First "ERAvsCORONA" Action Plan

Comments by the Helmholtz Association

The Helmholtz Association welcomes the "ERAvsCORONA" Action Plan presented on April 7, 2020. It is only through pan-European research and development that we can overcome this ongoing health crisis, and we agree with the EU's strong focus on coordinated research efforts to facilitate this process. It is evident that pan-European collaboration is absolutely critical to understand and resolve this pandemic and to learn from it for the future. The first 18 EU-funded Covid-19 projects are a suitable first step.

It remains crucial to promote research into all aspects of SARS-CoV-2 and Covid-19, since today's "fundamental" research is the basis of tomorrow's "applied" research and graspable outcomes affecting our lives. This includes novel diagnostic tools and treatment options as well as decision-supporting models. It will be decisive to learn from this pandemic to better prepare for the next one.

Helmholtz strongly supports all ten priorities of the "ERAvsCORONA" Action Plan and is ready to support their implementation. We want to provide additional input to the following aspects:

3. New funding for innovative and rapid health-related approaches to respond to coronavirus and deliver quick results relevant to society and a higher level of preparedness of health systems

Helmholtz researchers contribute to solving this challenge in many ways from solutions provided by molecular biology to big data analytics. Evidently, the multidisciplinary identification, assessment, and production of a Covid-19 vaccine is of critical importance, and must remain one of the core goals of SARS-CoV-2 research.

Below we highlight the most important aspects of responding to this pandemic – the issues whose investigation offers multiple opportunities for intervention. These activities promise short-term results and even immediate help for infection control, such as contact tracing and prognosis on pandemic spread, and provide evidence for political decisions.

Major indirect impacts on health and wellbeing

The pandemic has major socioeconomic and psychosocial impacts that will affect health and wellbeing on short and long time scales. Assessing them now in large-scale population-based cohorts such as the German National Cohort and other European cohorts will be important to support political decisions and to protect public health in this vulnerable period. This population-based research can also pave a way to future sustainable European societies integrating the ambitions of the Green Deal through insight on the effects of pollutant exposure and other examples of environmental effects on human health.

Diagnostics

At the population level, the identification of immunized individuals is highly relevant. Multiplexed serological assays allow the testing of 100,000s of people for SARS-CoV-2-specific antibodies in their blood. This allows the precise determination of infection levels, mortality rates, and the proportion of serious disease courses that might help to derive decisions on non-pharmaceutical interventions. Helmholtz researchers follow this approach in collaboration with their partners. In addition, the Helmholtz Centre for Infection Research (HZI) is developing technologies for non-invasive sample collection from the lung relevant for the diagnosis of Covid-19.

The German Research Center for Environmental Health (HMGU) is specialized in research of the airways, the main entry route for most epidemic viruses including SARS-CoV-2 and the location of lethal complications. Furthermore, Helmholtz is involved in or plans to work on the assessment of Covid-19 on the most vulnerable high-risk groups like patients suffering from diabetes, asthma, chronic lung disease, or allergies.

Modelling

Mathematical modelling efforts are required to enable informed public policy measures against the spread of Covid-19. The interdisciplinary nature of Helmholtz brings together complementary expertise covering biological science, systems theory and high performance computing (HPC). We emphasize the need for multiscale predictive models and simulations (as opposed to the current descriptive ones) with adequate resolution in space and time to develop decision support tools for policymakers.

Epidemic monitoring

Real-time and complete epidemic surveillance is of utmost importance for the coordination of countermeasures: It would provide data on the current state and thus enable both *ad hoc* and model-based decisions. However, EU countries currently do not have appropriate tools, e.g., for contact follow-up. Helmholtz Centers have developed different mobile app-based solutions to this end, including Surveillance Outbreak Response Management and Analysis System (SORMAS) and Prospective Assessment of Incident Health Events (PIA) for individual monitoring. They have the potential to be rolled out by health authorities in other Member States as well.

Antiviral drug identification

Development of new antiviral drugs (structure-based rational drug design and conventional compound screening) will help to be better prepared for the next pandemic outbreak. Both specific (e.g. anti-Spike) and generic (anti-RNA polymerase) approaches will be needed.

Moreover, novel antiviral compounds are identified from natural sources (e.g. plants or marine organisms), some of which are already recommended for supplementary antiviral therapy. Additional collaborations between pharmaceutical science and research on marine and other organisms can be vital to the discovery of novel available compounds.

In addition to research into *novel* antiviral drugs for future epidemics, Helmholtz researchers are screening compound libraries for existing drugs by high performance computing. These drugs may be beneficial to Covid-19 patients. Repurposing and combining existing, approved drugs accelerates their transfer into clinical practice remarkably, because their safety has already been proven.

In addition to antiviral drugs *per se,* drugs for the treatment of Covid-19 symptoms such as cytokine release and kidney failure is useful.

Helmholtz scientists are establishing an effective Artificial Intelligence (AI) and HPC-based platform to generate and analyze protein targets from pandemic microorganisms by combining different methods (X-ray, cryo-electron microscopy, neutrons, and others). This will lead to a sustainable infrastructure for a fast scientific response to future pandemic scenarios. The infrastructure will be further supported by workflow schemes for biochemical and cellular screening tests for candidate molecules.

4. Increasing support to innovative companies

Helmholtz supports this point; in fact, Helmholtz Centers are collaborating with companies from all over Europe in projects covering SARS-CoV-2 and other topics. Collaborations between academia and industry are crucial, particularly for the discovery and application of novel and repurposed drugs, vaccines, and other pharmaceutical interventions such as antibodies.

A key inherent challenge of newly emerging infections is that we cannot predict which virus will cause the next outbreak. Consequently, off-the-shelf antivirals are not available, and the pharmaceutical industry is hesitant to

invest in such activities. Therefore, it is *crucial* to set incentives for start-ups and SMEs to develop innovative solutions. Access to research infrastructures at academic institutions can be part of this.

6. Establish a one-stop shop for Coronavirus R&I funding

To provide researchers across the EU with the resources they need to combat and end this pandemic, it is *important* to provide them with easily accessible information on available funding and to ensure that the application procedures are as simple as possible. Thus, Helmholtz particularly welcomes this initiative.

7. Establish ad-hoc High Level R&I Task Force on the Coronavirus

As the largest scientific organization in Germany and one of the largest in Europe, Helmholtz is determined to contribute to the solution of this societal challenge by providing its expertise in all fields related to the Covid-19 pandemic. Selected experts from its Research Fields Health, Information, Earth & Environment, Energy, Matter, as well as Aeronautics, Space, and Transport stand ready to advise national and international policymakers and provide up-to-date insights from their cutting-edge research. Experts from the LifeTime consortium (see below) can contribute to these activities.

One role of this R&I Task Force could be to deliver the scientific basis towards the harmonization of anti-pandemic measures all over Europe. Currently, each Member State uses its own set of criteria for administering SARS-CoV-2 tests, quarantine regulations, and rules regarding the flow of people and goods across borders. This is in sharp contrast to the pandemic itself, which affects all of Europe, and thus differing rules between Member States could lead to viral spread or the formation of virus reservoirs. The R&I Task Force could help standardize and coordinate these approaches if experts from all related fields come together to share their knowledge.

8. Access to Research Infrastructures

We highly appreciate the EU's emphasis on the role of research infrastructures. A wide variety of research infrastructures have already contributed strongly to the international fight against SARS-CoV-2. Many of the Helmholtz research infrastructures are available to members of the scientific community for their projects on SARS-CoV-2: large-scale sequencing facilities, cryo-electron microscopes, HPC-based screening of molecules, high-field NMR facilities for structural biology in drug development, particle accelerators, and Europe's most powerful supercomputers. Helmholtz drug research specialists joined forces as well, offering facilities and expertise to partners.

The Partnership for Advanced Computing in Europe (PRACE) published a call for proposals for compute time to mitigate the effects of the Covid-19 pandemic. Photon and neutron facilities respond to the challenges posed by SARS-CoV-2 by establishing priority actions and offering their capabilities to the entire scientific community. Some of these efforts are summarized on the websites of the League of Advanced European Neutron Sources (LENS) and League of European Accelerator-Based Photon Sources (LEAPS).

Established ESFRI infrastructures like the biobank network BBMRI and the mouse model databank INFRAFRONTIER offer information on standardized sample collection as well as resources, emergency archiving services and SARS-CoV-2-specific mouse strains to the global research community.

In this particular situation, access to these and other specific research infrastructures – such as biosafety laboratories and vaccine development infrastructures – within Helmholtz is especially important.

9. Research data sharing platform

The delayed publication of Covid-19-related research results would lead to a delayed response in saving patients' lives. Thus, Helmholtz strongly welcomes the sharing of all Coronavirus-related research findings.

It is crucial to follow the "one-stop shop" approach here as well: If data are distributed across multiple platforms, they will be diluted and hard to navigate. Therefore, we welcome the collaboration with EMBL-EBI to build the Covid-19 Data Portal presented in April 2020.

A common approach for data sharing is a priority for this portal and others focusing on laboratory and/or patient data, such as the Lean European Open Survey on SARS-CoV-2-Infected Patients (LEOSS). The Europe-wide federated data and compute platform FENIX, an EU-funded infrastructure of the Human Brain Project, supports the offer of PRACE regarding supercomputing resources with data capacity in the petabyte range and extended data services provided by the Human Brain Project, which are linked to international repositories.

The LifeTime consortium (see below) and its member institutions coordinate and harmonize sample collection and processing, clinical data records as well as data analysis and management at the European level.

The data sharing platform could be further expanded by incorporating non-health data, such as data on mobility behavior, psychology, environmental effects etc. Covid-19 is a rare example of a natural experiment, and the data gathered during this time will be valuable to prepare society for future pandemics, and will also have relevance in other areas (e.g. the environmental dimension of teleworking).

The "ERAvsCORONA" Action Plan contains priorities concerning the most relevant aspects of research activities regarding Covid-19. It remains crucial to continue involving all relevant stakeholders who contribute to fighting this pandemic and be better prepared for the next one.

In addition to these ten priorities, **we suggest an eleventh priority: Research for Preventing and Coping with Future Pandemics.** Relevant topics here include the connections between climate change and disease outbreaks, the maintenance of key infrastructures during a pandemic, the development of smart city infrastructures that raise society's resilience to future crises of this sort.

The LifeTime consortium, comprising of life scientists, computational experts and mathematicians, technologists and clinicians from leading institutions across Europe supported by the European Commission, aims to advance healthcare by tracking and understanding human cells during disease, including during infections. LifeTime is coordinated by a Helmholtz Centre, the Max Delbrück Center for Molecular Medicine (MDC) in Berlin, and the Institut Curie in Paris with the active participation of other Helmholtz Centers in the Research Field Health.

LifeTime proposes a single-cell and data-driven approach to understanding an individual patients' immune response to SARS-CoV-2 infection. A fundamental issue that requires single-cell analysis to understand the basis for the broad range of observed clinical symptoms in patients. In the short-term this will enable the selection of more effective therapeutic options for individual patients, while providing a new path to developing and testing new drugs and therapies in the longer term.

It is crucial that our societies draw further insight on infectious disease outbreaks and the science-based measures to end them. Helmholtz will continue to combat the Covid-19 pandemic with its expertise and in collaboration with its European and international partners. We believe that it is only through scientific progress in a collaborative spirit that this crisis will be defeated.

Brief portrait of the Helmholtz Association

Helmholtz contributes to solving major challenges facing society, science, and the economy through top-level scientific achievements in six Research Fields: Energy, Earth and Environment, Health, Key Technologies/Information, Matter, and Aeronautics, Space, and Transport. With more than 40,000 employees at 19 Research Centers and an annual budget of around 4.8 billion euros, Helmholtz is the largest scientific organization in Germany. Its work is rooted in the tradition of the great natural scientist Hermann von Helmholtz (1821–1894).

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