COVID-19 Scientific and Public Health Policy Update[1] – (08 September 2020)

In addition to our Weekly Outbreak Brief on the spread of COVID-19 and the actions that Africa CDC is taking to help African Union Member States. Africa CDC shares a weekly brief detailing the latest developments in scientific knowledge and public health policy from around the world, as well as updates to the latest guidance from WHO and other public health agencies. Contents of this document are not intended to serve as recommendations from the Africa CDC; rather, it is a summary of the scientific information available in the public space to Member States. It is important to note that the outbreak is evolving rapidly and that the nature of this information will continue to change. We will provide regular updates to ensure Member States are informed of the most critical developments in these areas.

A. Executive summary

- Results from two open non-randomised phase I/II studies with 76 participants assessed the safety and immunogenicity of rAd26 and rAd5 vector-based COVID-19 vaccine in Russia. Findings suggest that the heterologous rAd26 and rAd5 vector-based COVID-19 vaccine has a good safety profile and induced strong humoral and cellular immune responses in participants. Further investigation is needed for the effectiveness of this vaccine for prevention of COVID-19.
- The study presents a phylogenetic analysis suggesting a likely origin for SARS-CoV-2 in Rhinolophus spp. bats. Findings suggest that host-switching occurs more frequently and across more distantly related host taxa in alpha- than beta-CoVs, and is more highly constrained by phylogenetic distance for beta-CoVs.
- An open-label, randomised clinical trial in Brazil assessed whether adding azithromycin to the standard of care, which included hydroxychloroquine, would improve clinical outcomes of patients admitted to the hospital with severe COVID-19. Findings do not support the routine use of azithromycin in combination with hydroxychloroquine in patients with severe COVID-19.
- A prospective meta-analysis with pooled data from seven randomized clinical trials evaluated the efficacy of corticosteroids (systemic dexamethasone, hydrocortisone, or methylprednisolone) in 1,703 critically ill COVID-19 patients across 12 countries. Findings suggest the administration of systemic corticosteroids, compared with usual care or placebo, was associated with lower 28-day all-cause mortality.
- Reports of COVID-19 reinfections have been reported, two infections in each person were separate events, the Hong Kong and Nevada teams each sequenced the viral genomes from the first and second infections.

[1] This update compiled for use by Africa CDC and African Union Member States and is developed in collaboration with the World Health Organization - Regional Office for Africa. **This is a preliminary summary of information and not considered policy, guidance, or final conclusions of the Africa CDC or the African Union**.

B. New guidelines and resources

Since 01 September 2020,

- Africa CDC has published new guidance and resources on:
  - Guidance for Awake Prone Ventilation in the non-intubated Conscious Patient
  - COVID-19 Infection Prevention and Control: Your Questions Answered
- WHO has published new guidance and resources on:
  - COVID-19 management in hotels and other entities of the accommodation sector;
  - Promoting public health measures in response to COVID-19 on cargo ships and fishing vessels;
  - Annex to the advice on the use of masks in the context of COVID-19, interim guidance, 5 June, 2020; advice on the use of masks for children in the community in the context of COVID-19 interim guidance;
  - Considerations for quarantine of contacts of COVID-19 cases;
  - Home care for patients with suspected or confirmed COVID-19 and management of their contacts;
  - Public health surveillance for COVID-19;
  - Strategies for surveillance of COVID-19 human infection caused by SARS-CoV-2 virus. Guidance v1;
  - Considerations for the provision of essential oral health services in the context of COVID-19;
  - Advice and Q&A on the use of masks for children in the context of COVID-19 – Masks for Children;
  - Considerations for quarantine of contacts of COVID-19 – IPC > Considerations for Quarantine;
  - Guidance on home care for patients with suspected or confirmed COVID-19 and management of their contacts – Home Care;
  - Q&A on home care for families and caregivers) IPC > Home Care;
  - Q&A on home care for health workers and administrators IPC > Home Care;
  - Updated Emergency global supply chain catalogue - Essential Resources Planning > Global Supply Chain Catalogue;
  - Interim guidance on public health surveillance for COVID-19 – Surveillance > Global Surveillance Guidance;
  - COVID-19 case definition Surveillance > Global Surveillance Guidance
  - Scientific briefing on status of environmental surveillance for COVID-19 Surveillance > Environmental Surveillance;
  - Updated surveillance reporting forms - Surveillance > Reporting Forms.

The full list of latest guidance and resources from WHO and other public health institutions can be found in this link.

C. Scientific updates

Basic Science

- This study evaluated T-cell memory in 42 patients following recovery from COVID-19 (28 with mild disease and 14 with severe disease) and 16 unexposed donors, using interferon-γ-based assays with peptides spanning SARS-CoV-2 except for ORF1. The breadth and magnitude of T-cell responses were significantly higher in severe as compared with mild cases. In mild cases, higher proportions of SARS-CoV-2-specific CD8+ T-cells were observed. The identification of T-cell responses associated with the milder disease will support an understanding of protective immunity and highlights the potential of including non-spike proteins within future COVID-19 vaccine design.
- This study reports the correlation between the magnitude of neutralizing antibody (NAb) responses and the disease severity in COVID-19 patients in a cohort of 59 recovered patients with disease severity including severe, moderate, mild, and asymptomatic. Findings suggest a positive correlation between serum neutralizing capacity and disease severity, in particular, the highest NAb capacity in sera from the patients with severe disease, while a lack of ability of asymptomatic patients to mount competent NAbs.
- Using a bayesian statistical framework and a large sequence data set from bat-CoVs (including 630 novel CoV sequences) in China, researchers explore the macroevolution, cross-species transmission and dispersal. Findings suggest that host-switching occurs more frequently and across more distantly related host taxa in alpha- than beta-CoVs, and is more highly constrained by phylogenetic distance for beta-CoVs. The study presents a phylogenetic analysis suggesting a likely origin for SARS-CoV-2 in Rhinolophus spp. bats.

Epidemiology

- Researchers from the University of Hong Kong's Li Ka Shing Faculty of Medicine Department of Microbiology report the first confirmed case of COVID-19 reinfection in 33 year old man using whole genome sequencing. Findings suggest that the viral genomes from first and second episodes belong to different clades/lineages. The second episode of asymptomatic infection occurred 142 days after the first symptomatic episode in an apparently immunocompetent patient. The results suggest SARS-CoV-2 may continue to circulate among the human populations despite herd immunity due to natural infection or vaccination.
- This case study describes the data from an investigation of two instances of SARS-CoV-2 infection in the same individual, in Nevada. Through nucleic acid sequence analysis, the viruses associated with each instance of infection were found to possess a degree of genetic discordance that cannot be explained reasonably through short-term in vivo evolution. Findings suggest that it is possible for humans to become infected multiple times by SARS-CoV-2, but the generalizability of this finding is not known.

- This study reports the first animal to human SARS-CoV-2 transmission events documented in mink farms, an in-depth investigation of outbreaks on 16 mink farms and humans living or working on these farms, using whole-genome sequencing. Genetic analysis suggested that workers had introduced SARS-CoV-2 to mink, which spread the virus back to workers, who might then have passed it on to other people. Findings suggest that after the detection of SARS-CoV-2 on mink farms, 68% of the tested farm workers and/or relatives or contacts were shown to be infected with SARS CoV-2, indicating that contact with SARS-CoV-2 infected mink is a risk factor for contracting COVID-19. *(Preprint, not peer reviewed)*
- In this cohort study of 128 individuals and case investigation of a community outbreak of COVID-19 in Zhejiang province, those who rode a bus with air recirculation and with a patient with COVID-19 had an increased risk of SARS-CoV-2 infection compared with those who rode a different bus. Airborne spread of SARS-CoV-2 seems likely to have contributed to the high attack rate in the exposed bus. These results suggest that future efforts at prevention and control must consider the potential for airborne spread of SARS-CoV-2, which is a highly transmissible pathogen in closed environments with air recirculation.
- This case series of children with COVID-19 was conducted in 20 hospitals and 2 nonhospital isolation facilities in Korea, suggests symptom screening fails to identify most COVID-19 cases in children, and SARS-CoV-2 RNA in children is detected for an unexpectedly long time.Heightened surveillance using laboratory screening will allow detection in children with unrecognized SARS-CoV-2 infection.
- A systematic review of 39 observational studies with 662 patients describes the typical presentation and outcomes of children diagnosed with Multisystem inflammatory syndrome. Findings suggest 71·0% of children were admitted to the intensive care unit, Multisystem inflammatory syndrome is a new pediatric disease associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that is dangerous and potentially lethal.
- A living systematic review and meta-analysis of 77 studies reports that pregnant and recently pregnant women are less likely to manifest COVID-19 related symptoms of fever and myalgia than non-pregnant women of reproductive age and are potentially more likely to need intensive care treatment for COVID-19. Pre-existing comorbidities, high maternal age, and high body mass index seem to be risk factors for severe COVID-19.
- This study measured antibodies in serum samples from 30,576 persons in Iceland, using six assays (including two pan-immunoglobulin [pan-Ig] assays), findings indicate that antiviral antibodies against SARS-CoV-2 did not decline within 4 months after diagnosis.Antibody levels rose during the two months after diagnosis, plateaued and then remained at the same level for the duration of the study. Findings estimate that 0.9% of Icelanders were infected with SARS-CoV-2 and that the infection was fatal in 0.3%, and also estimates that 56% of all SARS-CoV-2 infections in Iceland had been diagnosed with qPCR.

Care and Treatment

- An open-label, randomised clinical trial at 57 centres in Brazil assessed whether adding azithromycin to the standard of care, which included hydroxychloroquine, would improve clinical outcomes of patients admitted to the hospital with severe COVID-19. In patients with severe COVID-19, adding azithromycin to the standard of care treatment (which included hydroxychloroquine) did not improve clinical outcomes. Findings do not support the routine use of azithromycin in combination with hydroxychloroquine in patients with severe COVID-19.
- A prospective meta-analysis that pooled data from 7 randomized clinical trials evaluated the efficacy of corticosteroids (systemic dexamethasone, hydrocortisone, or methylprednisolone) in 1,703 critically ill patients with COVID-19 across 12 countries. The risk of death was 32% for patients treated with steroids and 40% for those treated a placebo. Findings suggest the administration of systemic corticosteroids, compared with usual care or placebo, was associated with lower 28-day all-cause mortality.
- A living systematic review and network meta-analysis compared the effects of treatments for COVID-19, findings suggest glucocorticoids probably reduce mortality and mechanical ventilation in patients with COVID-19 compared with standard care.
- A randomised double-blind sequential trial compared the effect of low-dose hydrocortisone vs placebo on treatment failure (death or persistent respiratory support dependency) at 21 days in 149 critically ill patients with COVID-19 and acute respiratory failure in France. Findings suggest low-dose hydrocortisone, compared with placebo, did not significantly reduce treatment failure (defined as death or persistent respiratory support) at day 21. The study was stopped early and likely was underpowered to find a statistically and clinically important difference in the primary outcome.
- An open-label clinical trial compared the effects of dexamethasone vs usual care on the number of days alive and free of mechanical ventilation at day 28 among COVID-19 patients with moderate to severe acute respiratory distress syndrome (ARDS), in Brazil. Findings indicate intravenous dexamethasone plus standard care, compared with standard of care alone, resulted in a statistically significant increase in the number of days alive and free of mechanical ventilation over 28 days.
- This open-label randomised trial compared the effects of fixed-dose vs shock-dependent vs no intravenous hydrocortisone on organ support–free days among COVID-19 patients admitted to critical care units. Among patients with severe COVID-19, treatment with a 7-day fixed-dose course of hydrocortisone or shock-dependent dosing of hydrocortisone, compared with no hydrocortisone, resulted in 93% and 80% probabilities of superiority with regard to the odds of improvement in organ support–free days within 21 days.
- Findings from this study suggest that feline coronavirus drug, prodrug GC376, a dipeptide-based protease inhibitor and its parent GC373, are effective inhibitors of the Mpro from both SARS-CoV and SARS-CoV-2 with IC50 values in the nanomolar range. GC373 and GC376 are potent inhibitors of SARS-CoV-2 replication in cell culture. They are strong drug candidates for the treatment of human coronavirus infections because they have already been successful in animals.

- A systematic review and meta-analysis of 27 studies suggest that angiotensin-converting enzyme inhibitors (ACEi) and angiotensin-receptor blockers (ARB) ACEi/ARB exposure does not seem to increase the risk of having the SARS-CoV-2 infection or developing severe stages of the disease including mortality. The potential benefits observed in mortality of hypertensive patients reassure safety, but robust studies are required to increase the confidence in the results.
- A multicenter observational study evaluates the possible relationship between worse clinical outcomes and the use of angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) in 247 hospitalized COVID-19 patients. Findings suggest the presence of hypertension and use of ACEIs/ARBs were not significantly associated with poor primary clinical outcomes; however, neutrophil-to-lymphocyte ratio (NLR) and D-dimer level were strong predictors of clinical worsening.

Vaccines

- Two open non-randomised phase I/II studies with 76 participants in Russia, assessed the safety and immunogenicity of two formulations (frozen and lyophilised) of the heterologous COVID-19 vaccine consisting of two components, a recombinant adenovirus type 26 (rAd26) vector and a recombinant adenovirus type 5 (rAd5) vector. Findings suggest that the heterologous rAd26 and rAd5 vector-based COVID-19 vaccine has a good safety profile and induced strong humoral and cellular immune responses in participants. Further investigation is needed of the effectiveness of this vaccine for prevention of COVID-19.
- A randomized, placebo-controlled, phase I/II trial evaluating the safety and immunogenicity of the NVX-CoV2373 (rSARS-CoV-2) vaccine in 131 healthy adults, reports that 35 days, NVX-CoV2373 appeared to be safe, and it elicited immune responses that exceeded levels in COVID-19 convalescent serum. The Matrix-M1 adjuvant-induced CD4+ T-cell responses that were biased toward a Th1 phenotype.
- This study analyses the in vitro and in vivo safety and efficacy of lyophilized vaccine candidates inactivated by gamma-irradiation (OZG-3861 version 1 (V1) is an inactivated SARS-CoV-2 virus vaccine, and SK-01 version 1 (V1) is the GM-CSF adjuvant added vaccine candidate). Preliminary results in vaccinated mice, reports that when considered in terms of T and B cell responses, the vaccine models containing GM-CSF as an adjuvant caused significant antibody production with neutralization capacity in absence of the antibody-dependent enhancement feature. (*Not peer-reviewed)*

Infection, Prevention and Control

- This study investigates environmental SARS-CoV-2 contamination in the isolation rooms of severe COVID-19 patients requiring mechanical ventilation or high-flow oxygen therapy. Of the 48 swab samples collected in two of the rooms, only samples from the outside surfaces of the endotracheal tubes

tested positive for SARS-CoV-2, in another patient's room, 13 of the 28 environmental samples (fomites, fixed structures, and ventilation exit on the ceiling) showed positive results. Air samples were negative for SARS-CoV-2. Environmental contamination of SARS-CoV-2 can be a route of viral transmission.

- Recognizing the importance of handwashing in preventing the spread of COVID-19, concerns have arisen about the condition of millions of Africans who lack access to hygiene facilities and clean water services. This paper compiles evidence from the WHO-UNICEF data to show the health disparities that limit the capacity of African countries to effectively address the COVID-19 disease along with recommendations for addressing the challenge.

Diagnostics

- A head-to-head evaluation of ten point-of-care-style lateral flow assays (LFAs) and two laboratory-based enzyme-linked immunosorbent assays to detect anti-SARS-CoV-2 IgM and IgG antibodies in 5-d time intervals from symptom onset and studied the specificity of each assay. Test specificity ranged from 84.3% to 100.0% and was predominantly affected by variability in IgM results.
- This study reports that sampling of oropharyngeal secretions (OSs) helped improve detection of SARS-CoV-2 RNA by nucleic acid amplification testing of potential patients with COVID-19.The nasopharyngeal swab test has a risk of sending home more patients (59%) who still have the infection, while the oropharyngeal secretion test will make such an error in fewer patients (14%).
- Findings from a a pilot study of four serological assays assessing the amounts of anti–SARS-CoV-2 antibodies in serum samples obtained from healthy individuals and individuals hospitalized with COVID-19, suggests that in hospitalized patients with COVID-19, seroconversion and virus neutralization occurred between 5 and 14 days after symptom onset. Seropositivity was detected in 32% of mildly symptomatic individuals within 15 days of symptom onset and in 3% of healthy blood donors.
- This study assessed the analytical performances, sensitivity and specificity, of two rapid tests (Covid- Presto® test and NG-Test®) and one automated immunoassay (Abbott) for detecting anti- SARS-CoV-2 antibodies.An excellent agreement was also observed between the two rapid tests ($\kappa = 0.937$). Specificity for IgM was 100% and 86.5% for Covid-Presto® test and NG-Test®, respectively. Specificity for IgG was 92.0%, 94.9% and 96.5% for Covid-Presto®, NGTest ®, and Abbott, respectively.

Non-Pharmaceutical Interventions

- The coronavirus disease 2019 (COVID-19) pandemic has affected many countries with increasing morbidity and mortality. Interestingly, many of the actions and policies adopted in countries are linked to the social determinants of health (SDH). The SDH are critical determinants of health and health inequalities that are not directly within the health sector. The effectiveness of many of the other SDH in reducing the burden of the COVID-19 pandemic hinges on effective communication, especially crisis and risk communication.

Although many countries are adopting different communication strategies during the COVID-19 crisis, effective crisis and risk communication will lead to building trust, credibility, honesty, transparency, and accountability.

- This study highlight's South Korea's response, the average number of new cases per day fell to 6.4 in the first week of May and currently 90% of all confirmed cases have fully recovered after a massive outbreak in February 29. South Korea has flattened the curve of COVID-19 by combining testing, early isolation, and free treatment of positive cases combined with digital technologies without taking to "lockdown" measures. South Korea disclosed all information on COVID-19 to the public in an open and transparent manner and secured the civic participation and voluntary engagement of citizens and businesses.

Other

- Demand for rice consumption in Africa has outstripped the current local production capacities. As a result, African markets have become heavily dependent on importation, especially from Asia. During the COVID-19 pandemic, rice production in both Asia and Africa is likely to be reduced. It is also likely that the major Asian rice exporting countries will resort to stockpiling of their local production, and restrict volumes of (or ban) rice exportation. Such measures could affect demand–supply dynamics and trigger a price crisis in African rice markets. Based on the lessons learnt from the Ebola and Severe Acute Respiratory Syndrome (SARS) epidemics and the 2007–08 food price crisis, African nations need to moderate the impact of such a crisis through appropriate policy actions.

D. Summary of travel restrictions implemented by Member States

Contents of this section include only publicly announced public health policies. Sources of this section include official government communique, embassy alerts and press search. (As of 06 September 2020)

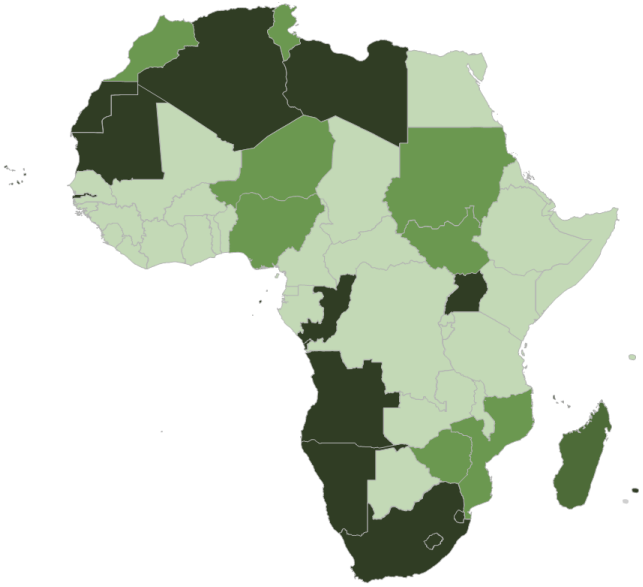
17 Full border closures[1]

2 International air traffic closures

6 Travel restrictions to and from specific countries

32 Entry/ Exit restrictions[2]

Most Member States have imposed **mandatory quarantine** for all travelers or travelers arriving from high risk areas



1 Some countries still allow cargo, freight and emergency transport into and out of the country; Some MSs will still allow citizens and residents to enter but all borders are essentially closed
2 Entry or exit of passengers through COVID-19 screening

For further detailed information for each country, refer to the full table here.

E. Registered Clinical Trials in Africa (84)

Key updates:

Clinical trial initiatives and networks

- The European Innovative Medicine Initiative (IMI) has launched CARE (Corona Accelerated R&D in Europe), a 5 years project involving a consortium of 37 globally-renowned academic institutions, research organisations and pharmaceutical companies aiming to accelerate the discovery and development of urgently needed medicines to treat COVID-19.
- On 27 August 2020, NIH launched the Centers for Research in Emerging Infectious Diseases (CREID). Supported research will aim to identify previously unknown causes of febrile illnesses in humans and investigate animal sources of pathogens. Investigators will develop reagents and diagnostic assays to improve detection of emerging pathogens and study human immune responses to new or emerging infectious agents. In Africa, focus will be on Rift Valley fever virus and MERS (East and Central) as well as on Ebola and Lassa virus (Western).

Vaccine trials

- On 24 August 2020, Novavax announced the initiation of the Phase II portion of Phase I/II clinical trial of its COVID-19 Vaccine candidate, which is currently under phase IIb clinical trial evaluation in South Africa. This phase II clinical trial will expand the age range of the phase I portion by including approximately 50 percent of participants ≥60 years of age at 40 sites in the United States and Australia, in order to characterize immune responses in the older population.
- On 31 August 2020, the NIH announced the launch of the phase III clinical trial of Astrazeneca AZD1222, a non-replicating ChAdOx1 vector vaccine candidate initially developed by Oxford University for the prevention of COVID-19. Approximately 30,000 volunteers 18 years and older will be enrolled across 80 sites in the United States.
- On 03 September 2020, the updated WHO landscape of COVID-19 vaccines was published. Thirty-four vaccine candidates were at the clinical evaluation stage and 142 candidates at the preclinical stage.
- On 04 September 2020, a review on the updated overview of the vaccine R&D landscape presenting the current pipeline of COVID-19 vaccine candidates was published. A total of 321 vaccines candidates were listed including: 201 at the exploratory stage, 88 at the preclinical phase, ten at phase I, sixteenth at phase I/II or II and six at phase IIb/III or III clinical trial phases. Notably, 8 vaccine candidates at the clinical phase are included in the portfolio of the CEPI, Gavi and WHO led COVAX initiative which aims to deliver two billion vaccine doses for global allocation by the end of 2021.
- Further, a second review presented the COVID-19 vaccine trials landscape in Africa.
- A third review published on 04 September 2020 looked at immunological principles to consider in the development of COVID-19 vaccine strategies, scientific and practical challenges in the R&D process for a successful vaccine and the prospective evolution of COVID-19 vaccine strategies over time.
- The UK government's innovation agency has awarded £1.9million to the Cambridge University spin-out company DIOSynVax to begin the clinical evaluation of its innovative DIOS-CoVax2 vaccine candidate. DIOS-CoVax2 is based on libraries of computer-generated genetic sequences of all known coronaviruses (i.e. MERS, SARS, etc.) including those from bats, to produce beneficial antiviral responses. It is expected that the vaccine will protect from SARS-CoV-2, but also other related coronaviruses.

Therapeutics trials:

- On 4th september 2020, the Mansoura University Faculty of Medicine in Egypt registered the open label clinical trial aiming to assess the efficacy and safety of Sofosbuvir plus the anti HCV Daclatasvir drug for the treatment of COVID-19.

Immunotherapy trials:

- On 31st August 2020, GSK announced the launch of the Phase 2/3 COMET-ICE study, which will investigate the safety and efficacy of the VIR-7831 monoclonal antibody in preventing COVID-19 related hospitalisations VIR-7831 is directed against SARS-CoV-2 spike protein and has demonstrated potent viral neutralization activity. This trial will enrol approximately 1,300 patients worldwide.

Other clinical studies:

- The COVID-19 Prevention Network & the NIAID are conducting the CoVPN 5001 prospective study of innate and adaptive immune responses during acute COVID-19 infection and convalescence in order to help develop better diagnostic tests and help in developing future vaccines. Eight African countries are participating: Botswana, Kenya, Malawi, Mozambique, South Africa, Tanzania, Zambia, Zimbabwe.
- On 01 September 2020, the NIH announced a study to track prevalence and impact of SARS-CoV-2 among 16,000 pregnant women in LMICs, conducted by the Global Network for Women's and Children's Health Research. Women will be followed up through pregnancy and 12 months after childbirth to compare maternal, foetal and newborn outcomes between COVID-19 infected and uninfected participants. Kenya, Democratic Republic of Congo and Zambia will participate.

For further detailed information for each country, refer to the full table here

Contributors

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