

Standardization of Immune Response Assays to COVID-19 Vaccines
A Year’s Experience Transferring Assays to a Global Network of Labs

# The webinar was co-organized by CEPI and BEBPA and held on the 31st August 2021. It dived into the lessons learned during tech transfer of immunological assays to a global network of laboratories to standardize the evaluation of the immune response elicited by different SARS-CoV-2 vaccines.

# Session 1: A Year in Review

**Intro and Webinar Logistics**

*Laureen Little, BEBPA, President*

[**Chair Introduction to the Webinar**](https://www.bebpa.org/2021-eur-bioassay-abstracts/#solzin)

 *Ivana Knezevic, WHO, Team Leader, Norms and Standards for Biologicals, Quality, Safety and Standards; COVAX, Co-Lead of the Enabling Sciences SWAT Team*

**Overview of CEPI & COVAX**

*Paul Kristiansen, CEPI, Head of Biological Standards & Assays, Preclinical Immunology; COVAX, Co-Lead of the Enabling Sciences SWAT Team*

**CEPI Centralized Laboratory Network: Key Features**

 *Valentina Bernasconi, CEPI, Scientist, Project Leader of Centralized Laboratory Network*

**Lessons Learned from One Year of Transferring Assays to a Global Network of Laboratories**

*Arun Kumar, CEPI, Scientist, Co-lead of Centralized Laboratory Network*

**Expert Panel Discussion & Audience Q&A**

# Session 2: The Future - Routine Testing

**CEPI Centralized Laboratory Network: Planning for the Future**

*Valentina Bernasconi, CEPI, Scientist, Project Leader of Centralized Laboratory Network*

**Future Pandemics and the Clinical Trial Directive**

 Bassam Hallis, Public Health England, Head of Pre-Clinical Dev & General Project Manager National Infection Service

**Future Planning Q&A/Panel Discussion**

**CEPI Centralized Laboratory Network: How to Become Involved?**

*Ana Paula De Almeida Aranha, CEPI, Project Manager of Centralized Laboratory Network*

# Executive summary

# Session 1: A Year in Review

CEPI is a global coalition made up of public, private, philanthropic and civil society organizations with the mission to accelerate the development of vaccines against emerging infectious diseases and enable equitable access to these vaccines for affected populations during outbreaks in order to create a world in which epidemics are no longer a threat to humanity. To achieve this goal, CEPI funds numerous vaccine development projects and cross cutting enabling science activities.

In addition to COVID-19, CEPI’s target pathogens include Ebola virus, Lassa virus, Middle East Respiratory Syndrome coronavirus, Nipah virus, Rift Valley Fever virus and Chikungunya virus. CEPI also invested in platform technologies that can be used for rapid vaccine and immunoprophylactic development against unknown pathogens (Disease X). A full list of all the vaccine candidates we fund and their status in clinical development can be found on the CEPI website.

COVAX is the vaccines pillar of the ACT Accelerator, a collaboration between CEPI, Gavi and the World Health Organization, with key delivery partner UNICEF. COVAX provides countries access to the world’s largest portfolio of vaccine candidates, actively managed by CEPI’s R&D experts.

Over 200 million COVAX doses have been delivered worldwide. COVAX also provides cross-cutting support to vaccine developers through SWAT teams. This webinar is organized by the Enabling Sciences SWAT team, which supports COVID-19 vaccine developers in the area of standards, assays and animal models.

The genetic sequence of SARS-CoV-2 was published on 11th January 2020 and this triggered an intense global R&D activity to develop a vaccine against the virus. At present, more than 400 vaccine developers are active worldwide to develop a vaccine against it. You can imagine how comparing immune responses induced by different vaccine candidates is extremely challenging. These vaccines are at different stages of development, use different technology platforms, samples are collected, transported, stored in different ways and the lack of standardization among different assays with different readouts and different testing laboratories makes the comparison very difficult.

To improve immunological assay standardization, CEPI, WHO and the National institute for Biological Standards and Control have worked together to develop and make available worldwide reference serum panels, the First WHO International Standard for anti-SARS-CoV-2 immunoglobulin and First WHO International Reference Panel for anti-SARS-CoV-2 immunoglobulin. These reagents are of fundamental importance to harmonize serological assay results across different vaccine candidates. During the preparation of the First WHO International Standard for anti-SARS-CoV-2 immunoglobulin, research reagents have been made available since May 2020 as an intermediate solution for improving the interpretation of the results from the assays. Conversion factor was also provided to bridge the data generated before the establishment of the WHO International Standard.

In parallel, as a synergistic approach to improve immunological assay standardization worldwide, CEPI has created a Centralized Laboratory Network selecting laboratories with the highest quality standards using a core set of assays needed for key immunogenicity and efficacy end point evaluation and harmonizing protocols and key reagents across the laboratories.

The CEPI Centralized Laboratory Network is open to all vaccine developers worldwide to test samples from pre-clinical to Phase III clinical studies to facilitate rapid evaluation, approval, and dissemination of the most effective vaccine candidates and support their pathway towards licensure, increasing the chances of finding successful Covid-19 vaccines.

The Network counts today 9 laboratories across the globe, 3 in North America (Nexelis in Canada, Q2 Solutions in the US and the National Autonomous University of Mexico in Mexico), 4 in Europe (Public Health England and the National Institute for Biologic Standards and Control in the UK, Vismederi in Italy and Viroclinics in the Netherlands) and 2 in Asia (Translational Health Science and Technology Institute in India and the International Centre for Diarrheal Disease Research in Bangladesh).

The Laboratories of the network are performing ELISA for spike protein, receptor binding domain and N protein, pseudo virus and wild type virus neutralization assays and IFNy/IL-5 ELISPOT using the exact same protocols and the same standardized reagents to ensure harmonization and comparability of results. The assays are qualified and validated and are being technically transferred to all the labs of the network.

Nexelis is transferring ELISA, pseudo virus neutralization assay and ELISPOT to every lab of the network, while Public Health England is transferring a wild type (live) virus neutralization assay to the labs that have BSL-3 capacity. The results from binding and neutralizing antibody measurements are bridged to the WHO International Antibody Standard and are expressed in binding antibody units (BAU).

The technical transfer process was developed to ensure harmonization across laboratories. Some of the elements of success that were included in the transfer were:

-The use of key reagents produced by the same source and distributed to all the labs equally. For example, serum panels, reference reagents, coating antigens and viruses

-A well-developed technical transfer protocol which included:

* Assay overview
* Gap analysis to highlight differences reference labs and recipient labs and mitigate the impact of the gaps
* Laboratory comparison assessment to ensure that comparable results can be obtained across laboratories
* Assay performance evaluation at recipient laboratories to ensure assay performances were not impacted by the transfer (precision, dilutional linearity, clinical specificity)
* QC charts and proficiency panel to assess the assay performance over time

- Online training and ad hoc teleconferences

-Fast and transparent communication to make sure all the participants to the program are aligned

-Team work

All the assays available in the Network are based on the original SARS-CoV-2 strain. However, as everyone knows, all viruses, including SARS-CoV-2, change over time. The CEPI Centralized Laboratory Network is now open for testing of vaccines performance against SARS-CoV-2 variants Alpha, Beta, Gamma and Delta. CEPI is also actively monitoring new circulating SARS-CoV-2 strains that might arise in the future.

To identify how to sustain strengths and improve weaknesses on the project and to define recommendations to improve future performance, CEPI runs lessons learned exercises every 6 months since project initiation. The areas of focus are: 1) Agreements and contracts 2) Communication, teams and project management 3) Technical transfer process 4) SOPs, instructions and training 5) Supply of key reagents and consumables. A detailed outcome of the lessons learned exercise can be found of the slide deck.

# Session 2: The Future - Routine Testing

Epidemic and pandemic diseases affect us all – they do not respect borders. In its short history, CEPI has had an outsized influence in shaping the global R&D ecosystem, accelerate the development of vaccines against emerging infectious diseases and enable equitable access to these vaccines for affected populations during outbreaks.

COVID-19 has killed millions and destroyed the livelihoods of hundreds of millions of people. CEPI has set out an ambitious strategy to build a world that is better equipped to deal with pandemics and epidemics. CEPI’s plan includes:

- Strengthening our defenses against COVID-19 and reducing the risk of future coronavirus pandemics

-Developing vaccines for known threats

-Working to compress vaccine development timelines to 100 days

-Producing a library of prototype vaccines

-Establishing global networks for lab capacity, assays, and preclinical models

-Supporting the efforts of low- and middle-income countries to take full ownership of their national health security

CEPI has developed a five-year plan to prepare for known threats, transform the response to the next novel outbreak, and connect and enhance global collaboration to strengthen global preparedness.

CEPI 2.0 strategy will deal with the:

-The development of vaccines and promising biologics against the most prominent known threats, building on COVID-19 achievements and CEPI 1.0; this will help us ending the COVID-19 pandemic and eliminating the risk of new coronavirus pandemics and accelerating the development of vaccines and other biologics against known high-risk pathogens

-The use of vaccine development innovations to significantly reduce the global vulnerability to threats of novel pathogen outbreaks

-Design a more robust and effective global preparedness and response building collaboration which will enable a faster response

The Centralized Lab team responsibility is to align to the CEPI 2.0 objectives to:

-Create a Network of laboratories to accelerate testing of vaccines against SARS-CoV-2 and use the Network for the other CEPI priority pathogens such as Lassa, MERS, RVF, Nipah and Chikungunya

-Invest in innovations so vaccine testing is cheaper and faster

-Build a strong, post-pandemic global network, push for collaboration and solutions which will enable a faster system-wide response, coordinating a scalable on-demand testing network and aligning with other initiatives worldwide

One of CEPI’s objectives is to compress vaccine development timelines to 100 days from pathogen characterization to clinical data for deciding emergency use. We need to work on a strategy to reduce bottle necks we are likely to encounter based on what we have learnt from experience with SARS-CoV-2 tackling issues from the release of the virus sequence, train staff and develop protocols, source convalescent sera and scale up reagents production, the lab capacity for testing and the data handling. We have exciting times ahead in which we’ll work towards expanding the CL network to include new labs, tackle new diseases, align with CEPI 2.0 objectives to be prepared for the future.

It was recognized that the CEPI Centralized Lab Network can set an example by using the secondary standard calibrated against the First WHO International Standard for anti-SARS-CoV-2 immunoglobulin and expressing the results of the neutralization assays from clinical trials in the International Units. That would make a major step forward in the comparison of the clinical data generated for various vaccine candidates.