Ebola Data Sharing Platform: 
Draft Research Agenda for Public Consultation

PART I: Retrospective Clinical Data Collection

A. Natural History/Pathophysiology

1. What is the evolution of patient symptoms and clinical signs over time?
   a. Earliest symptoms/signs at disease
   b. Frequency of symptoms/signs at presentation
   c. Development of symptoms/signs over time
   d. Can clinical symptoms be linked/related to host factors, viral factors
      and/or health care factors?

2. What psychological symptoms and mental health consequences were
   most common in patients with EVD and how did they change over time?

3. What is the evolution of clinical biomarkers over time in patients?
   a. Viral load
   b. Cycle Threshold
   c. White Blood Cell Count
   d. Haemoglobin
   e. Platelets
   f. C-reactive protein
   g. Electrolytes
   h. Creatinine
   i. Liver transaminases
   j. CPK
   k. Lactic Acid
   l. Base Excess
   m. PTT
   n. Antibody titers
   o. Others

4. Do clinical presentation, psychological symptoms and biomarkers vary by
   time and geographic location over the course of the epidemic?

5. Which host factors are associated with increased mortality risk and
   particular time point of death?
   a. age
   b. pregnancy
   c. co-infections / co-morbidities,
   d. clinical signs
   e. biological signs of organ failure
   f. host genetics
   g. time of onset of symptoms
h. presence and duration of virus in different body fluids
i. health worker status/occupation
j. nutritional status
k. others

6. Which viral factors are associated with increased mortality risk and particular time point of death?
   a. viral sequence
   b. viral exposure level
   c. antibody titers / viral load evolution
   d. others

7. Which health care factors are associated with increased mortality risk and particular time point of death?
   a. previous treatment
   b. previous vaccination, time to vaccination
   c. time to admission, diagnosis and/or treatment
   d. type of supportive treatment, therapeutics and/or nutrition,
   e. isolation
   f. previous admission in holding center and timing
   g. length of stay
   h. others

B. Infectivity

1. What is the duration of the presence of virus (RT-PCR, virus isolation, gene sequencing, culture) in the different body compartments and in the different body fluids?
   a. Is there a difference according to patients characteristics like age, pregnancy, co-morbidities, onset of symptoms?
   b. Is there a difference according to viral factors like viral sequence or exposure?
   c. Is there a difference according to health services factors like time and type of treatment or vaccinations received?

2. What is the link between presence of (viable) virus or positive qRT-PCR results and infectivity?
   a. Does infectivity duration differ according to viral diversity, initial viral load, characteristics of the disease, age, host genetics, co-morbidities, treatment received or other potential co-founding factors?

3. What is the infectivity of infected person with no symptoms or sub clinical presentation? Which body fluids or body compartments are the most likely to be infectious?
4. How long does the virus survive and is potentially infectious on fomites, medical material, equipment and in the environment?
   a. What are factors contributing to prolonging or shortening the infectivity of the virus outside of human or animal bodies?

5. What biomarkers are associated with (or which could predict) infectivity, transmissibility or virulence?

6. What is the proportion of nosocomial infections in patients in transit or holding centers, treatment centers, and non-Ebola health care centers?

7. What is the proportion and type of documented risk exposure (needle stick injury, PPE breach, etc.) faced by health care and frontline workers? What is the proportion of these having received:
   a. RT-PCR diagnosis and follow up
   b. Positive RT-PCR test
   c. PEP
   d. Treatment
   e. Outcome

C. Diagnosis

1. How do we use the clinical and outbreak data to revise and risk stratify the case definition?
   a. How well did various case definitions (MSF, WHO, etc) perform in practice?
   b. What is the best clinical model (combination of clinical/epidemiologic signs) for predicting EVD infection?
   c. Do biomarkers improve upon the clinical prediction of EVD?
   d. What is the best clinical model for EVD surveillance in a low transmission state (outside of an outbreak setting)?

2. What are the test characteristics of different rapid tests for EVD?
   a. Sensitivity, specificity, and reliability
   b. Differences based on assay, setting used, patient characteristics

3. What biomarkers could be used for diagnosis prior to clinical manifestation in exposed persons?
   a. What biomarkers are associated with (or predict) subclinical or mild infections?

4. What are the test characteristics of RT-PCR testing?
   a. Sensitivity and specificity of testing
   b. Differences between assays and types of samples
   c. Geographic, demographic and epidemiologic differences
5. What is the proportion of suspected cases with a second positive RT-PCR after a first negative RT-PCR?
   a. What is the time span between the two tests?
   b. What is the difference in the different geographical locations, management centers, lab platform used?
   c. Is there a difference according to patients’ characteristics like age, pregnancy, co-morbidities, main symptoms, onset of symptoms…?
   d. Are there significant differences in outcome: mortality, complications, early and late survivors’ symptoms?

D. Monitoring

1. Which are the most important vital signs and clinical signs to monitor in an ETU setting?
   a. Which signs are most common over time in patients
   b. Which signs best predict changes in clinical course and mortality
   c. Which signs are most easiest or more difficult to collect?
   d. How does collection of signs (oral versus infrared thermometer for temperature) affect accuracy or usefulness of signs?

2. What are the most important biomarkers to collect in patients with EVD?
   a. What biomarkers are associated with (or predict) effective control, or outcome, of an infection at early, middle or late stages in the course of illness?
   b. What biomarkers are associated with (or predict) different viral loads?
   c. What early biomarkers are associated with (or which could differentiate between) different presentations (syndromes)?
   d. How do identified biomarkers differ in human recipients of different vaccines and therapies compare to those observed in natural infections or untreated infections?

3. What would be the most important biomarkers to follow for EVD survivors with or without symptoms? How frequent and how long should the selected biomarkers be followed?

E. Treatment

1. What measures constitute optimal supportive therapy?
   a. What is the effectiveness of oral and intravenous rehydration?
   b. What is the effectiveness of prophylactic antimalarial/antibacterial medications?
   c. What is the effectiveness of vitamin supplementation? Which vitamins are most helpful?
d. What is the effectiveness of gastric prophylactic medications on reducing gastrointestinal symptoms?

e. What is the effectiveness of various other treatments in alleviating symptoms?

2. What are the types of psychosocial support utilized for patients?
   a. Which forms of psychosocial support were most commonly utilized?
   b. What was the effectiveness of different psychosocial interventions?

3. What are the criteria to engage in palliative care?
   a. Which forms of palliative care are most feasible and effective in the ETU context?

4. Which antiviral therapy is most effective?
   a. Which indication should be used for the different antiviral therapies?
   b. What combination of different therapies would be most optimal and in which indications?
   c. What combination of different therapies should be avoided?
   d. What is the optimal dosing regimen?
   e. What are the biomarkers to follow to adapt dose, duration of treatment?
   f. What are the main side effects?
   g. What are the biomarkers to monitor and treat side effects?
   h. What is the role of antiviral therapy in eradicating the virus?
   i. What is the role of antibody therapies in recrudescence?

5. What is the best option for PEP and what are the time limits for efficacy?
   a. In vaccinated and unvaccinated individuals?

F. Public Health

1. What are the viral, host, behavioural, and social factors explaining the heterogeneity in transmission and susceptibility including super spreader events?

2. How do we integrate genomic sequencing into new case investigation and contact tracing to differentiate chains of transmission and differentiate new spill over events?

3. What therapeutic options may be indicated to prevent or interrupt infection of contacts, those at risk, contacts of contacts (e.g. vaccine, drugs for prophylaxis)?
a. What are the best operational models for their deployment? (e.g. treatment/vaccination of contacts, social networks, rings, etc.)

b. What are the most important symptoms after vaccination (according to vaccine use) their severity and duration?

c. What are the most effective treatments for post vaccination symptoms?

d. What algorithms to use to differentiate post vaccination symptoms from suspected EVD symptoms?

4. What is an ideal way to monitor and detect EVD in a low transmission state (e.g. event-based surveillance, targeted death swabs, skin biopsy)?

5. What are the most effective strategies to maintain non-Ebola health services?
   a. Which would be the non-Ebola health activities to prioritize?
   b. What would be the best strategy for screening in primary health care services (case definitions, temperature monitoring, rapid detection assays...)?
   c. How should healthcare delivery differ? (e.g. hands-off consultation, modified surgical technique, adjusted triage criteria, etc.)

6. What role do health workers/alternative practitioners play in amplifying the epidemic? What is the impact of current PPE use and ICP training?

PART II: Survivor Data

1. What are the main survivors’ symptoms once in convalescence?
   a. What are the main early (within 4 weeks after discharge) survivors’ symptoms/pathologies?
   b. What are the main transient survivors’ symptoms/pathologies?
   c. What are the main persistent survivors’ symptoms/pathologies?

2. What host factors are associated with various post-Ebola psychological and clinical /biological syndromes:
   a. age
   b. co-infections / co-morbidities,
   c. clinical signs
   d. biological signs of organ failure
   e. host genetics
   f. presence and duration of virus in different body fluids
g. nutritional status
h. others

3. What viral factors are associated with post-Ebola syndromes and their resolution, complications or chronicity:
   a. viral sequence
   b. viral exposure level
   c. antibody titers / viral load evolution
d. others

e. others

4. What health care factors are associated with post-Ebola psychological and clinical/biological syndromes and their resolution, complications or chronicity:
   a. previous treatment
   b. previous vaccination, time to vaccination
c. time to admission, diagnosis and/or treatment
d. type of supportive treatment, therapeutics and/or nutrition,
e. isolation
f. previous admission in holding center and timing
g. length of stay
h. others

5. What biomarkers are associated with (or which could predict) post-Ebola syndromes/pathology and their evolution?

6. Which are the most important vital signs, clinical signs and biomarkers (including rqt-PCR of different bodily fluids) to monitor EVD survivors?

7. What treatments are most effective in post-Ebola syndromes/pathologies?

8. Which interventions are effective in preventing or reducing post-Ebola clinical and psychological syndromes (before, during and after disease care in ETC)?

9. Are there other options to detect viral RNA persistence in survivors bodily fluids that the existing qRT-PCR and RDT?
   a. What would be their indication of use and interpretation?

10. What are the criteria to define when survivors can undergo elective surgery for Ebola and non-Ebola related pathologies?

11. What are the precautions and specific infection prevention measures to take while doing invasive procedure or emergency surgery in survivors?
12. What are the risks for fetuses, newborns and infants when their mother is an EVD survivor?

13. What interventions are the most effective for psychosocial (including stigma) problems encountered by EVD survivors?

14. What is the importance of follow up of contacts of EVD patients?
   a. What is the prevalence of psychological syndromes and stigma in contacts?
   b. Which factors influence most psychological syndromes and stigma in contacts?
   c. What is the proportion of contacts with detectable EBOV antibodies?
   d. What is the proportion of contacts with detectable rQT-PCR in any of their bodily fluids?
   e. What are the most important clinical and psychological signs and biomarkers to follow in contacts?
   f. What is the proportion of contacts that has died and what are the main causes?
   g. What is the proportion of contacts that has been vaccinated?

PART III: Data, information and knowledge

1. How best to develop a strategy to collect meta data?

2. How best to develop a strategy to link or integrate laboratory, epidemiological, and clinical data?

3. How best to develop a strategy to further the harmonization, accessibility, and interpretability of data production?