

**Note for the attention of
the Members of the EU scientific advice platform on COVID-19**

This note follows an agreement at the most recent meeting of the EU scientific advice platform on COVID-19 on 7 January to provide information on the EU-wide clinical trial networks for therapeutics and vaccines as well as other EU-funded projects, which are relevant for the questions addressed in this forum.

1. EU-wide network for COVID-19 therapeutics

Priority action two of the ERAvsCORONA action plan¹, identifying a first set of 10 actions in the area of research and innovation to be implemented at EU level period, refers to the EU commitment of extending and supporting large EU-wide clinical trials for the clinical management of COVID-19 patients.

The recently set up EU-wide network for COVID-19 therapeutic trials is based on two large-scale adaptive platform trials, the second-generation DisCoVeRy trial and the REMAP-CAP for COVID trial². These trials are funded with around EUR 30 Million through the EU-RESPONSE³ and RECOVER⁴ projects, respectively, and are enrolling several thousand patients in numerous European countries.

A coordination mechanism between the two trials, a common Trial Coordination Board, promotes complementarities, helps to avoid redundancies, and facilitates cooperation, also with other European and international initiatives in the field, in order to maximise the robustness of trial outcomes and speed-up discoveries of therapeutics to treat COVID-19.

Working in close coordination, these projects will deliver a comprehensive development strategy for COVID-19 platform trials in Europe, providing a streamlined access for new therapies to be tested, setting priorities for compounds to be tested, and offering support for the setting up of new platform trials as relevant.

On January 7th 2021, the REMAP-CAP trial reached an important conclusion: two medicines, Tocilizumab and Sarilumab, that are monoclonal antibodies normally used to treat rheumatoid arthritis, were found to cut the relative risk of death of severely-ill COVID-19 patients by 24%^{5,6,7}.

¹ https://ec.europa.eu/info/files/first-eravs-corona-action-plan-short-term-coordinated-research-and-innovation-actions_en

² <https://www.remapcap.org/coronavirus>

³ <https://eu-response.eu/>

⁴ <https://www.recover-europe.eu/>

⁵ https://ec.europa.eu/info/news/eu-funded-clinical-trial-finds-new-treatments-be-effective-against-covid-19-2021-jan-08_en

⁶ <https://medrxiv.org/cgi/content/short/2021.01.07.21249390v1>

⁷ <https://www.theguardian.com/world/2021/jan/07/covid-arthritis-drugs-could-help-save-lives-of-seriously-ill-patients-research-finds>

In addition, on December 22 2020, the REMAP-CAP trial data showed that among critically ill COVID-19 patients requiring intensive care, therapeutic anticoagulation drugs did not improve outcomes⁸.

Results from the DisCoVeRy trial, launched in March 2020 by INSERM, analysed in the framework of the WHO Solidarity trial, suggest that the treatments Hydroxychloroquine, Lopinavir and Interferon have no effect on the clinical improvement of patients⁹.

- ➔ Such results are important to identify which treatments have been proven to make a difference and to halt treatments that previously seemed promising but actually have no benefit.

2. EU-wide clinical trial networks for Vaccines

Building on the example of the EU-wide network for COVID-19 therapeutics, it is planned to set up an EU-wide network for COVID-19 vaccine trials to facilitate large-scale trials in Europe for large industry, SME and academic developers, and contribute to answering public health questions to inform vaccination strategies.

The network will:

- **Provide a single entry point** for industry/SMEs which would like to use the trial sites to test their vaccine candidates and for Public Health Authorities, ECDC and EMA to articulate public health related research questions to be addressed in phase II/III trials;
- **Keep a systematic overview of ongoing and planned vaccine trials**, in collaboration with Member State competent authorities and EMA. Such continuous mapping that would include information from the EU clinical trials database (EudraCT) and help identifying the potential gaps in scientific questions that need to be investigated, in particular from a public health perspective;
- **Facilitate the discussions on harmonised trial protocols and data standardisation**. Collaboration and coordination between Member States around complementary trial protocols is paramount to yield sufficiently powered trials that can provide the evidence critically needed by public health authorities;
- **Build capacity** for conducting vaccine trials across Europe; and
- **Conduct trials**. Should the proposed funds from Horizon 2020 allow, small-scale trials could already be funded.

This network will capitalise on the extensive experience and infrastructures across Europe, and where possible use previous investments. The German Centre for Infection Research (DZIF) carried out an extensive mapping exercise¹⁰, providing a comprehensive overview on

⁸ <https://www.umcutrecht.nl/en/about-us/news/article/statement-from-the-remap-cap-trial-international-trials-of-blood-thinners-pause-enrollment-of-critically-ill-covid-19-patients>

⁹ <https://presse.inserm.fr/en/lessai-solidarity-discovery-livre-ses-premiers-resultats-sur-lefficacite-des-traitements-repositionnes-contre-la-covid-19/41642/>

¹⁰ <https://www.euvap.eu/>

existing vaccine trial sites and infrastructure in the Member States, as well as the extent to which these are organised as (national) networks with a central hub.

Thanks to the close cooperation with the Horizon 2020 Programme Committee for Health Research up to now 23 Member States and 8 Associated Countries (including the UK, Switzerland and Israel) signed up to participate in this network. In agreement with Member States, Germany assumed the coordinating role for the network under the lead of Professor Cornely at the University Hospital of Cologne (DE). Participating countries are asked to identify country co-ordinators or country-nodes, which bring together the vaccine trial sites in their respective country.

The proposal with the work description, its operations and governance will be submitted to DG R&I by end of January. After a rapid evaluation, if positive, the grant can be concluded so that the network might be ready to start already end of February/early March.

The vaccine trials network will work in close collaboration and coordination with EMA and ECDC, which are overseeing the post-authorisation safety and effectiveness monitoring studies. In addition, both agencies will actively contribute to identifying priority research questions to be addressed in phase II/III trials.

Input from the Expert Panel on COVID-19, the EU scientific advice platform on COVID-19 and/or the Vaccine Steering Board is welcome to ensure that the most pressing and relevant research questions can be addressed through comprehensive studies and reliable scientific evaluations. Any views the members of the COVID-19 platform may have in this regard, will be transmitted to the network for consideration.

Considering the scale and time it takes to deliver such results and the capacity of the network that will just start, the results to these questions are expected rather in the mid-term.

The network could for example address questions such as:

- the possibility of vaccinating with a combination of different vaccines;
- the possibility of re-vaccinations ('booster doses') with vaccines differing from the first one given ('mix and match');
- comparative studies when several vaccines, and different types of vaccines, with different price levels will become available.

Members of the EU scientific advice platform on COVID-19 are invited to encourage the relevant contacts in their respective countries who did not yet sign up for the vaccine trials network to join as well.

Both clinical trials networks constitute an important investment to further build and strengthen EU capacity to carry out large-scale clinical trials, contributing to better preparedness for future epidemics or pandemics.

3. EU-wide cohort studies: ORCHESTRA

The newly started EU-funded project ORCHESTRA¹¹ will provide recommendations on the best vaccines and vaccination strategies for the different categories of persons in the population.

The consortium will characterize the immunological response induced by the different vaccines and assess their efficacy in terms of protection against the various forms of the COVID-19 disease. It will also be able to study the important open question, if the vaccine protects not only against disease but also against transmission of the SARS-CoV-2 virus. The project could also study the serological status, i.e. the development of a protection by the immune system, of people who received a delayed 2nd dose, if institutions participating in the project are from countries that apply this strategy. Finally, the project is also equipped to study, if emerging new viral variants are able to escape vaccines and to feed this information back to vaccine developers.

4. COVID19 data sharing portal

The Commission in collaboration with the EMBL's European Bioinformatics Institute (EMBL-EBI), with Member States and Associated Countries and research partners such as ELIXIR¹², launched the European Open Science Cloud's (EOSC) COVID-19 Data Platform¹³ on 20 April. This allows the scientific community to share, analyse, and process data rapidly, openly and effectively.

This data platform offers access for researchers around the world to publications on Coronaviruses (>132,000), assembled viral sequences (>44,500), raw viral sequence reads (>174,000), and other bio-molecular data (>1000 protein records). By the end of 2020, the portal had more than 110,000 users, and more than 3.5 million web requests for data, from over 170 countries.

- ➔ The COVID19 data sharing portal can help with the timely and harmonised sharing of genomic sequences, which in turn can facilitate the analysis and follow-up of new variants.

For additional information, please contact

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¹¹ <https://orchestra-cohort.eu/>

¹² <https://elixir-europe.org/about-us/who-we-are/nodes/france>

¹³ <https://www.covid19dataportal.org/>