This document considers the clinical trials that are planned as part of the Ebola outbreak response from a sociological and anthropological perspective. It develops a series of critical and empirical questions to guide research that should be conducted within, alongside or separate from clinical interventions. This document primarily focuses on trials that will be conducted in countries currently experiencing intense transmission of Ebola.

Introduction

As the West African Ebola Outbreak continues to elude conventional methods of containment, novel therapeutics and vaccines have been presented as a reason for hope. The acceleration of pharmaceutical development is, in many ways, unprecedented: from the international collaborative consortia organized to fund, conduct and share the outcomes of clinical trials to the support from regulatory agencies, WHO, NGOs and African governments to loosen the restrictions on the use of non-validated agents in afflicted populations. Promising candidates have moved from preclinical studies to human trials in a matter of months; after initial Phase I safety and dosage trials in North America and Europe, investigations with African volunteers have already begun, with tens of thousands to be enrolled by early 2015.

The fast-tracking of production has, remarkably, also been characterized by a deliberative robustness. A series of multi-agency, international and interdisciplinary consultations have been organized at the WHO to consider the appropriateness of placebo, randomization and informed consent for investigations in an outbreak context (WHO, 2014). Adaptive trial designs that include cluster randomization, single-armed and stepped-wedge studies—characterized by frequent interim analysis and stopping rules for efficacy—have been suggested as a way to balance the urgent therapeutic needs of afflicted populations and the regulatory imperatives of generating sound safety and dosage data (e.g. Halloran et al., 2010). These compromises between efficiency and rigor are hardly straightforward; departure from the ‘gold standard’ has precipitated polarized discussions about standards of care and the moral burden of compassion for dying populations as opposed to the undue risks posed to vulnerable subjects.

The ethical repercussions of the randomized design and placebo in an emergency context have been debated at length (e.g. Adebamowo et al 2014; Marshall 2007; Rid & Emmanuel 2014; Shaw 2014). In terms of meting out the moral principles of clinical equipoise (Freedman 1987) of experiments in an emergency context, there is little we
would hope to add. Rather our aim is to situate these debates within the broader socio-cultural dynamics, histories and politics of global health research, raising some practical concerns about how clinical trials will touch ground in afflicted communities. In what follows, we address the proposed interventions—vaccines, therapeutics and convalescent blood or plasma—in turn. Parsing the particular set of issues these fast-tracked investigations raise, we aim to provoke more nuanced consideration of the everyday realities of research in these contexts. Ultimately, we argue that attention to these complex social dynamics provide insight into enhancing clinical trial design, ethical conduct, performance and outcomes in the context of a medical humanitarian emergency.

The Platform Working Group on Clinical Trials is developing a set of questions and concerns oriented towards a specific array of investigations. These issues will be briefly summarized in the second part of this document and expended upon in separate working documents on vaccines, therapeutics and convalescent blood. In addition, the Working Group has begun to develop a set of cross-cutting themes on emerging biomedical tools for Ebola.

Cross-cutting themes for anthropological study on Ebola trials

Understanding Publics
Ultimately, these trials are to be carried out under the goal of improving public health. Anthropologists have previously highlighted that the ‘public’ in public health is plural (Prince & Marsland, 2014), with different groups seen as target beneficiaries in different programmes and agendas, but that this multiplicity is often obscured in the way public health is talked about. The current Ebola trials evoke different publics of public health, with different possibilities for benefit. We seek to examine multiple the “publics” involved in CTs and showcase how differences in material, conceptual and interpretive worlds are likely to influence them: how, for instance, CTs evoke expectations and amplify anxieties, generate rumors and entrench inequalities. We will seek to give ethnographic depth to the social networks, power relations, forms of stigma, therapeutic care, socio-political realities that foster fear and expectations.

Key foci of research include:

a) Building Partnerships: How meaningful partnerships will be built, for example with local investigators that include local scientists and those responsible for both social research and community engagement. What arrangements will be put in place for training and mentorship, collaboration and capacity building and how might they acknowledge and address inequalities? (Geissler & Okwara 2014)

b) Identifying the community: With whom engagement will be required, how should they be involved and then who is the wider public? This will differ depending
on the research protocol, the target group, immediate community of potential participants, and different layers of stakeholders. In development interventions more broadly, there are often misconceptions about how the selection of people to participate in research operations and advisory groups happens and what the benefits (or costs) of inclusion might be. Often those identified as gatekeepers in a community (e.g. chiefs) are viewed by other members as hoarding resources, or perceived to grant access to these resources on an unfair basis. This means also engaging with different kinds of leaders/stakeholders, i.e. not only chiefs and secret society elders but also those who are less officially identifiable (e.g. youth leaders, occupational associations/social clubs leadership). This might be one way to overcome very low levels of trust in international/government actors, while also recognising that there may be lack of trust inside communities. Additional attention should be paid to socially marginalized population groups and subpopulations as they may lack representation or be missed entirely—e.g. nomadic groups, men who have sex with men or others.

The Social Lives of Protocols
In a context characterized by severe staff shortages and poor infrastructures, designing and maintaining protocols for CTs at the local level, enrolling participants, ensuring that standards across disparate clinical contexts and negotiating patient/family preferences for treatment/care, presents some serious challenges. The disparate clinical and geographical contexts involved in these CTs may create unforeseen challenges in this regard that should be noted and explored (e.g. Lawton et al, 2012). To grapple with the realities of clinical research, we will focus on the translation of global guidelines into local settings. Contextualizing the research process could provide valuable insights to guide practice, and situate data. Such attention to how the protocol travels, can encourage a flexible mode of engagement, ensuring local anxieties are meant and responded too, reinforcing trust in the research team.

a) Communicating inclusion/exclusion. Addressing the perception that certain communities are being helped while others are not will be a highly sensitive area. Local interpretations of such ‘selection’ are inevitable, and may evoke concerns both about exclusion from what is perceived as a positive intervention or about inclusion in a dangerous one, and are likely to become politicised. Attending to these, and responding in a timely and appropriate manner, may help to avoid distrust.

b) Informed consent: A number questions remain about obtaining informed consent and conveying the experimental nature of these trials in a situation where there is a lack of existing preventative and curative solutions. Beyond ensuring patients are informed, what is critical is understanding the social process of the exchange of information and care, which entails responsibilities beyond the signing of a document.
c) **Taking of Blood:** Addressing potential concerns about taking blood as part of the trial; the amount that will be taken, where it will be sent to, what tests will be done on this blood, as related to people’s understandings of the relations between blood and strength/wellbeing, as well as to perceptions of a transnational political economy in blood.

d) **Reimbursement:** Reimbursement of participants; how, what amount, when? How do perceptions of likely payment (grounded or otherwise) affect willingness to participate?

**Hope and Trust**

In contrast to the AIDS epidemic where patients became actively involved and a force in the design of trials, here they rely on family, and local instantiations of government to indicate levels of acceptability and voice concerns. What needs to be borne in mind is that these trials, despite the uniqueness of the consortia, are still being conducted by pharmaceutical companies despite taking place in a situation widely described as “market failure” (Lezaun & Montgomery 2014; Moran and Stevenson 2013), where public-private partnerships have become the primary means to address the lack of financial incentive companies appear to need to indemnify risky expenditure on “neglected diseases of the poor”. Also although vaccines and therapeutics offer significant hope there are many unanswered questions about the dose or supportive care needed and for vaccines, the duration of protection offered. It is important to bear this uncertainty in mind because there is a risk that the ‘hope’ and investment placed in vaccines and therapeutics by the international community could overshadow the need to focus attention on the need to rebuild health systems.

a) **Rumours & Representation.** Dealing with rumours and concerns requires developing a comprehensive engagement strategy with a variety of local stakeholders in an emergency context. This demands pragmatism, and increasing levels of involvement over time. To be successful, there is a need to critically assess who should be involved. There is a need to understand public perceptions of existing research institutions; what other non-government programmes should be involved in trial implementation (e.g. Medicines sans Frontiers, Save the Children) who may be playing a dual role of clinical-researchers for the first time? Such institutions need to gain trust and build partnerships, but how? This will be complex given that trials are primarily led by international organisations and local public health institutions, some of whom have been subject to conspiracy theories.

**Resources, Care and Capacity Building**

Whether investigating preventative or curative agents, trials will require substantial resources in order to produce the level of evidence needed to assure efficacy and to guard against potential negative effects. There are questions over whether investments into these investigations will come at the costs of longer-term investments in public health infrastructure. A requirement of clinical trials is to prioritise based on urgency
of immediate treatment, highest standards of care and particular harms/benefits analyses. However, clinical trials bring with them financial and clinical resources which could be directed towards the training of local staff, improving health centers and even strengthening communities through engaging and compensating volunteers—activities that could have an immediate impact as well as long-term. A critique of short-term compensation (e.g. in public work schemes) has been that once the intervention is over, individuals find themselves in the same position as before, but with heightened social pressures as they are perceived as having had access to resources—so perhaps important to consider how these can be made sustainable long term as well. Decisions on how trials are set up, run, resourced and integrated locally will be key to realizing this positive potential of trials.

a) *Financing and impact on services.* How these clinical trials will be financed and how this will affect the provision of other essential health care services. Given the fragile health infrastructure as well as diverse epidemiological, social, historical and political contexts in Guinea, Sierra Leone and Liberia, how can clinical trial teams ensure longer-term sustainability, and protocols that are relatively standardized and comparative across very different clinical contexts? What can be done to ensure that communities where trials take place (in addition to individuals participating in trials) experience longer term material benefits from treatment and vaccine trials? Might this access be extended to all potential future sufferers on a humanitarian basis?

b) *Indemnity and access to medical care* during and post-trial: who will cover this? Discussions about this between pharmaceutical companies and the World Bank need to be opened up to wider discussion with representation from wider shareholder groups (i.e., the public funders of research and development). Securing funding, availability and rapid access of the successful vaccines for future outbreaks needs attention at this stage.

**The Political Economy of Clinical Trials**

Biomedical solutions provide the optics of tangible “successful outcomes” for donors. But they tend to prioritize short-term investments over long-term capacity and social mobilization. We suggest the current drive might best be situated within lessons learned from AIDS and malaria vaccine work. We plan to follow the funding, mergers, donor agendas, social construction of knowledge, and power; tracking financial flows relative to the actual cost/benefit and harms of trials.

a) *Funding:* Who is getting funded and why? Do experts agree about the safety and efficacy of these experimental therapies and, if so, what propels an experimental vaccine through to regulatory approval?

b) *Collaboration:* How are CT teams formed and coordinating with government and non-government agencies? It has been suggested that coordination and governance gaps are opening up between global agencies and governments
(New York Times, 2014). Are there gaps in this collaboration and coordination? How much money is going into these CTs relative to other emergency response areas? These trials appear to be attracting a huge amount of attention in the international media – what does this reflect and what does it neglect?

c) **Reading Results:** How are protocols developed in emergency settings? How are international teams established, local investigators involved, and how are protocols translated and implemented in practice between Industry, Principal Investigators (PIs), national and local health authorities, local researchers and then nurses/fieldworkers and participants? What is lost and transformed in translation and how does this influence the scientific data and interpretation of results? This requires close review to ensure that trials are conducted with due reference to optimal humanitarian values that include cultural considerations whose dismissal can account for potential problems that undermine the integrity of data and the trust of participants and local stakeholders. Recognizing the need for urgent response, investigators need to take great care that study procedures are feasible, coherent and understood in the local context, and implemented in a sensitive manner.

**Questions around specific investigations**

For each investigation type (vaccines, therapeutics and convalescent blood/plasma) we list candidates known to us, and information on their modes of action, how they will be implemented in trials and logistics of that candidate, as far as we know at this time.

**Vaccines**

<table>
<thead>
<tr>
<th>Candidate*</th>
<th>Manufacturer</th>
<th>Mode of Action</th>
<th>Investigation</th>
<th>Logistics</th>
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<tbody>
<tr>
<td>cAd3-ZEBOV</td>
<td>GSK/NIAD</td>
<td>Non-replicating chimpanzee adenovirus, EVD surface protein, 100% efficacy in NHP, bivalent (Zaire &amp; Sudan) and monovalent products (Zaire) are available</td>
<td>Phase 1 USA/UK; Results in 20 volunteers are promising, bivalent studies are also planned but only monovalent for scale-up; phase 2 in early 2015 in affected countries, design undecided</td>
<td>Storage at -70C, sterile injection, HCWs can administer</td>
</tr>
<tr>
<td>rVSV-delta GZEOV</td>
<td>Newlink Genetics/Public Health Agency of Canada/Merck</td>
<td>The rVSV live vaccine aims to induce EVD-specific immune responses, 100% efficacy in NHP</td>
<td>Phase 1, Canada, Germany, USA, Gabon and Kenya; Phase 2 2015 in affected countries; Phase 2/3 in Guinea with health workers – ring immunization around cases with one group immunised immediately and</td>
<td>Same as above</td>
</tr>
<tr>
<td>MVA-BN® Filo</td>
<td>Baeverian Nordic, Crucell, Johnson &amp; Johnson</td>
<td>This vaccine platform Modified Vaccinia Ankara, MVA, but it contains the same Ebola gene as the cAd3-EBO Z vaccine. It also contains the genes for proteins specific to the Zaire and Sudan strains of the Ebola virus and 1 gene for a protein from Marburg virus.</td>
<td>Part of Phase 1 Oxford trial of cAd3-ZEBOV. 30 trial participants given this booster at different doses. Further plans to use this or similar vaccine in Phase 1 trials in Europe in African (areas not affected by the current Ebola outbreak) Phase 2 trials will be conducted by INSERM and Phase 1 &amp; 3 by LSHTM. Phase 3 will take place in West Africa possibly using a ring-fenced cluster randomized design.</td>
<td>Same as above</td>
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*Please note other candidates are undergoing pre-clinical testing and may be ready for phase 1 & 2 testing within the lifecycle of this Ebola outbreak.

Advanced as one of the greatest public health tools, vaccines hold the promise not only of prevention but also of disease eradication. The history of vaccines and particularly, childhood immunization in Africa, however, is particularly fraught—mass immunization campaigns have had variable successes and failures. Unsafe vaccines and immunization practices in the colonial period arguably precipitated the spread of blood borne infections. The militarized framework of vaccine implementation embodies a legacy of unequal power relations and violence (e.g. Lachenal et al 2010; Moulin 1996; Vaughan 1991; White 2000). Fears that vaccines would lead to sterilization thwarted immunization programs in Cameroon (Savelsberg et al, 2000) in the 1990s and similar concerns, coupled with anti-Muslim violence, brought a polio campaign to a halt in Nigeria (Ghinai et al., 2013; Jegede A.S., 2007). At the same time, injections have been seen as particularly powerful and thus favoured by many populations, even to the extent of being taken up as the preferred mode of delivery for some ‘traditional’ medicines (Whyte et al 2002).

Deployed through national programs and targeted at young children, vaccines trigger great expectations and anxieties in populations in both the developed and the developing world (Fairhead & Leach 2007). The Ebola vaccines come at a time of considerable fear and mistrust by populations of international and national governments. In contrast with therapeutics, which target those who are in immediate need, experimental vaccines will likely be given to those at greatest risk, for example front line workers in contact with Ebola sufferers. Front line workers are a vastly heterogeneous population, ranging from highly trained medical personnel to new burial team recruits who have little or no education. Given the rapidly changing emergency situation and the demand to accelerate vaccine development and production, there is urgent need to pay attention to developing engagement with and between different stakeholders e.g. industry, government and nongovernmental
agencies, health workers, and appropriate public representatives to address existing and emergent concerns.

The Platform Working Group on Clinical Trials are developing a set of questions and concerns to incorporate into plans and research alongside vaccine trials. These include the following:

a) *Selection criteria:* Balancing fair selection of study population and ‘at-risk status’: Rid and Emmanuel (2014) suggest that trained health care workers belong to a privileged group. They emphasize that care must be taken to ensure that all vulnerable groups are considered. Whilst the public may accept that health workers and first line responders are at high risk and there is a moral duty to protect them, a case could be made that others are just as vulnerable. Health facilities have not been able to accommodate all people presenting with Ebola symptoms, which has meant that isolation has not worked and family members and others have continued to be exposed and may have assumed care-giving duties without the necessary protection. There is also evidence of an increase in deaths from other untreated illnesses, including higher maternal mortality due to pregnant women not seeking care in facilities with high risks of contact with EVD and with higher mortality risk if they do contract Ebola.

b) *Vaccine anxieties and vulnerability:* In the context where rumours about immunization may be common it becomes increasingly important to care for the wellbeing of those participating. Observing, for instance, whether participation in a vaccine trial affords participants a false sense of security leading to less vigilance about protection; the use of contraception in female and male participants; communicating the risk (of both EVD transmission for a given period following treatment and after “cure”); as well as long-term follow-up of all participants, with special interest in cases such as children of women who become pregnant. These workers are facing some challenging social encounters with their families and communities (some are hiding the truth about their work). How might these considerations influence their participation in vaccine trials? What potential longer term benefits may be possible for these health workers, for example long-term commitments to training of highly qualified personnel.

c) *Immunization Programmes:* Ebola vaccines may not become part of a routine immunization programme since it is difficult to predict where outbreaks will occur, and there are also different strains of the virus. So whilst a licensed vaccine will be an invaluable tool for response strategies it may not necessarily be of long-term benefit to the communities where trials take place if they do not have ready access in future. How, should CTs integrate with existing systems for vaccine safety monitoring and response, such as the Expanded Programme for immunization (EPI) and the Global Vaccine Safety Blueprint within and subsequent to the CTs? GAVI support may mean that the introduction of Rotavirus vaccination may be delayed, for example. Also how will Ebola
vaccination research and programmes affect the re-establishment of the EPI primary immunization programme towards the end of the outbreak and post-outbreak? How might political will for capacity building be sustained and community health care workers be trained and involved in identifying, monitoring and responding to all infectious diseases as well as adverse events following immunization (Graham et al 2012)?

**Therapeutics**

<table>
<thead>
<tr>
<th>Candidate*</th>
<th>Company</th>
<th>Mode of Action</th>
<th>Investigation</th>
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<tbody>
<tr>
<td>brincidofovir</td>
<td>Chimerix, USA</td>
<td>Lipid conjugate antiviral against cytomegalovirus or adenovirus infections, successful in mice.</td>
<td>Open-label, non-randomized, single-arm trial; site still under negotiation between CDC &amp; Liberian gov. but likely an ETU in Monrovia, inclusion sequential, 140 survival, 14 days survival</td>
</tr>
<tr>
<td>favipiravir/avigan</td>
<td>Toyama Chemical, Japan</td>
<td>Anti-influenza drug inhibits replication of viral genetic material by blocking the enzyme RNA polymerase that is required for multiplication of viral particles after they infect the cells. In Phase 3 trials (for flu) in the US demonstrating safety, successful in four cases of Ebola in France, Germany, Spain and Norway.</td>
<td>Non-comparative, proof-of-concept, phase Ib sequential trial to take place across three sites EVD centres in Guinea, Guéckédou, Guinea, French Institute of Health Research (INSERM), funded by the European Commission; 160 people &gt;than 12 years who; interim efficacy analyses every 20 patients. Primary assessment in 60 adults begin treatment within 48 hours of symptoms. Move into 2b into 3 and design of trial in Liberia yet to be worked out.</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Italian non-governmental organisation Emergency.</td>
<td>Amiodarone, a multi-ion channel inhibitor and adrenoceptor antagonist, showed in preclinical studies to be a potent inhibitor of filovirus cell entry. Used for decades on millions of patients, its problematic safety profile is well known in N. well resourced settings for arrhythmia (but it can cause serious noncardiac toxicity and may be less well suited in resource-poor countries). In a controversial case, the NGO Emergency administered the drug as a compassionate therapy to 65 patients in a treatment centre in Lakka in 2014.</td>
<td>A phase III trial is expected to start, when a 100 bed hospital recently built by the UK Department for International Development will be entrusted to Emergency. The hospital is one of six built as part of Britain’s £250m (€314m; $395m) effort to fight the Ebola virus in Sierra Leone.</td>
</tr>
<tr>
<td>ZMapp</td>
<td>(LeafBio, Inc.), a San Diego based arm of Mapp Biopharmace</td>
<td>ZMappTM is not a serum or serum derived product. It is composed of three monoclonal</td>
<td>Plans for a trial are being discussed</td>
</tr>
<tr>
<td>LeafBio created ZMapp in collaboration with its parent and Defyrus Inc., each of which had developed its own cocktail of antibodies, called MB-003 and ZMab.</td>
<td>Antibodies directed against the Ebola Zaire virus strain. The component monoclonal antibodies were licensed from Defyrus (Toronto) and USAMRIID, humanized and recombinantly manufactured in a variety of tobacco (Nicotiana benthamiana)</td>
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*Other drug candidates are also being developed and may be ready for human trials during the course of this Ebola outbreak.

Conducting medical research in resource-poor contexts engenders a raft of logistical, political and ethical challenges. The so-called ‘therapeutic misconception’, or the tendency of populations to confuse clinical trials with medical benefits, is one of the most glaring discrepancies between scientific protocols and local health care realities (e.g. Geissler & Molyneux 2008; Molyneux, Peshu, & Marsh, 2004). These local standards of care underpinned the scandalous short-course AZT trials conducted across Africa in the mid-1990s, whereby treatment known to prevent mother-to-child transmission of HIV/AIDS was compared with a placebo (c.f. Angell 1997). While the case was made for rapid, clear and contextually relevant results, the advantages of structural inequities in reducing the costs of trials were hard to ignore (Petryna 2005).

The Ebola drug trials will take place in the shadow of AZT, and other related experiences (Page-Shafer et al., 2005; Ezeome and Simon, 2010; Calain, 2014). What is distinctly different about the regimens on trial is that they have not been tested and there is a genuine lack of knowledge about their safety and efficacy. Also they are targeting a disease with a known, rapid and high fatality rate (unlike slow onset AIDS) and therefore populations are likely to want access to these drugs as they present hope for a possible treatment. A recent expert consultative meeting concluded that: “for all these drugs, there is only suggestive preclinical evidence of efficacy” (WHO, 2014). However, questions around the standards of care will remain central to how populations respond to these experiments. The fact that this outbreak is the direct result of poor health infrastructure is uncontested (Abramowitz, 2014; Petit et al, 2013; Svoronos et al, 2014). Liberia had one doctor for every 100,000 patients, before the number of health workers were decimated by Ebola. Leaving aside for the moment the logistics of conducting complicated trials in such a context, the question of what should be compared looms large (e.g., Adams et al., 2005). While there is no currently authorized treatment for Ebola, expats who have been spirited away have done rather well – regardless of whether they have received experimental treatment. Indeed, one of the arguments put forward for undertaking trials is to provide improved standard of care. Paul Farmer, for instance, has boldly claimed that with early diagnosis and
aggressive supported care including rehydration and blood transfusions as many as 90% will survive (Farmer 2014).

Comparing drugs against a standard of care that involves overcrowded and understaffed health centers, stressed doctors with limited resources could produce some clear and quick results as to the efficacy of these treatments. With their frontline staff unused to carrying out experimental research, MSF will be providing the care in the brincidofovir trial. This will be of the highest standard and, following adaptive design, all patients will receive the treatment if proven effective. However, the training needed to conduct research, maintain drug regimens and observe and manage side effects, far exceeds the capacity of local health workers and charities. The critical question then becomes whether the highly resourced clinical contexts that will necessarily be built up around the experiments will run in parallel to the health care system, only to evaporate once these projects have concluded (Kelly 2010; Street 2014), and providing evidence of efficacy of drugs provided together with high quality case management, but no evidence of how such drugs would perform in the absence of such resource intensive care, which seems the typical picture across affected countries.

The Platform Working Group on Clinical Trials are developing a set of questions and concerns to incorporate into plans and research alongside trials of new therapeutics. These include the following:

a) **Staff Shortages:** How staff shortages will be managed, particularly considering that delivery of a trial drug requiring a two hour intravenous infusion involves two nurses, able to work for only an hour at a time in required PPE – so four nurses would be required per trial participant. Although primarily a practical question, social science can help inform trade-offs that might need to be made such as reducing numbers of trial participants, or randomizing, which can have social implications in the interpretation of these decisions.

b) **Medical Pluralism:** In hospital settings in Africa, therapeutic landscapes between biomedicine (offered privately or through public systems) and local “traditional” medicines are often mixed as nurses and patients develop innovative ways to deal with scarcity (see Langwick, 2008). This relates to local therapeutics for Ebola that are emerging to deal with uncertainty and the lack of cure. How will CT teams negotiate this pluralistic medical landscape – will they attempt to deny patients from taking other treatments, over-look it or will the allure of a biomedical treatment marginalize other therapies in the eyes of participants? Could the range of therapies being offered to Ebola patients outside Africa be extended as ‘choices’ to Ebola patients in Africa?

**Convalescent Blood and Plasma**
Convalescent blood and plasma is currently being prioritized for investigation by the WHO—this requires the identification and use of Ebola survivors. Using this population is complicated for multiple reasons. Survivors of Ebola have faced ostracism by their communities (Catholic Relief Services et al. 2014; De Roo 1998). Stigmatization and other forms of social exclusion may be related to Ebola’s high mortality rate and unclear origins that associate survivors with invisible networks of power or nefarious plans of the West (Bolten 2014). Following the death of kin and the depletion of their social networks, survivors may also find it difficult to integrate back into communities; they may also face dire economic situations as all their belongings, including their house, working tools and food may have been burned (c.f. Hewlett & Amola 2003; Hewlett & Hewlett 2005). In turn these circumstances can lead to further marginalization. They may also face expectations to become involved in the care of Ebola patients and whilst for some this may be a welcome opportunity others may not feel up to this and may struggle with such moral obligation.

The collection of blood may also pose a particular challenge: anthropologists working across the region have noted that blood is understood as a ‘vital force’ associated not only with good health but also with individual strength and prosperity. A similar set of logics link illness and misfortune to reductions in the quality and quantity of blood (e.g. Bierlich, 2000; Fairhead, Leach, & Small, 2006; Leach et al 2008) or the ‘drying of the body’ brought about through a wasting of blood, which had formerly been plentiful (Ferme & Schmitz, 2014). This ‘blood calculus’ is further amplified in contexts where volunteer blood banks are not supported by systems of national health care and where blood transfusion demands sacrifices from relatives or can result in expensive charges, which in turn, can lead to the clandestine purchase and sale of blood. The HIV/AIDS epidemic and the politics associated with access to therapies has also played a role in the association between the drawing of blood and access to social, political and economic resources (Nguyen, 2010).

Concerns about blood theft, sale and vampirism are common across the Africa continent (e.g. Fairhead, Leach, & Small, 2006; Geissler 2005; Kelly 2012; White 2000). While often dismissed as ‘misunderstandings’, ‘traditional beliefs’, ‘rumours’, ‘metaphors’ or ‘coded expressions of resistance’, anthropologists and historians have shown that these anxieties reflect upon, and make sense of, ambiguous exchanges, resource flows, new technologies and forms of labour—dynamics particularly characteristic of medical research (Geissler & Pool 2006). In addition, anthropologists and clinical researchers have argued that the management of these concerns should become an intrinsic component of clinical research as they present a bottleneck for the ethical conduct of research. The ethical principle of respect for persons, widely recognized as a pillar of medical research implies the specific duty of being sensitive to other cultural perspectives (Peeters Grietens et al., 2014; Bannister-Tyrrell et al., forthcoming).

Blood theft stories are not merely the province of the uneducated and far-flung, often highly nuanced observations interweaving common sense and observations, rumours articulate collective anxieties grounded in long-term engagements with
biomedicine, legacies of unequal relations of power, extraction and exchange (Birungi 1998; Feldman-Savelsberg et al. 2000.). The deep ambivalence about giving blood relates to it being a matter of significance that engenders concerns about its distribution and the need to ensure that this distribution is equitable, that benefits are balanced, and volunteering or host communities are appropriately cared for. With reference to contextualizing anxieties surrounding vampirism Bolten (2014) has an interesting perspective on how notions of witchcraft and vampirism relating to Ebola reflect fears about social breakdown and the deterioration of social relations. This means that anxieties around witchcraft are (as they seem to be) heightened at the moment and thus feed into both conspiracy theories about Ebola and the fear that may be associated with giving blood. Leach's (2014) lecture “Ebola and Beyond” usefully ties notions of sorcery to history and political economy, framing it as a way of making sense of inequality and disempowerment. An understanding of these dynamics may help in designing communication strategies in trials.

The Platform Working Group on Clinical Trials are developing a set of questions and concerns to incorporate into plans and research alongside clinical trials of convalescent whole blood and blood plasma.

a) **Significance of Blood Donation:** In what ways does the cultural significance of blood underpin responses to donation? How might a history of engagement with HIV shape acceptability of uptake and the overlaps between donation and diagnosis? In what ways do the circulation of blood work relate to other substances of contagion, creation and cure i.e. semen? How is the gift of blood shaped by the institutional context in which it is given? Might community members perceive “blood donations” as an exchange for access to resources or an indication of infection (like HIV/AIDS)?

b) **Reciprocity, Compensation and Demands:** What are the understandings of the gift and forms exchange are at work through the act of donation? In what ways are kinships networks and previous expectations relevant for recruitment? What kinds of expectations are placed on trial participants beyond blood donation? What happens at the end of trials?

c) **Stigmatization and Trust:** Considering survivors’ life chances it is important to consider the importance of social networks for survival (both in the sense that one’s status is dependent on access to networks but also, perhaps more importantly, that actual survival in the absence of safety nets is entirely dependent on the ability to rely on ties of reciprocity with others). Being without social networks also breeds a level of mistrust within communities, which might make survivors even less willing to give blood for fear of being further stigmatized.
Contributors
We gratefully acknowledge the following people, in alphabetical order, who contributed to this statement as part of the Clinical Trials Working Group coordinated by the Ebola Response Anthropology Platform:

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Ebola Response Anthropology Platform
The Ebola Response Anthropology Platform (www.ebola-anthropology.net) brings together anthropologists from around the world to provide advice on how to engage with crucial socio-cultural and political dimensions of the Ebola outbreak and build locally-appropriate interventions.

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