TERMS OF REFERENCE for Unity Studies network sites in the WHO SEARO Region

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PURPOSE

The WHO Investigations and Studies global and regional initiative, also branded Unity Studies, is a suite of enhanced surveillance activities that are harmonized to help provide detailed insights into the epidemiological characteristics of emerging or re-emerging respiratory pathogens of pandemic and epidemic potential (ex. influenza viruses, coronaviruses, etc). They are critical tools to supplement routine surveillance systems to address specific questions, particularly in the early stages of a pandemic, or epidemic, but also over time through a continuous, periodic, or alert-driven (e.g. emergence of a new sub-type, variant or lineage) assessment process. These insights are essential for projections of likely impact of an emerging infectious threat, aiding identification of effective and proportionate response strategies. The study types include population-based age-stratified sero-epidemiological investigations, transmission and severity investigations, vaccine effectiveness protocols and others.

To meet these early surveillance objectives, in-country investigators must be 'shovel ready' in advance of a health emergency. Preconditions for timely and effective implementation include ethically approved protocols for defined populations, clearly identified resourcing, roles and responsibilities to achieve study tasks, and established data governance, sharing, analysis and reporting arrangements.

The COVID-19 pandemic has demonstrated that such studies add value and are achievable in both high and low-middle income country settings with WHO support, supporting capacity development and equity objectives.

The WHO is establishing a global network of sites which will be ready to conduct these investigations and

studies rapidly in the event of a pandemic, or epidemic of an emerging or re-emerging pathogen, and share relevant information with WHO. The network will ensure response readiness for rapid evaluation of influenza viruses of pandemic potential, coronaviruses of pandemic potential and any emerging or re-emerging respiratory transmitted pathogens. Chosen sites will be primed to conduct country-specific standardized, pre-planned and pre-approved studies, exercised during respiratory infection seasons. Sites could be national institutes of health, national research bodies and universities for example and may run multiple study sites within a country. Multi-sectorial co-ordination will be required between Ministries of Health, other ministries and independent academic institutions.

The establishment of operational study sites in the interpandemic period will help to identify local strengths and areas for development to enable sites to be ready for when a pandemic occurs. This process will provide a focused opportunity for skills and capacity building in aspects of study implementation, laboratory testing, data management, epidemiological and modelling analyses, results sharing, global collaboration, and reporting. Joint training activities will promote the development of local, regional, and global collaborations and build local capacity and resilience for responding to future epidemics and pandemics.

DESCRIPTION OF DUTIES

1. **Inter-pandemic**
   - The sites *should*, with WHO technical guidance and support and in close collaboration with the Ministry of Health, **prepare themselves to be sites for the collection of early information and data** in alignment with WHO generic protocols in the case of a pandemic (also referred to as readiness capacity before a pandemic event), or an epidemic of an emerging or re-emerging pathogen.
   - As part of preparing themselves, sites *should* **exercise one or more of the investigations and studies protocols at least once a year** (either whole protocol or certain aspects of it) during a seasonal influenza epidemic or a respiratory virus outbreak (ex: MERS-CoV). Following an exercise, where necessary, sites should adapt protocols based on the learning from the exercise.
   - Sites should coordinate and advocate with their Ministry of Health or national public health body to **include this element as a core action in their respiratory pathogens and /or influenza pandemic preparedness plans.**

2. **During a pandemic, or epidemic of an emerging or re-emerging pathogen**
   - The sites will **undertake one or more of the investigations and studies during a future respiratory pathogen pandemic,** or epidemic of an emerging or re-emerging pathogen, in accordance with arrangements made with WHO prior to the pandemic.
   - The sites *will* **submit timely information and results** gathered through the investigations and studies as soon as possible (specific timeframe to be defined when pandemic occurs) to WHO, in line with the 'WHO Unity Studies data and early information terms of submission' guidance (*link to be added when finalised, will cover whether information is encrypted line listing individual information or aggregated anonymized information.*). A WHO data repository platform (NB: to be built) will collate results in "real time".
   - The sites *should* **participate in conference calls** relevant to the **investigation study/studies that**

the site has committed to, so that any issues can be identified and solved early and collaboratively by the global network of sites with support from WHO. This will also be a forum to share early global findings and promote international collaboration in the response effort.

- On request, the sites will present results transparently showing progress of work, as well as outcomes of final investigations and studies amongst Unity Studies sites and partners to promote the sharing of experience and knowledge within and external to the network and to promote the sharing of early findings to inform action.

3. Interpandemic and during a pandemic

- The sites *must* ensure that the investigations and studies are conducted **in accordance with the relevant national and international ethical regulations and principles** and should endeavor to obtain ethical review board pre-approval, and other relevant regulations, if needed, to help ensure rapid commencement of the study(ies) during a pandemic.
- The sites *may be requested* to **assist in providing technical assistance/mentoring to other sites that are inside the network** (upon request, mostly remotely) before and during the next respiratory pandemic through the sharing of experience, knowledge, relevant skills and resources to consolidate the global network and to foster further collaboration.
- The sites *may be requested* to **assist in providing technical assistance/mentoring to sites that are outside the network but which are ready to join** when the next pandemic will hit, through the sharing of experience, knowledge, relevant skills and resources to foster regional and global evidence -based response and collaboration.
- The sites *should* ensure coordination of financing and mobilization of resources with support from WHO.

DESCRIPTION OF BENEFITS

1. The results from the investigations and studies will:
    a. **Inform the appropriate level of response** nationally, regionally and globally, and,
    b. Help **to target intervention activities effectively to reduce the impact on the population of the next respiratory pathogen pandemic**.
2. Ensuring the timely collection and sharing of early results/information during a future respiratory pandemic will allow an **evidence-based and so optimal response based on available information.** Standardized data collection can rapidly inform local action, and provision of this information to WHO is key to informing regional and global risk assessments.
3. Sites will be formally **recognized as a WHO Investigations and Studies network champion site**, after having fulfilled the ToR for two years.
4. Sites will **be recognized as a center of expertise regionally and globally**: to globally unlock, mobilise and connect the experience, knowledge, data and information, and resources of the sites that transcend the geographic transmission zones, languages and disciplinary (e.g., surveillance, laboratory, modelling, ethics) boundaries of our sites.

5. Sites and their respective Member States will be **capacity built by WHO and partners** to fulfill their network duties: opportunity for skills and capacity building in aspects of study implementation, laboratory testing, data management, analytics and modelling analyses and reporting and participation in joint training activities.
6. **Access to scientific and technical peer review support from the other sites of the network and to a community of best practice**: sites will know whom to call to get rapid and trustable inputs or support.
7. Access to high quality **standardized and harmonized tools and materials** to collect, analyze, visualize and disseminate data and information: such as tools (e.g. generic field questionnaires, data collection tools, R scripts for data analysis and modelling), methodologies, systems (e.g. generic field investigation protocols), processes (e.g., data and early information on terms of submission) to promote the interoperability of sites.
8. Participation in the network will support sites and their respective Member States to reach pandemic influenza preparedness and readiness goals helping to **fulfil IHR preparedness and readiness country mandates**.
9. **Funding** for these activities should be the responsibility of the country, however, WHO and partners will make efforts to seek supporting funds to allow the piloting of investigations and studies (before the pandemic) and the running of them (early on in the pandemic), primarily in low to medium income countries.
10. **Participation in a regional or global network meeting:** annually or every two years.

SITE SELECTION CRITERIA

While investigations and studies do not necessarily need to be implemented in every setting, broad representation will be ensured by initial purposive recruitment of target study sites across regions, country income levels, population demography and health systems resources and context. It is anticipated that countries will differ in existing capability and resources to conduct these studies, with some requiring more support than others.

In a pandemic, there is a need to gather evidence from geographical areas where data is scarce whilst also making sure the highest possible quality of data is obtained from areas with already well-functioning surveillance systems. WHO Investigations and Studies initiative aims to fill those gaps, and particular attention will be paid to supporting areas where surveillance is suboptimal or without well-functioning established surveillance systems.

Essential criteria:

1. **Commitment from the sites** to participate in the Unity Studies network according to the duties described above through the acceptance and signature of the ToR.
2. Having a **designated, active Focal Point/Principal investigator/Support Center** in the country (or across several countries) to **coordinate** the envisioned investigations and studies and to liaise with WHO CO, RO and HQ for the latest guidance. Special coordination arrangements can be made in the case of joint investigation by several sites in various countries from already existing global networks.
3. Having **access to a laboratory** designated by WHO as a National Influenza Center (NIC) or as a reference laboratory for respiratory viruses like coronaviruses, such as WHO Coronavirus Network (CoViNet) reference laboratory, with sufficient existing **capacity for molecular diagnostics** for respiratory viruses, as well as freezer **storage capacity (-20°C, -70°C) for**

respiratory, blood and serum samples and experience with the transport of infectious diagnostic specimens and/or pathogens (Category B +/- Category A) domestically and internationally. For sites who do not have direct access to a NIC or other national respiratory virus reference laboratory, having rapid access to a WHO Collaborating Centers for any respiratory viruses (ex influenza, coronaviruses) or working with the WHO Public Health Laboratory recognition programme for pathogens with epidemic and pandemic potential.

4. Having **previously conducted** high quality investigations and studies during the COVID-19 pandemic.

Desirable criteria:

1. Having **previously successfully collaborated with the COVID-19 Unity Studies initiative** and conducted at least one well implemented study aligned with one of the COVID-19 Unity Protocols and shared results timely with WHO.
2. Having access (inside or outside the country) to a laboratory competent with capacity for multiple relevant methods including serologic testing, genomic sequencing, insilico analysis (even if outside of the country).
3. Regular sharing of Severe Acute Respiratory Infections (SARI) / Influenza-like illness (ILI) data with WHO through virological and epidemiological data submission to the WHO global system, RespiMART (formerly FluMART).
4. Regular sharing through material transfer agreements of influenza or SARS-CoV-2 virus isolates and/or respiratory specimens with WHO Collaborating Centers, CoViNet Reference Laboratories and/or WHO BioHub.
5. Having access or links to a national Field Epidemiology Training Programme (FETP), to perform rapid investigation and response to perform the required range of investigations and studies.
6. Having access to data analytics team.

To support site selection/designation, WHO may consider other criteria that are relevant to a specific investigations and studies protocol. These criteria are described in the relevant protocol annexes.

LANGUAGE:

These Terms of Reference were drafted in English. It will be translated into other WHO official languages for convenience and use only, and the English language text shall prevail.

CONTACT

If you have any questions or would like further information about how to join this global initiative, please contact: unity@who.int or regional focal points.