plasma, and their parents or guardians should not overrule their decision regarding donation.

Other persons with diminished autonomy[5]

The acceptance of individuals with diminished autonomy (e.g., individuals with current or recurring mental health problems) as blood donors should depend on (1) an assessment of their ability to give informed consent to the donation process, including the testing of their blood (31), and (2) the existence of sufficiently robust mechanisms to ensure that donors with diminished autonomy are neither coerced to donate or subject to exploitative practices. Such mechanisms could include an ethics committee that reviews these requests on a case-by-case basis. Where the criteria above are met, both the individual with diminished autonomy and a family member or legal representative should provide appropriate informed consent.

3.6.3 Confidentiality

The identities of people who have recovered from Ebola virus disease must be carefully protected from wider disclosure to protect individual freedom to refrain from donation. Likewise, transfusion should be anonymized, which means that the identities of donors and recipients should be

[5] An individual is considered to have diminished autonomy when he/she has restricted capability of deliberation about personal goals and limited ability to act under the direction of their deliberations.

confidential. To do this, sites should consider storing the donated blood and plasma rather than conducting one-to-one transfusion services with direct donation of blood or plasma to a specific person such as family members or friends (see also section 3.6.1.3 above). To further protect the confidentiality of donors, treatment centres should store blood and plasma units using only ID numbers instead of identifiable information and ensure adequate disposal of unused units. Access to areas where confidential donor, patient or staff records are stored should be restricted to authorized staff *(32)*.

3.6.4 Reimbursement for donation

Donation is considered an act of solidarity, compassion and altruism, and there is international agreement that individuals should not receive payment for donating blood or plasma *(33)*.[6] Nevertheless, reimbursing donors for any expenses directly associated with donation, such as travel expenses, is reasonable.[7] In the context of Ebola virus disease, other non-financial forms of recognition such as public recognition of donors as community heroes and dietary supplementation – especially for repeated donors – could also be considered depending on the context. At a different level, people who have recovered from Ebola virus disease may be in a desperate financial situation themselves *(23,24)* and may demand payment for their donation of blood or plasma, thereby exploiting the people who currently have Ebola virus disease. The health system should guard against such situations by providing social support for people who have recovered from Ebola virus disease and having clear guidelines and regulations against such practices. For example, as suggested in the WHO interim guidance on community engagement being prepared, communities could consider providing people who have recovered from Ebola virus disease with integration support packages containing basic household amenities if these have been destroyed.

3.7 Recipient-related issues

This section outlines ethical issues related to the recipients of convalescent whole blood or plasma transfusion, whether they are part of a research study or participating in monitored emergency use of unregistered and experimental interventions.

3.7.1 Fair selection of people with Ebola virus disease

Since the need for transfusion of convalescent whole blood and convalescent plasma may exceed the available supply, the principles used to set priorities for the intervention should be agreed through a consultative process. Utilitarian principles suggest that priority should be given to those who are most likely to benefit from the intervention, or to those who are most likely to benefit the health system if the treatment is successful. On the other hand, equity considerations suggest that those who are sicker or those who are more vulnerable, such as pregnant women and those with diminished autonomy (including children and people with mental disabilities) should not be arbitrarily excluded from these interventions. Public engagement and involving relevant stakeholders should be part of the priority-setting activity. The process used to develop the priority-setting criteria should be fully transparent and involve the governments of the affected countries or their representatives, a panel of experts in infectious diseases, transfusion medicine and ethics as well as communities in a

[6] WHO has adopted the Code of Ethics for Blood Donation and Transfusion *(29)*.

[7] This is in accordance with the principles of voluntary, non-remunerated donation found in the Code of Ethics for Blood Donation and Transfusion *(29)*.

participatory and inclusive manner to avoid creating a perception of unfair allocation, frustration or public distrust of health systems and health actors, national and/or international.

3.7.2 Autonomy

3.7.2.1 Voluntariness

The ultimate choice of whether to receive convalescent whole blood or convalescent plasma must rest with the people with Ebola virus disease, and their choice should not affect the care they would otherwise receive: standard supportive care should always be provided. Accordingly, people with Ebola virus disease should be given the option to opt out of treatment with convalescent products at any time. For minors, consent from parents or guardians and assent from older minors should be obtained. An objection by a minor to take part in research should generally be respected even if the parents have given permission *(35)*. However, when the investigational therapy shows promise of therapeutic benefit and there is no alternative therapy, a parent or guardian may override the child's objections to participate *(35)*. When a child who is nearly capable of independent informed consent objects, the investigator should seek the specific approval of the scientific and ethical review committees before giving the investigational therapy. Situations of disagreement between the parent or guardian and the clinician regarding transfusion should be anticipated and mechanisms put in place to ensure that the child's well-being is protected.

Given the many children who have lost either one or both parents to Ebola virus disease *(36)*, parents or guardians may not always be available to consent for the participation of their children in research. To ensure that orphans are not unfairly excluded from research, especially if it has potential therapeutic benefit, because they lack an adult representative to consent for them, countries should appoint responsible committees (such as the ethics committee or the management committee of the treatment centre) to make the necessary decisions on a case-by-case basis.

3.7.2.2 Informed consent[8]

The extent of uncertainty about the efficacy and safety of convalescent whole blood and convalescent plasma in treating people with Ebola virus disease should be clearly acknowledged and transparently communicated to each potential person with Ebola virus disease, whether they are part of a research study or of monitored emergency use of unregistered and experimental interventions, to avoid fostering unfounded expectations and to ensure that prospective people with Ebola virus disease make informed decisions regarding treatment. Information should also be provided to patients with Ebola virus disease regarding the possible uses of their medical records and of any biological material collected in the course of the intervention (for research or monitored emergency use of unregistered and experimental interventions). Further, recipients should be told whether collected data and biological specimens are planned to be destroyed at the end of the intervention, and if not, details should be provided about their storage and possible future use. Patients with Ebola virus disease should have the right to decide about such future use, to refuse storage and to have the material destroyed. The informed consent of recipients should also be amended if

[8] The WHO technical interim guidance on use of convalescent whole blood or plasma collected from patients recovered from Ebola virus disease for transfusion, as an empirical treatment during outbreaks *(30)* provides an example of a consent form for Ebola treatment with experimental convalescent whole blood or plasma therapy.

new information becomes available that could affect the willingness of subjects to receive convalescent whole blood or convalescent plasma.

Innovative approaches to the standard informed consent process (such as video or audio recordings and surrogate consent) may need to be considered to account for the contextual limitations outlined below.

- Patients are treated in isolation wards, and limited numbers of health-care workers are allowed inside the treatment area.
- Health-care workers can only spend a limited amount of time inside the treatment area and are in personal protective equipment, which limits the opportunity for normal communication-
- The patients' relatives or next of kin are not allowed inside the treatment area.
- Some patients may be illiterate.

Researchers should anticipate that there will be situations when the person with Ebola virus disease is unconscious or otherwise too unwell to understand the risk–benefit ratio of these therapies and obtain prior ethics approval for seeking consent from the next of kin. Information and possible consent should be considered from the severely sick patient, as soon as he or she becomes well enough to discuss the treatment. Situations in which a person with Ebola virus disease is unable to give consent to participate in research and the person's representative is not available should be anticipated, and prior ethics approval should be sought, especially when convalescent whole blood or convalescent plasma is planned to be given as part of a research trial.

3.7.3 Maintaining a positive risk–benefit ratio for recipients

It is ethically imperative that the risks to people with Ebola virus disease be minimized as much as possible. Given the uncertain efficacy of using convalescent whole blood and convalescent plasma in treating patients with Ebola virus disease and given the prevalence of other transfusion-transmissible infections in the communities where the Ebola virus disease epidemic is occurring, no shortcuts should be taken in screening donor blood for other infections and for signs of residual Ebola infectivity (for example, RT-PCR as a surrogate for infectivity). Complying with safety standards avoids adding risks to an intervention of unknown benefits and thus maintains a positive benefit–risk balance. Thus, strictly applying protocols to ensure compatibility between the donor and the recipient and safety regarding transmissible infections is mandatory. Developing haemovigilance systems to monitor, investigate, manage and record any adverse transfusion events is also highly recommended.

3.7.4 Confidentiality

The confidentiality of patients with Ebola virus disease should be protected to the maximum extent possible. In particular, the data and biological samples should be coded (assigning an ID code or number), and all documents that allow identification should be accessible to authorized staff only.

3.8 Issues related to health workers and research and ancillary staff

Handling infectious blood samples is associated with several types of risks. Personnel working in donation and treatment sites therefore need to be provided with adequate safety standards, including appropriate personal protective equipment. They also need to be adequately trained in international standard procedures for preventing Ebola virus transmission and for treating patients with Ebola virus disease with convalescent whole blood and convalescent plasma. Health-care workers and research and ancillary personnel also need to be well informed about the risks of the procedures they may undertake and agree to be implementers of these interventions, whether they are part of research or part of monitored emergency use of unregistered and experimental interventions. In any case, the risks associated with these procedures need to be minimized as much as possible.

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Appendix I

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Prof Arthur Caplan	Drs. William F and Virginia Connolly Mitty Professor Director of the Division of Medical Ethics NYU Langone Medical Center's Department of Population Health	USA
Dr Marion Danis	Head, Section on Ethics and Health Policy; Chief, Bioethics Consultation Service, National Institutes of Health	USA
Prof Ogobara Doumbo	Director Malaria Research and Training Centre,University of Bamako, Mali	Mali
Prof Jennifer Gibson	Sun Life Financial Chair in Bioethics; Director, Joint Centre for Bioethics; Associate Professor, Institute of Health Policy, Management & Evaluation, University of Toronto	Canada
Ryuichi Ida	Member of the Expert Panel on Bioethics (National Bioethics Committee), Japan	Japan
Dr. Amar Jesani	Independent Researcher and Teacher (Bioethics, Public Health); Editor: Indian Journal of Medical Ethics (https://ijme.in); Visiting Professor: Centre for Ethics, Yenepoya University, Mangalore.	India
Robinah Kaitiritimba	Community representative, Makerere University IRB; Uganda National Health Consumers' Organisation (UNHCO)	Uganda
Dr Bocar Kouyate	Special advisor to the Minister of Health (earlier, Chair of National Ethics Committee); Patient representative	Burkina Faso

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Prof Melissa Leach	Director, Institute of Development Studies	United Kingdom
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Prof Oyewale Tomori	President, Nigeria National Academy of Sciences	Nigeria
Dr Aissatou Touré	Head, Immunology Department; Pasteur Institute Member, National Ethics Committee	Senegal
Prof Ross Upshur	Canada Research Chair in Primary Care Research Professor, Department of Family and Community Medicine and Dalla Lana School of Public Health, University of Toronto	Canada
Cong Yali	Associate professor of medical ethics, Department of Medical Ethics, Peking University China	China