World Health Organization

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The World Health Organization presents its compliments to Member States and has the
... honour to attach information related to the current outbreak of COVID-19.

This Circular Letter and the attached information is being dispatched through electronic mail to the official email addresses provided by Member States in response to circular letters C.L.38.2017 and C.L.25.2018 requesting Member States to provide an electronic address or electronic addresses where official correspondence can be sent.

This Circular Letter and the attached information has also been sent to representatives in the Permanent Missions to the United Nations Office and other International Organizations at Geneva.

WHO representatives and liaison officers have also received this Circular Letter and the information and are requested to follow-up with Member States as appropriate.

It is envisaged that the Secretariat will continue to share information and requests to Member States through this mechanism for rapid and timely engagement.

The World Health Organization takes this opportunity to renew to Member States the assurance of its highest consideration.

GENEVA, 23 September 2020

... ENCL.: (1)

COVID-19: Call for Countries to Participate in the Global WHO SOLIDARITY Protocol for COVID-19 Vaccines trials

The Director-General would like to express appreciation to all WHO Member States for their solidarity and extraordinary measures being implemented towards containing the COVID-19 pandemic.

The Director-General would also like to express appreciation to WHO Member States for continued support to the Secretariat's ongoing work to establish research priorities and facilitate international collaboration towards the development of countermeasures to prevent and treat COVID-19.

With a view to accelerate and enhance the likelihood of finding several effective COVID-19 vaccines, and to ensure critical and reliable evaluation of these essential products, WHO is coordinating the international SOLIDARITY vaccines trial – an adaptive design COVID-19 vaccines trial protocol designed to provide sufficient evidence of safety and vaccine efficacy against COVID-19 to support decision-making about global vaccine deployment.

In the context of the WHO-spearheaded Access to COVID-19 Tools (ACT) Accelerator, and the R&D Blueprint mechanism, WHO Member States are invited to join this international, randomized controlled clinical research trial for COVID-19 vaccines.

Goal of the SOLIDARITY Vaccines Trial

The goal of the trial is to coordinate prompt, efficient, and reliable evaluation of the many preventive candidate SARS-CoV-2 vaccines under development, to assess their safety and efficacy and to identify those that are likely to be appropriate for deployment to end the acute phase of the pandemic. WHO has designed this scientifically robust protocol alongside leading research methodologists and vaccine experts so that several different candidate vaccines can be evaluated rapidly and robustly.

Unique Advantages of the SOLIDARITY Vaccines Trial

The WHO SOLIDARITY vaccines trial seeks to achieve rapid, reliable results by the simplicity of the trial design, and through increasing the likelihood of finding highly effective vaccines by: including multiple promising vaccine candidates in the trial; establishing a robust and transparent processes to support preclinical evaluation and to rigorously identify the vaccines with the greatest promise; and promoting efficient allocation of world-wide clinical trial resources and continuous use of established clinical trial infrastructure.

High enrolment rates facilitated by flexible trial design and hundreds of study sites in high-incidence locations also increase the potential to yield results on short-term efficacy for each vaccine within a truncated time period. Evaluation of multiple COVID-19 vaccines with standardized methodology will also facilitate regulatory and deployment decisions, and afford an opportunity for promising vaccines to be evaluated in an internationally recognized trial whereas, in the alternative, they may not have such an opportunity to demonstrate scientific viability.

Please find attached a summary of the trial protocol that provides additional details concerning the trial design.

In order to proceed in the affirmative, WHO requests the nomination of your Government's designated national research trial coordinator who can liaise with WHO's Chief Scientist, Dr Soumya Swaminathan (swaminathans@who.int) to advance this trial.

Global collaboration in vaccine development can contribute to a global solution that will ensure equity in access to vaccines across the world with one goal: to reduce the burden of the COVID-19 pandemic by addressing the cause. In this regard, WHO looks forward to your confirmation.

World Health Organization

An international randomised trial of candidat vaccines against COVID-19

(draft summary)

R&DBlueprint
Powering research
to prevent epidemics

An international randomized trial of candidate vaccines against COVID-19

Summary

This large, international, randomized controlled clinical trial is designed to enable an expeditious, agile and concurrent evaluation of the benefits and risks of multiple candidate preventive vaccines against COVID-19 at international sites with sufficient COVID-19 attack rates. Different candidate vaccines may be available or suitable to enter the trial at different times; for each candidate vaccine, the primary efficacy results are expected within 3-6 months of the vaccine entering the trial.

The trial will rapidly enroll and individually randomize very large numbers of adult participants in many different populations. Each participant will be contacted weekly for information as to whether any potentially relevant symptoms have arisen, with laboratory testing triggered if the report suggests COVID-19. By using a shared placebo/control group and a common Core protocol to evaluate multiple candidate vaccines in the trial, resources allocated to the evaluation of each candidate vaccine are judiciously saved while a high standard of scientific rigor and efficiency is ensured.

The trial is designed to provide sufficient evidence of safety and vaccine efficacy against COVID-19 to support decision-making about global vaccine deployment, which may include licensure and/or WHO pre-qualification. Final decisions about COVID-19 deployment will be made in each jurisdiction.

Goal of the trial

The goal of the trial is to coordinate prompt, efficient, and reliable evaluation of the many preventive candidate SARS-CoV-2 vaccines under development, to assess their safety and efficacy and to identify those that are likely to be appropriate for deployment to influence the course of the pandemic.

Adaptive design

While the expectation is that the trial will rapidly enroll sufficient numbers of participants to expeditiously evaluate all included vaccines, the design of the trial incorporates adaptive features that respond to changes in standards of prevention and care, varying availabilities of candidate vaccines at different times, and uncertainties about the course of the epidemic in different geographic locations and populations. High enrollment rates are expected, and various adaptive features will assure that the trial achieves results in a defined and short period of time. These adaptive features are:

1) Choice of vaccines under evaluation - Candidate vaccines may be added to the trial as soon as they become available and meet prioritization criteria (to be defined via Criteria for COVID-19 Vaccine Prioritization).

2) Choice of success criteria and number of COVID-19 events required to trigger efficacy analyses of a vaccine - While the trial will start with criteria required for success that allow rapid identification of vaccines that will be of high value in the current public health setting, success criteria may be revised after initiation of the trial to accommodate unanticipated circumstances, including changes in the time available to conduct the trial, blinded attack rates, and observed participant enrollment rates. Likewise, the number of COVID-19 events required to trigger efficacy analyses of vaccines may be changed, depending on these factors. Accrual and the blinded COVID-19 attack rate will be monitored, with defined guidelines and operational boundaries indicating unacceptably slow progress to assess vaccine efficacy. Reaching an operational boundary alerts the Steering Committee to consider adjusting the trial design and conduct to ensure its ability to meet the study objective in a timely manner.

3) Choice of study population - If deemed necessary to increase the likelihood that the study will identify efficacious vaccines, the blinded Steering Committee may also modify the number of study sites, the sample size at all or selected study sites, or refocusing the accrual to certain sub-populations. Some sites may use a mobile trial structure, allowing flexible redirection to populations with high attack rates.

4) Monitoring of efficacy - Each candidate vaccine will be monitored for early evidence of benefit and for early evidence of lack of benefit using prespecified monitoring guidelines and boundaries that may lead to halting further randomization of participants into a vaccine arm. Early monitoring for benefit is critical for obtaining and reporting data that could support rapid deployment of efficacious vaccines. Monitoring for lack of benefit targets trial resources to the study of vaccines that are more likely to be successful.

5) Choice of control group - The placebo comparator is an integral component of the study design. All participants in study vaccine and placebo groups will receive the current, local standard of prevention of COVID-19. Randomization to placebo will continue until it is no longer considered appropriate. In this situation, a vaccine regimen that has been found to be efficacious may serve as a positive control for the evaluation of other candidate vaccines currently in the trial or later added to the trial, and new benefit and lack-of-benefit criteria will be introduced.

Features and Advantages

This large international multicenter trial to test vaccines is consistent with the collaborative spirit underlying COVID vaccine development and will foster international deployment with equity of access. As compared with conducting separate trials for each candidate vaccine, the trial design, which evaluates candidate vaccines in parallel with a common placebo group:

1. allows the most rapid and rigorous conclusions to be reached by:
    a. expeditiously enrolling many participants who are at high risk for COVID-19 at sites with high rates of COVID-19, enabling successful vaccines to meet a stringent lower statistical confidence bound on efficacy;
    b. achieving high efficiency (fewer required total participants for evaluation of each vaccine) through use of a shared placebo group;
    c. increasing the consistency of the evaluation process across vaccines by standardizing the populations enrolled, study screening and follow-up procedures, and endpoint determination; and
    d. standardizing success criteria across vaccines, assuring that all vaccines receive a rigorous evaluation of their efficacy that will be sufficient to support broad deployment of an effective vaccine; and
2. has the potential to evaluate a large number of vaccines that have a chance of being effective, increasing the likelihood of finding highly effective vaccines by:
    a. including multiple promising vaccine candidates in the trial; and
    b. promoting efficient allocation of world-wide clinical trial resources, reducing the likelihood that sites with high incidence of COVID-19 will contribute only to the evaluation of an ineffective vaccine; and
3. increases the likelihood that participants receive one of the candidate vaccines (relative to placebo) and provides all trial participants a fair chance at receiving ultimately successful vaccines; and
4. has advantages for developers/funders by:
    a. providing rapid evaluation of the efficacy of their vaccine;
    b. reducing uncertainties in endpoint acquisition rates, increasing the likelihood of enrolling enough trial participants to rapidly assess efficacy of each vaccine;
    c. permitting vaccines to enter the trial when ready;
    d. eliminating the inefficiency of designing and conducting separate trials; and
    e. decreasing overall costs of vaccine evaluation.